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# Economic Analysis for the Proposed Per- and Polyfluoroalkyl Substances National Primary Drinking Water Regulation Appendices

# Economic Analysis for the Proposed Per- and Polyfluoroalkyl Substances National Primary Drinking Water Regulation Appendices

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# Acronyms and Abbreviations

| | |
|---|---|
| AE | Adverse Events |
| AFFF | Aqueous Film Forming Foam |
| AHRQ | Agency for Healthcare Research and Quality |
| ANGIDX | Angina, or Angina Pectoris, As Defined in the Medical Exposure Panel Survey |
| APFO | Ammonium Perfluorooctanoate Production |
| ASCVD | Atherosclerotic Cardiovascular Disease |
| ATSDR | Agency for Toxic Substances and Disease Registry |
| BEA | Bureau of Economic Analysis |
| BIRTH | Birth Characteristics |
| BLS | Bureau of Labor Statistics |
| BP | Blood Pressure |
| BW | Birth Weight |
| CAGR | Compound Annual Growth Rate |
| CDC | Centers for Disease Control and Prevention |
| CHD | Coronary Heart Disease |
| CHDDX | Coronary Heart Disease, as Defined in the Medical Exposure Panel Survey |
| CHMS | Canadian Health Measures Survey |
| CI | Confidence Interval |
| COI | Cost Of Illness |
| CPI | Consumer Price Index |
| CVD | Cardiovascular Disease |
| DBP | Disinfection Byproduct |
| DL | Detection Level |
| DS | Distribution System |
| EA | Economic Analysis |

| | |
|---|---|
| EBCT | Empty Bed Contact Time |
| EIA | Energy Information Administration |
| EJ | Environmental Justice |
| EPA/OST | U.S. Environmental Protection Agency Office of Science and Technology |
| EP | Entry Point |
| FIPS | Federal Information Processing Standards |
| GAC | Granular Activated Carbon |
| GDP | Gross Domestic Product |
| GFR | Glomerular Filtration Rate |
| GW | Ground Water |
| HCUP | Healthcare Cost and Utilization Project |
| HDLC | High-Density Lipoprotein Cholesterol |
| HESD | Health Effects Support Document |
| HMO | Health Maintenance Organization |
| ICER | Incremental Cost-Effectiveness Ratio |
| ICR | Information Collection Request |
| IR | Incidence Ratio |
| IS | Ischemic Stroke |
| KC | Kidney Cancer |
| LBW | Low Birth Weight |
| LCB | Lower Confidence Bound |
| MCL | Maximum Contaminant Level |
| MDEM | Maternal Demographic and Socioeconomic Characteristics |
| MEPS | Medical Expenditure Panel Survey |
| MIDX | Heart Attack, or Myocardial Infarction, as Defined in the Medical Exposure Panel Survey |
| MR | Point of Maximum Residence |

| | |
|---|---|
| mRCC | Metastatic Renal Cell Carcinoma |
| MRF | Maternal Risk and Risk Mitigation Factors |
| MRL | Minimum Reporting Level |
| NCCN | National Comprehensive Cancer Network |
| NCHS | National Center for Health Statistics |
| NHANES | National Health and Nutrition Examination Survey |
| NPDWR | National Primary Drinking Water Regulation |
| NVSS | National Vital Statistics System |
| OGWDW | Office Of Groundwater and Drinking Water |
| OHRTDX | Other Kind of Heart Disease or Condition, As Defined in the Medical Exposure Panel Survey |
| OLS | Ordinary Least Squares |
| OSHA | Occupational Safety and Health Administration |
| OW | Office of Water |
| PAF | Population Attributable Fraction |
| PBPK | Pharmacologically Based Pharmacokinetic |
| PDV | Present Discounted Value |
| PDYPP | Personal Disposable Income Per Capita |
| PFAS | Poly- and Perfluoroalkyl Substances |
| PFBS | Perfluorobutane Sulfonic Acid |
| PFDA | Perfluorodecanoic Acid |
| PFNA | Perfluorononanoic Acid |
| PFOA | Perfluorooctanoic Acid |
| PFOS | Perfluorooctanesulfonic Acid |
| PK | Pharmacokinetic |
| PPPM | Per Patient Per Month |
| PWS | Public Water Systems |

| | |
|---|---|
| PWSID | Public Water System ID |
| QALY | Quality-Adjusted Life-Years |
| RCC | Renal Cell Carcinoma |
| ROB | Risk of Bias |
| RSSCT | Rapid Small-Scale Column Tests |
| SAB | Science Advisory Board |
| SD | Standard Deviation |
| SDWIS | Safe Drinking Water Information System |
| SE | Standard Error |
| SEER | Surveillance, Epidemiology, and End Results |
| STRKDX | Stroke Diagnosis, As Defined in the Medical Exposure Panel Survey |
| SW | Surface Water |
| TC | Total Cholesterol |
| TOC | Total Organic Carbon |
| THM4 | Four Regulated Trihalomethanes |
| TSD | Treatment Study Database |
| UCB | Upper Confidence Bound |
| UCMR | Unregulated Contaminant Monitoring Rule |
| VSL | Value of a Statistical Life |
| WS | Water System Facility Point |
| WTP | Willingness to Pay |

# Appendix A. Framework of Bayesian Hierarchical Markov Chain Monte Carlo Occurrence Model

This appendix is adapted from Cadwallader et al. (2022) and details the Bayesian hierarchical Markov chain Monte Carlo model developed by EPA to estimate national occurrence of poly- and perfluoroalkyl substances (PFAS) at public water systems (PWSs) prior to the implementation of drinking water treatment technologies and under theoretical regulatory scenarios (Cadwallader et al. (2022). EPA used the occurrence model to define the universe of PWSs that could be required to treat their drinking water to reduce PFAS levels under the regulatory alternatives. EPA has used similar hierarchical model structures to inform analyses in previous regulatory actions (U.S. EPA, 2000a; U.S. EPA, 2005).

## A.1 Data Selection

Data collected for the third Unregulated Contaminant Monitoring Rule (UCMR 3) served as the primary dataset for this model due to its nationally representative design. While large PWSs included in UCMR 3 represent a census, not all small PWSs were required to monitor. Rather, a statistically representative national sample of 800 small PWSs were selected using a population-weighted stratified random sampling design to select small PWSs with broad geographic distribution representative of all source water types and size categories (U.S. EPA, 2012). Because UCMR 3 included only a sample of small systems, there is greater uncertainty in the occurrence estimates for small systems compared to large systems.

Because there was a relatively small fraction of UCMR 3 samples with PFAS concentrations reported above minimum reporting levels (MRLs), EPA incorporated state PFAS monitoring datasets to supplement UCMR 3 data in the occurrence model. These datasets, which have generally been collected more recently than UCMR 3, generally have lower reporting limits because the analytical methods have matured rapidly over the last 10 years, allowing laboratories to reliably measure PFAS at concentrations approximately 3 and 30 times lower than for UCMR 3. While the model can incorporate results below reporting limits in the fitting process via cumulative distribution functions, such results are less informative than reported values. Thus, state datasets using lower reporting limits than those used in UCMR 3 helped to inform the model through higher fractions of reported values. The introduction of additional state datasets consisting of samples that were collected more recently than UCMR 3 broadened the temporal range of data used to fit the model. EPA anticipates that, if temporal trends are significant, the addition of more recent state data will only bias the results towards present day.

EPA collected state occurrence data using broad internet searches[1] and downloaded publicly available monitoring data from state government websites as of August 2021. While comprehensive information about methods used and reporting was not fully available for all of the state monitoring programs, nearly all (at least 97.1%) of the state data incorporated in the occurrence model were analyzed using EPA-approved PFAS drinking water analysis methods, including EPA Methods 533, 537, and 537.1. Of these methods, the most commonly used method was EPA Method 537.1.

[1] Search terms included “PFAS”, “drinking water”, “occurrence”, “monitoring”, and “state”, or a specific state name.

Additionally, if the state data met certain specifications, EPA assumed that they were statistically comparable with the UCMR 3 data and could be used to inform the national occurrence model. In making these determinations, EPA performed quality assurance on the state data as they were reported and described online. The implemented quality assurance procedures included verifying that the data utilized to inform the national model were inclusive of finished drinking water samples only, reporting or detection limits were available for any samples reported as below a reporting limit, PFOA, PFOS, PFHpA, and PFHxS were reported as individual chemical analytes, and reported state data were for distinct state monitoring efforts (*i.e.*, they were not also a part of UCMR 3 monitoring). If any of this information could not be verified based on the descriptions that states provided on their public websites or within the downloadable data, those state data were not incorporated within the national occurrence model.

Further, the supplemental state data were limited to samples collected from systems that were also included in UCMR 3. The purpose of this was to prevent biasing the dataset towards states for which the data from additional PWSs were available and to maintain the nationally representative set of systems selected for UCMR 3. Using these criteria, 17 states were identified as having some state monitoring data to be included in fitting the national occurrence model. These states included: Arizona, California, Colorado, Delaware, Georgia, Illinois, Kentucky, Maine, Massachusetts, Michigan, New Hampshire, New Jersey, North Dakota, Ohio, Pennsylvania, South Carolina, and Vermont (Arizona Department of Environmental Quality, 2021; California Division of Drinking Water, 2020; Colorado Department of Public Health and Environment, 2020; Delaware Office of Drinking Water, 2021; Georgia Environmnetal Protection Division, 2020; Illinois Environmental Protection Agency, 2021; Kentucky Department for Environmental Protection, 2019; Maine Department of Environmental Protection, 2020; Massachusetts Department of Energy and Environmental Affairs, 2021; Michigan Environment, 2021; New Hampshire Department of Environmental Services, 2021; New Jersey Department of Environmental Protection, 2021; North Dakota Department of Environmental Quality, 2020; Ohio Department of Health, 2020; Pennsylvania Department of Environmental Protection, 2020; South Carolina Department of Health and Environmental Control, 2020; Vermont Department of Environmental Conservation, 2021). According to state websites, these state data represent samples collected between March 2016 through May 2021.

The dataset used to fit the model included all data available in the final UCMR 3 dataset for PFOS, PFOA, PFHpA, and PFHxS[2] (U.S. EPA, 2017). This amounted to 36,972 samples each for PFOS, PFOA, and PFHpA, and 36,971 UCMR 3 samples for PFHxS. Of these four PFAS, 1,114 samples had results reported at or above the UCMR 3 MRL[3]. The additional state datasets included to supplement the UCMR 3 data included 6,645 PFOS samples, 6,656 PFOA samples, 4,715 PFHpA samples, and 5,114 PFHxS samples collected at systems that were included in UCMR 3. Of these samples, 2,200 (33%) were reported values for PFOS, 2,694 (40%) were reported values for PFOA, 932 (20%) were reported values for PFHpA, and 1,269 (25%) were reported values for PFHxS. The remainder were listed as being below their respective reporting limits.

[2] PFBS and PFNA were not included in this model because 19 reported values across the country from the primary dataset (UCMR 3) were insufficient for fitting the national model (Cadwallader et al., 2022).

[3] MRLs under UCMR 3 were as follows: PFOS 40 ppt; PFOA 20 ppt; PFNA 20 ppt; PFHxS 30 ppt; PFHpA 10 ppt; and PFBS 90 ppt.

Table A-1 provides information on the number of systems and samples included in each supplemental state dataset. Reporting limits in state datasets varied both across and within datasets but were primarily in the lower single digits in parts per trillion (ppt) for all four PFAS included in the model, though for some samples the limits reported were as high as the UCMR 3 limits or as low as sub-1 ppt. The particularly low limits associated with some samples may be associated with method detection limits rather than more conservative reporting limits.

**Table A-1: System and Sample Counts for Contributions to the Supplemental State Dataset by State**

| State | Systems Included | PFOS Samples | PFOA Samples | PFHpA Samples | PFHxS Samples |
|---|---|---|---|---|---|
| AZ | 2 | 190 | 189 | 0 | 0 |
| CA | 65 | 1,913 | 1,913 | 1,721 | 1,723 |
| CO | 52 | 95 | 95 | 95 | 95 |
| DE | 1 | 34 | 34 | 0 | 0 |
| GA | 1 | 2 | 2 | 2 | 2 |
| IL | 97 | 321 | 321 | 319 | 319 |
| KY | 23 | 25 | 25 | 25 | 25 |
| MA | 65 | 434 | 434 | 436 | 436 |
| ME | 1 | 3 | 3 | 3 | 3 |
| MI | 58 | 160 | 160 | 151 | 160 |
| ND | 1 | 1 | 1 | 1 | 1 |
| NH | 20 | 334 | 336 | 176 | 331 |
| NJ | 148 | 2,676 | 2,686 | 1,566 | 1,566 |
| OH | 145 | 234 | 234 | 0 | 234 |
| PA | 51 | 91 | 91 | 91 | 91 |
| SC | 31 | 104 | 104 | 101 | 100 |
| VT | 10 | 28 | 28 | 28 | 28 |

Abbreviations: PFOA – perfluorooctanoic acid; PFOS – perfluorooctanesulfonic acid; PFHpA – perfluoroheptanoic acid; PFHxS – Perfluorohexane sulfonate.

Further, there were several instances where approximate values were provided in state data when the sample results were above a method detection limit but below the quantitation limit. In these cases, EPA used the reported values assuming that the uncertainty introduced by using these values would be small in comparison to within-system variability. While certain systems may have adapted treatment since the time that data were collected, the data included in the occurrence model represent a best estimate of the current state of occurrence. Note that both samples with results reported as specific measured concentrations and samples with concentrations reported as lower than a reporting limit were used to fit the model. While the latter help to provide information to the model, samples providing a measured result are much more informative.

## A.2 Conceptual Model Structure

The Bayesian hierarchical model presented here uses log transformed data. Unless otherwise noted, all of the following discussions, equations, distributions are based upon the use of PFOA, PFOS, PFHpA, and PFHxS data that have been log transformed with the natural log.

EPA tested several model variants. These variants all featured a hierarchical structure with a multivariate normal distribution of system-level means and system-level normal distributions, which were assumed to have been the parent distributions for the individual sample results. Thus, for each variant, EPA assumed lognormality for system-level medians as well as within-system occurrence. Lognormality is a common assumption for environmental contaminant concentrations and constitutes a core assumption made here (Lockwood et al., 2001; Ott, 1995). The exploration of alternative distributions is inhibited by the large fraction of samples found below their respective reporting limits. Similar Bayesian hierarchical model approaches have been used in past drinking water occurrence assessments conducted by EPA and others, including for arsenic and Cryptosporidium parvum (Crainiceanu et al., 2003; Lockwood et al., 2001; Ott, 1995). The exploration of alternative distributions is inhibited by the large fraction of samples found below their respective reporting limits.

Model variants differed by inclusion of parameters specific to system size (small versus large) and source water type (ground water versus surface water). These parameters included: independent correlation matrices, between-system standard deviations, within-system standard deviations, and fixed factor shifts of system-level means. EPA included fixed factor shifts in model variants to allow the model to explore whether systems of certain categories (*e.g.*, large or small, ground water or surface water), might generally appear to have higher or lower concentrations of each chemical. EPA compared these model variants using 5-fold cross validation. EPA selected the model that performed best in the 5-fold cross validation exercise (described below).

EPA assumed that system-level means were distributed multivariate normally. This was done to allow the model to fit and utilize a covariance matrix among system-level means for the four PFAS included. Before adjustment for system-specific factors, the system-level means for PFOS, PFOA, PFHpA, and PFHxS were assumed to be distributed as:

Equation A-1:

$$mu_{raw,i} \sim MVNorm(MU, \Sigma)$$

Where *i* is the system index and equal to 1, …, $n_{sys}$ , $n_{sys}$ is the number of PWSs informing the model, $mu_{raw,i}$ is a vector of length 4, with the four values indicating unadjusted system-level means for PFOS, PFOA, PFHpA, and PFHxS. $MU$ is a vector of length 4 providing the grand national means for large PWSs, Σ is the covariance matrix for system-level means. Σ is related to the correlation matrix and between-system standard deviation as shown in Equation A-2.

Equation A-2:

$$\Sigma = diag(\sigma_B) * \Omega * diag(\sigma_B)$$

Where $\sigma_B$ is a vector of between-system standard deviations and Ω is the correlation matrix of system-level means for PFOS, PFOA, PFHpA, and PFHxS. For small systems, a fixed factor shift was then applied to $mu_{raw,i}$. This is shown in Equation A-3.

Equation A-3:

$$mu_i = mu_{raw,i} + (bSM * SM_i)$$

Here $bSM$ is a vector of length 4 indicating an adjustment to be added to the unadjusted system level mean ($mu_{raw,i}$) if a system is small. $SM_i$ is a binary indicating whether system $i$ is small (1) or large (0). $mu_i$ is a vector of length 4, with the four values indicating adjusted system-level means for PFOS, PFOA, PFHpA, and PFHxS. Samples are then assumed to be normally distributed according to Equation A-4: if the sample is either from a large system (serving more than 10,000) or is a PFHpA or PFHxS sample.

Equation A-4:

$$y_{ijk} \sim Norm(mu_{i,k}, \sigma_{W,k})$$

Where $y$ represents sample results and $j$ is a sample index and equal to 1, …,$n_{samp}$, where $n_{samp}$ is the total number of samples . Here $i$ is the indicator for the system at which the sample $y_{ijk}$ was collected and $k$ is an indicator for the contaminant that $y_{ijk}$is a sample of (i.e., PFOS, PFOA, PFHpA, or PFHxS). Thus, $y_{ijk}$ represents the $j^{th}$ sample of contaminant $k$ collected from system $i$. $mu_{i,k}$ represents the $k^{th}$ element of $mu_i$ shown in Equation A-3, $\sigma_W$ is a vector of length 4 providing the within-system standard deviation for each chemical included in the model. Thus $\sigma_{W,k}$ represents the $k^{th}$ element of $\sigma_W$.

Within-system standard deviations specific to small systems were fit for PFOS and PFOA. $\sigma_{Wsm}$ replaces $\sigma_W$ in Equation A-4 when the sample is either PFOS or PFOA collected at a small (sm) system. Model variants that included within-system standard deviations specific to small systems for all 4 chemicals as well as no within-system standard deviations specific to small systems were both included in the cross-validation model comparison, but both were outperformed by the model presented here. The limited reported values of PFHxS and PFHpA at small systems relative to PFOS and PFOA made the fitting of within-system standard deviations specific to small systems highly uncertain for these chemicals and adversely affected the model's predictive performance. Because of this, EPA used within-system standard deviations pooled across both system size categories for PFHxS and PFHpA.

## A.3 Model Implementation

EPA conducted the data import, model setup, and assessment of model output using the R programming language and the RStudio IDE (R Core Team, 2021; RStudio Team, 2020). The Agency used Rstan to access the Stan probabilistic programming language and execute the model (Stan Development Team, 2020; Stan Development Team, 2021). The R packages *reshape2* and *dplyr* were used for data handling (Wickham, 2007; Wickham et al., 2020). The R packages *bayesplot*, *ggplot*, and *ggpubr* were used for data visualization (Gabry et al., 2020; Kassambara, 2020; Wickham, 2016).

Stan uses Hamiltonian Monte Carlo No-U-Turn-Sampling for Markov chain Monte Carlo. EPA ran models with 4 chains of 5,000 iterations, 2,000 of which were warmup, thinned by 3. Thinning was used to balance memory limitations with desired effective sample size. Additional sampler parameters included: *adapt_delta = 0.95*, *max_treedepth = 12*, and *seed = 1337*. EPA used Shinystan (Gabry et al., 2018) to confirm that the effective sample size exceeded 1,000 for all parameters that were not predefined values, such as the diagonal of a correlation matrix, which is 1 by definition. EPA also used Shinystan to confirm chain mixing. No divergent samples were observed.

For samples that were reported values (i.e., observed), the log probability was incremented using the log of the normal density for the reported value given the system-level mean and within-system deviation. For samples reporting the result as below the reporting limit rather than an observed value, the log probability was incremented as the log of the cumulative normal distribution at the reporting limit given the system-level mean and within-system standard deviation.

EPA optimized the model via non-centered parameterization and Cholesky factorization of the multivariate normal distribution. Additional information on handling of samples below a reporting limit and model reparameterization are available in the *Stan User's Guide* sections on "Censored data" and "Reparameterization", respectively (Stan Development Team, 2021). EPA used weakly informative prior distributions. Prior distributions serve as a way to reflect probabilistic beliefs for model parameters prior to seeing data. The decision to use weakly informative priors allowed for the improvement of computational efficiency by providing loose guidance towards sensical values for model parameters without influencing posterior distributions in any substantive matter.

# Appendix B. Affected Population

This appendix describes the data sources used to evaluate the population potentially affected by human health risk reductions due to reductions in drinking water exposure to per- and polyfluoroalkyl substances (PFAS). Table B-1 describes the data elements used to assess the affected population in EPA's analysis of the benefits of reducing PFAS levels in drinking water. These elements include the Safe Drinking Water Information System (SDWIS) 2021 quarter 4 (Q4) dataset (U.S. EPA, 2021b), and U.S. Census Bureau (2020).

The EPA SDWIS dataset provides information reported by states on drinking water systems, as required by the Safe Drinking Water Act. The dataset generally includes information on system name, identification number (public water system [PWS] ID), the cities or counties served, the number of people served, the type of system (community, transient, or non-transient), whether the system operates year-round or seasonally, and characteristics of the system's source water.

The U.S. Census provides detailed county-level population data by 5-year age-range, sex, race, and ethnicity from 2010 to 2019. EPA first calculated, for each county, the average population for each age-range/sex/race/ethnicity cohort over this 10-year period to determine a "typical-year" demographic distribution for each county. EPA then calculated the proportion of each county's population in each age-range/sex/race/ethnicity cohort in each of the 10-years. Finally, EPA estimated the proportion of each county's population in each age/sex/race/ethnicity cohorts by equally distributing the population in each 5-year age-range equally over the five years.

To determine the population proportions for each PWS, EPA took the following steps:

1. For PWSs for which EPA had information on the boundary of the PWS service area (see Chapter 9):

    a. Calculate the population-weighted proportion of the PWS's service area in each county.

    b. Use the values from (a) as weights, along with the county-level age-specific sex/race/ethnicity population cohort data, to estimate the PWS's population served in each age/sex/race/ethnicity cohort.

2. For PWSs for which EPA did not have information on the boundary of the PWS service area:

    a. Developed a crosswalk between the primary SDWIS county name and the county Federal Information Processing Standards (FIPS) codes used by the US. Census.

    b. Used the PWS primary county age/sex/race/ethnicity population cohort data to determine the PWS's population served in each age/sex/race/ethnicity cohort.

3. For PWSs for which EPA did not have information on the boundary or the primary county:

    a. Used national age/sex/race/ethnicity population cohort data to determine the PWS's population served in each age/sex/race/ethnicity cohort.

**Table B-1: Summary of Inputs and Data Sources Used to Estimate Affected Population**

| Data Element | Modeled Variability | Data Source | Notes |
|---|---|---|---|
| Initial Total Population | Location: PWS | SDWIS 2021 (U.S. EPA, 2021b) | Public water system inventory from EPA's SDWIS Q4 in 2021. EPA uses the SDWIS 2021 population data as the initial total population per PWS. |
| Percentage of Population in a Demographic Population Subgroup | Age: integer ages 0–84, 85+<br>Sex: males, females<br>Race/Ethnicity: non-Hispanic White, non-Hispanic Black, Hispanic, other<br>Location: U.S. counties | U.S. Census Bureau (2020): Annual County Resident Population Estimates by Age, Sex, Race, and Hispanic Origin: April 1, 2010 to July 1, 2019. | The original data source contains total population by race/ethnicity, sex, and 5-year age groups. |

Abbreviations: PWS – public water system; SDWIS – Safe Drinking Water Information System.

# Appendix C. Cost Analysis Results

This appendix provides additional cost output details. Section C.1 provides PWS-level costs by system type, primary source water, ownership, and system size category. Costs are provided for all systems as well as for only those systems that must treat or change water source to comply with the regulatory option. Section C.2 provides estimates of household costs.

## C.1 PWS-Level Cost Details

Section C.1 provides PWS-level costs by system type, primary source water, ownership, and system size category. Costs are provided for all systems as well as for only those systems that must treat or change water source to comply with the regulatory option.

### *C.1.1 Mean Annual Cost for all Community Water Systems*

**Table C-1: Mean Annualized Cost per CWSs, Proposed Option (PFOA and PFOS MCLs of 4.0 ppt and HI of 1.0) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | 5th Percentile | Mean | 95th Percentile |
|---|---|---|---|---|---|
| Private | Ground | Less than 100 | $904 | $1,263 | $1,680 |
| Private | Ground | 100 to 500 | $1,357 | $1,941 | $2,598 |
| Private | Ground | 500 to 1,000 | $1,838 | $2,813 | $3,928 |
| Private | Ground | 1,000 to 3,300 | $2,975 | $4,484 | $6,261 |
| Private | Ground | 3,300 to 10,000 | $5,981 | $10,374 | $15,395 |
| Private | Ground | 10,000 to 50,000 | $67,442 | $82,756 | $98,919 |
| Private | Ground | 50,000 to 100,000 | $114,170 | $198,210 | $297,240 |
| Private | Ground | 100,000 to 1,000,000 | $252,900 | $405,310 | $626,760 |
| Private | Surface | Less than 100 | $1,040 | $1,704 | $2,533 |
| Private | Surface | 100 to 500 | $1,552 | $2,431 | $3,473 |
| Private | Surface | 500 to 1,000 | $1,762 | $3,380 | $5,380 |
| Private | Surface | 1,000 to 3,300 | $2,511 | $4,683 | $7,573 |
| Private | Surface | 3,300 to 10,000 | $5,265 | $10,990 | $18,306 |
| Private | Surface | 10,000 to 50,000 | $65,305 | $82,341 | $100,160 |
| Private | Surface | 50,000 to 100,000 | $106,190 | $153,630 | $203,000 |
| Private | Surface | 100,000 to 1,000,000 | $1,442,200 | $1,684,800 | $1,921,000 |
| Public | Ground | Less than 100 | $892 | $1,291 | $1,752 |
| Public | Ground | 100 to 500 | $1,412 | $2,055 | $2,787 |
| Public | Ground | 500 to 1,000 | $1,993 | $2,853 | $3,922 |
| Public | Ground | 1,000 to 3,300 | $3,408 | $4,995 | $6,879 |
| Public | Ground | 3,300 to 10,000 | $8,334 | $12,306 | $16,911 |
| Public | Ground | 10,000 to 50,000 | $81,937 | $90,066 | $98,714 |
| Public | Ground | 50,000 to 100,000 | $154,560 | $194,310 | $237,500 |
| Public | Ground | 100,000 to 1,000,000 | $628,370 | $781,090 | $960,360 |
| Public | Surface | Less than 100 | $1,103 | $1,838 | $2,810 |
| Public | Surface | 100 to 500 | $1,757 | $2,630 | $3,663 |
| Public | Surface | 500 to 1,000 | $2,247 | $3,533 | $5,140 |

**Table C-1: Mean Annualized Cost per CWSs, Proposed Option (PFOA and PFOS MCLs of 4.0 ppt and HI of 1.0) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | 5th Percentile | Mean | 95th Percentile |
|---|---|---|---|---|---|
| Public | Surface | 1,000 to 3,300 | $3,524 | $5,566 | $7,901 |
| Public | Surface | 3,300 to 10,000 | $8,909 | $13,241 | $18,217 |
| Public | Surface | 10,000 to 50,000 | $78,401 | $85,772 | $93,705 |
| Public | Surface | 50,000 to 100,000 | $122,530 | $143,390 | $165,420 |
| Public | Surface | 100,000 to 1,000,000 | $533,340 | $617,920 | $707,580 |

Abbreviations: CWS – Community Water System.

**Table C-2: Mean Annualized Cost per CWSs, Option 1a (PFOA and PFOS MCLs of 4 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | 5th Percentile | Mean | 95th Percentile |
|---|---|---|---|---|---|
| Private | Ground | Less than 100 | $888 | $1,261 | $1,680 |
| Private | Ground | 100 to 500 | $1,334 | $1,934 | $2,585 |
| Private | Ground | 500 to 1,000 | $1,854 | $2,796 | $3,868 |
| Private | Ground | 1,000 to 3,300 | $2,953 | $4,450 | $6,234 |
| Private | Ground | 3,300 to 10,000 | $5,979 | $10,261 | $15,410 |
| Private | Ground | 10,000 to 50,000 | $65,310 | $79,729 | $95,342 |
| Private | Ground | 50,000 to 100,000 | $91,548 | $172,320 | $268,120 |
| Private | Ground | 100,000 to 1,000,000 | $246,080 | $389,920 | $603,790 |
| Private | Surface | Less than 100 | $1,047 | $1,701 | $2,534 |
| Private | Surface | 100 to 500 | $1,547 | $2,425 | $3,447 |
| Private | Surface | 500 to 1,000 | $1,712 | $3,365 | $5,385 |
| Private | Surface | 1,000 to 3,300 | $2,425 | $4,660 | $7,553 |
| Private | Surface | 3,300 to 10,000 | $5,238 | $10,883 | $17,388 |
| Private | Surface | 10,000 to 50,000 | $64,728 | $80,458 | $98,766 |
| Private | Surface | 50,000 to 100,000 | $104,600 | $150,890 | $202,940 |
| Private | Surface | 100,000 to 1,000,000 | $1,390,600 | $1,623,400 | $1,861,700 |
| Public | Ground | Less than 100 | $871 | $1,289 | $1,808 |
| Public | Ground | 100 to 500 | $1,411 | $2,049 | $2,781 |
| Public | Ground | 500 to 1,000 | $1,921 | $2,840 | $3,933 |
| Public | Ground | 1,000 to 3,300 | $3,361 | $4,959 | $7,023 |
| Public | Ground | 3,300 to 10,000 | $8,276 | $12,164 | $16,853 |
| Public | Ground | 10,000 to 50,000 | $80,197 | $87,864 | $96,239 |
| Public | Ground | 50,000 to 100,000 | $151,640 | $189,130 | $231,820 |
| Public | Ground | 100,000 to 1,000,000 | $580,840 | $731,850 | $904,440 |
| Public | Surface | Less than 100 | $1,087 | $1,834 | $2,802 |
| Public | Surface | 100 to 500 | $1,754 | $2,622 | $3,663 |
| Public | Surface | 500 to 1,000 | $2,243 | $3,518 | $5,136 |
| Public | Surface | 1,000 to 3,300 | $3,509 | $5,541 | $7,863 |

**Table C-2: Mean Annualized Cost per CWSs, Option 1a (PFOA and PFOS MCLs of 4 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | 5th Percentile | Mean | 95th Percentile |
|---|---|---|---|---|---|
| Public | Surface | 3,300 to 10,000 | $8,879 | $13,154 | $18,087 |
| Public | Surface | 10,000 to 50,000 | $76,668 | $84,314 | $92,037 |
| Public | Surface | 50,000 to 100,000 | $120,050 | $140,270 | $161,820 |
| Public | Surface | 100,000 to 1,000,000 | $513,240 | $598,820 | $688,670 |

Abbreviations: CWS – Community Water System.

**Table C-3: Mean Annualized Cost per CWSs, Option 1b (PFOA and PFOS MCLs of 5.0 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | 5th Percentile | Mean | 95th Percentile |
|---|---|---|---|---|---|
| Private | Ground | Less than 100 | $730 | $1,016 | $1,383 |
| Private | Ground | 100 to 500 | $1,080 | $1,544 | $2,133 |
| Private | Ground | 500 to 1,000 | $1,476 | $2,205 | $3,136 |
| Private | Ground | 1,000 to 3,300 | $2,256 | $3,471 | $5,044 |
| Private | Ground | 3,300 to 10,000 | $4,489 | $7,926 | $12,195 |
| Private | Ground | 10,000 to 50,000 | $51,098 | $62,760 | $76,022 |
| Private | Ground | 50,000 to 100,000 | $68,449 | $131,150 | $212,960 |
| Private | Ground | 100,000 to 1,000,000 | $172,010 | $285,530 | $450,550 |
| Private | Surface | Less than 100 | $823 | $1,375 | $2,120 |
| Private | Surface | 100 to 500 | $1,229 | $1,941 | $2,812 |
| Private | Surface | 500 to 1,000 | $1,309 | $2,658 | $4,433 |
| Private | Surface | 1,000 to 3,300 | $1,693 | $3,605 | $6,021 |
| Private | Surface | 3,300 to 10,000 | $3,613 | $8,317 | $13,926 |
| Private | Surface | 10,000 to 50,000 | $48,955 | $63,164 | $78,915 |
| Private | Surface | 50,000 to 100,000 | $82,435 | $120,590 | $163,410 |
| Private | Surface | 100,000 to 1,000,000 | $1,176,200 | $1,387,000 | $1,610,600 |
| Public | Ground | Less than 100 | $712 | $1,038 | $1,413 |
| Public | Ground | 100 to 500 | $1,127 | $1,627 | $2,254 |
| Public | Ground | 500 to 1,000 | $1,507 | $2,232 | $3,098 |
| Public | Ground | 1,000 to 3,300 | $2,532 | $3,838 | $5,403 |
| Public | Ground | 3,300 to 10,000 | $6,179 | $9,366 | $13,160 |
| Public | Ground | 10,000 to 50,000 | $64,417 | $71,078 | $77,915 |
| Public | Ground | 50,000 to 100,000 | $119,530 | $150,760 | $185,190 |
| Public | Ground | 100,000 to 1,000,000 | $471,660 | $599,690 | $742,700 |
| Public | Surface | Less than 100 | $898 | $1,490 | $2,290 |
| Public | Surface | 100 to 500 | $1,364 | $2,075 | $2,962 |
| Public | Surface | 500 to 1,000 | $1,676 | $2,747 | $3,995 |
| Public | Surface | 1,000 to 3,300 | $2,680 | $4,252 | $6,096 |

**Table C-3: Mean Annualized Cost per CWSs, Option 1b (PFOA and PFOS MCLs of 5.0 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | 5th Percentile | Mean | 95th Percentile |
|---|---|---|---|---|---|
| Public | Surface | 3,300 to 10,000 | $6,721 | $10,102 | $14,011 |
| Public | Surface | 10,000 to 50,000 | $60,686 | $66,147 | $72,448 |
| Public | Surface | 50,000 to 100,000 | $88,688 | $106,470 | $125,280 |
| Public | Surface | 100,000 to 1,000,000 | $405,400 | $471,320 | $541,870 |

Abbreviations: CWS – Community Water System.

**Table C-4: Mean Annualized Cost per CWSs, Option 1c (PFOA and PFOS MCLs of 10.0 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | 5th Percentile | Mean | 95th Percentile |
|---|---|---|---|---|---|
| Private | Ground | Less than 100 | $393 | $528 | $702 |
| Private | Ground | 100 to 500 | $558 | $776 | $1,051 |
| Private | Ground | 500 to 1,000 | $691 | $1,059 | $1,519 |
| Private | Ground | 1,000 to 3,300 | $977 | $1,581 | $2,389 |
| Private | Ground | 3,300 to 10,000 | $1,722 | $3,538 | $5,974 |
| Private | Ground | 10,000 to 50,000 | $19,811 | $26,317 | $33,672 |
| Private | Ground | 50,000 to 100,000 | $19,453 | $45,545 | $87,450 |
| Private | Ground | 100,000 to 1,000,000 | $37,601 | $82,560 | $146,030 |
| Private | Surface | Less than 100 | $460 | $728 | $1,095 |
| Private | Surface | 100 to 500 | $637 | $987 | $1,450 |
| Private | Surface | 500 to 1,000 | $639 | $1,287 | $2,300 |
| Private | Surface | 1,000 to 3,300 | $697 | $1,618 | $2,943 |
| Private | Surface | 3,300 to 10,000 | $1,171 | $3,541 | $6,806 |
| Private | Surface | 10,000 to 50,000 | $19,238 | $26,682 | $35,690 |
| Private | Surface | 50,000 to 100,000 | $35,527 | $57,657 | $82,458 |
| Private | Surface | 100,000 to 1,000,000 | $532,810 | $692,740 | $855,930 |
| Public | Ground | Less than 100 | $371 | $541 | $754 |
| Public | Ground | 100 to 500 | $565 | $799 | $1,103 |
| Public | Ground | 500 to 1,000 | $707 | $1,042 | $1,449 |
| Public | Ground | 1,000 to 3,300 | $1,098 | $1,683 | $2,418 |
| Public | Ground | 3,300 to 10,000 | $2,633 | $4,038 | $5,760 |
| Public | Ground | 10,000 to 50,000 | $29,654 | $33,106 | $36,905 |
| Public | Ground | 50,000 to 100,000 | $52,779 | $70,554 | $90,600 |
| Public | Ground | 100,000 to 1,000,000 | $200,950 | $270,410 | $350,070 |
| Public | Surface | Less than 100 | $478 | $756 | $1,224 |
| Public | Surface | 100 to 500 | $696 | $1,012 | $1,435 |
| Public | Surface | 500 to 1,000 | $767 | $1,261 | $1,948 |
| Public | Surface | 1,000 to 3,300 | $1,086 | $1,764 | $2,620 |

**Table C-4: Mean Annualized Cost per CWSs, Option 1c (PFOA and PFOS MCLs of 10.0 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | 5th Percentile | Mean | 95th Percentile |
|---|---|---|---|---|---|
| Public | Surface | 3,300 to 10,000 | $2,616 | $4,135 | $5,953 |
| Public | Surface | 10,000 to 50,000 | $25,209 | $28,007 | $30,854 |
| Public | Surface | 50,000 to 100,000 | $30,672 | $38,542 | $47,165 |
| Public | Surface | 100,000 to 1,000,000 | $163,970 | $199,200 | $238,560 |

Abbreviations: CWS – Community Water System.

## *C.1.2 Mean Annual Cost for all Non-Transient Non-Community Water Systems*

**Table C-5: Mean Annualized Cost per NTNCWS, Proposed Option (PFOA and PFOS MCLs of 4.0 ppt and HI of 1.0) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | 5th Percentile | Mean | 95th Percentile |
|---|---|---|---|---|---|
| Private | Ground | Less than 100 | $1,023 | $1,421 | $1,918 |
| Private | Ground | 100 to 500 | $1,334 | $1,943 | $2,642 |
| Private | Ground | 500 to 1,000 | $1,543 | $2,487 | $3,614 |
| Private | Ground | 1,000 to 3,300 | $2,251 | $3,888 | $5,962 |
| Private | Ground | 3,300 to 10,000 | $1,919 | $8,285 | $16,229 |
| Private | Ground | 10,000 to 50,000 | $458 | $39,962 | $226,000 |
| Private | Surface | Less than 100 | $954 | $1,812 | $2,946 |
| Private | Surface | 100 to 500 | $1,378 | $2,665 | $4,499 |
| Private | Surface | 500 to 1,000 | $1,236 | $3,827 | $7,903 |
| Private | Surface | 1,000 to 3,300 | $1,769 | $5,369 | $10,507 |
| Private | Surface | 3,300 to 10,000 | $3,029 | $15,334 | $33,118 |
| Private | Surface | 10,000 to 50,000 | $8,885 | $70,753 | $154,530 |
| Private | Surface | 100,000 to 1,000,000 | $902 | $240,660 | $2,044,000 |
| Public | Ground | Less than 100 | $975 | $1,411 | $1,920 |
| Public | Ground | 100 to 500 | $1,320 | $1,959 | $2,676 |
| Public | Ground | 500 to 1,000 | $1,489 | $2,383 | $3,422 |
| Public | Ground | 1,000 to 3,300 | $2,272 | $3,973 | $6,106 |
| Public | Ground | 3,300 to 10,000 | $916 | $9,171 | $22,933 |
| Public | Ground | 10,000 to 50,000 | $39,264 | $122,780 | $233,030 |
| Public | Surface | Less than 100 | $746 | $1,853 | $3,638 |
| Public | Surface | 100 to 500 | $1,004 | $2,674 | $5,136 |
| Public | Surface | 500 to 1,000 | $647 | $3,685 | $9,165 |
| Public | Surface | 1,000 to 3,300 | $1,261 | $6,725 | $14,525 |

**Table C-5: Mean Annualized Cost per NTNCWS, Proposed Option (PFOA and PFOS MCLs of 4.0 ppt and HI of 1.0) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | 5th Percentile | Mean | 95th Percentile |
|---|---|---|---|---|---|
| Public | Surface | 3,300 to 10,000 | $1,247 | $13,484 | $35,246 |
| Public | Surface | 10,000 to 50,000 | $1,140 | $65,055 | $194,550 |
| Public | Surface | 50,000 to 100,000 | $591 | $83,260 | $506,000 |

Abbreviations: NTNCWS – Non-Transient, Non-Community Water Systems.

**Table C-6: Mean Annualized Cost per NTNCWS, Option 1a (PFOA and PFOS MCLs of 4 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | 5th Percentile | Mean | 95th Percentile |
|---|---|---|---|---|---|
| Private | Ground | Less than 100 | $1,018 | $1,417 | $1,917 |
| Private | Ground | 100 to 500 | $1,347 | $1,936 | $2,639 |
| Private | Ground | 500 to 1,000 | $1,594 | $2,476 | $3,614 |
| Private | Ground | 1,000 to 3,300 | $2,251 | $3,864 | $5,962 |
| Private | Ground | 3,300 to 10,000 | $1,919 | $8,228 | $16,227 |
| Private | Ground | 10,000 to 50,000 | $458 | $39,525 | $226,580 |
| Private | Surface | Less than 100 | $953 | $1,808 | $2,946 |
| Private | Surface | 100 to 500 | $1,286 | $2,656 | $4,499 |
| Private | Surface | 500 to 1,000 | $1,236 | $3,804 | $7,361 |
| Private | Surface | 1,000 to 3,300 | $1,597 | $5,325 | $10,471 |
| Private | Surface | 3,300 to 10,000 | $2,699 | $15,070 | $31,326 |
| Private | Surface | 10,000 to 50,000 | $8,885 | $68,997 | $148,280 |
| Private | Surface | 100,000 to 1,000,000 | $902 | $237,510 | $2,044,000 |
| Public | Ground | Less than 100 | $972 | $1,407 | $1,920 |
| Public | Ground | 100 to 500 | $1,328 | $1,953 | $2,676 |
| Public | Ground | 500 to 1,000 | $1,473 | $2,374 | $3,381 |
| Public | Ground | 1,000 to 3,300 | $2,090 | $3,950 | $6,105 |
| Public | Ground | 3,300 to 10,000 | $916 | $9,118 | $22,619 |
| Public | Ground | 10,000 to 50,000 | $36,094 | $119,980 | $223,080 |
| Public | Surface | Less than 100 | $746 | $1,849 | $3,732 |
| Public | Surface | 100 to 500 | $965 | $2,665 | $5,136 |
| Public | Surface | 500 to 1,000 | $647 | $3,670 | $9,709 |
| Public | Surface | 1,000 to 3,300 | $1,257 | $6,676 | $14,525 |
| Public | Surface | 3,300 to 10,000 | $1,183 | $13,313 | $33,960 |
| Public | Surface | 10,000 to 50,000 | $1,114 | $64,144 | $193,970 |
| Public | Surface | 50,000 to 100,000 | $591 | $81,895 | $506,000 |

Abbreviations: NTNCWS – Non-Transient, Non-Community Water Systems.

**Table C-7: Mean Annualized Cost per NTNCWS, Option 1b (PFOA and PFOS MCLs of 5.0 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | 5th Percentile | Mean | 95th Percentile |
|---|---|---|---|---|---|
| Private | Ground | Less than 100 | $812 | $1,143 | $1,549 |
| Private | Ground | 100 to 500 | $1,067 | $1,542 | $2,097 |
| Private | Ground | 500 to 1,000 | $1,195 | $1,951 | $2,811 |
| Private | Ground | 1,000 to 3,300 | $1,681 | $3,008 | $4,701 |
| Private | Ground | 3,300 to 10,000 | $1,129 | $6,329 | $13,742 |
| Private | Ground | 10,000 to 50,000 | $458 | $30,335 | $225,300 |
| Private | Surface | Less than 100 | $771 | $1,457 | $2,477 |
| Private | Surface | 100 to 500 | $987 | $2,118 | $3,665 |
| Private | Surface | 500 to 1,000 | $879 | $3,001 | $6,298 |
| Private | Surface | 1,000 to 3,300 | $1,125 | $4,173 | $8,294 |
| Private | Surface | 3,300 to 10,000 | $2,055 | $11,733 | $28,079 |
| Private | Surface | 10,000 to 50,000 | $6,347 | $55,661 | $135,260 |
| Private | Surface | 100,000 to 1,000,000 | $902 | $164,110 | $1,051,400 |
| Public | Ground | Less than 100 | $758 | $1,134 | $1,598 |
| Public | Ground | 100 to 500 | $1,049 | $1,550 | $2,136 |
| Public | Ground | 500 to 1,000 | $1,154 | $1,861 | $2,672 |
| Public | Ground | 1,000 to 3,300 | $1,570 | $3,060 | $4,809 |
| Public | Ground | 3,300 to 10,000 | $761 | $6,925 | $18,498 |
| Public | Ground | 10,000 to 50,000 | $32,771 | $99,358 | $203,830 |
| Public | Surface | Less than 100 | $588 | $1,491 | $3,104 |
| Public | Surface | 100 to 500 | $775 | $2,108 | $4,245 |
| Public | Surface | 500 to 1,000 | $556 | $2,867 | $7,962 |
| Public | Surface | 1,000 to 3,300 | $918 | $5,149 | $11,711 |
| Public | Surface | 3,300 to 10,000 | $1,048 | $10,131 | $28,423 |
| Public | Surface | 10,000 to 50,000 | $879 | $47,923 | $150,450 |
| Public | Surface | 50,000 to 100,000 | $591 | $58,768 | $489,030 |

Abbreviations: NTNCWS – Non-Transient, Non-Community Water Systems.

**Table C-8: Mean Annualized Cost per NTNCWS, Option 1c (PFOA and PFOS MCLs of 10.0 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | 5th Percentile | Mean | 95th Percentile |
|---|---|---|---|---|---|
| Private | Ground | Less than 100 | $435 | $595 | $793 |
| Private | Ground | 100 to 500 | $535 | $768 | $1,035 |
| Private | Ground | 500 to 1,000 | $560 | $911 | $1,396 |
| Private | Ground | 1,000 to 3,300 | $686 | $1,350 | $2,264 |
| Private | Ground | 3,300 to 10,000 | $751 | $2,775 | $7,244 |
| Private | Ground | 10,000 to 50,000 | $458 | $12,056 | $82,018 |
| Private | Surface | Less than 100 | $452 | $778 | $1,396 |
| Private | Surface | 100 to 500 | $569 | $1,080 | $2,093 |
| Private | Surface | 500 to 1,000 | $565 | $1,436 | $3,479 |
| Private | Surface | 1,000 to 3,300 | $647 | $1,863 | $4,444 |
| Private | Surface | 3,300 to 10,000 | $1,453 | $5,342 | $14,663 |
| Private | Surface | 10,000 to 50,000 | $3,279 | $26,457 | $78,374 |
| Private | Surface | 100,000 to 1,000,000 | $902 | $36,179 | $6,586 |
| Public | Ground | Less than 100 | $410 | $592 | $821 |
| Public | Ground | 100 to 500 | $515 | $761 | $1,087 |
| Public | Ground | 500 to 1,000 | $525 | $860 | $1,321 |
| Public | Ground | 1,000 to 3,300 | $639 | $1,309 | $2,218 |
| Public | Ground | 3,300 to 10,000 | $612 | $2,824 | $9,931 |
| Public | Ground | 10,000 to 50,000 | $2,556 | $46,452 | $110,060 |
| Public | Surface | Less than 100 | $386 | $763 | $1,935 |
| Public | Surface | 100 to 500 | $491 | $1,057 | $2,415 |
| Public | Surface | 500 to 1,000 | $449 | $1,349 | $3,768 |
| Public | Surface | 1,000 to 3,300 | $588 | $2,228 | $6,340 |
| Public | Surface | 3,300 to 10,000 | $840 | $4,285 | $17,050 |
| Public | Surface | 10,000 to 50,000 | $828 | $17,287 | $86,559 |
| Public | Surface | 50,000 to 100,000 | $591 | $11,283 | $6,000 |

Abbreviations: NTNCWS – Non-Transient, Non-Community Water Systems.

## C.1.3 Mean Annual Cost for Community Water Systems that Treat or Change Water Source

**Table C-9: Mean Annualized Cost per CWSs that Treat or Change Water Source, Proposed Option (PFOA and PFOS MCLs of 4.0 ppt and HI of 1.0) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | 5th Percentile | Mean | 95th Percentile |
|---|---|---|---|---|---|
| Private | Ground | Less than 100 | $13,793 | $15,375 | $17,165 |
| Private | Ground | 100 to 500 | $22,643 | $25,014 | $28,091 |
| Private | Ground | 500 to 1,000 | $30,327 | $35,471 | $41,384 |
| Private | Ground | 1,000 to 3,300 | $47,843 | $56,147 | $64,536 |
| Private | Ground | 3,300 to 10,000 | $98,144 | $122,540 | $149,250 |
| Private | Ground | 10,000 to 50,000 | $242,260 | $283,750 | $327,210 |
| Private | Ground | 50,000 to 100,000 | $453,640 | $642,690 | $873,600 |
| Private | Ground | 100,000 to 1,000,000 | $618,460 | $903,530 | $1,317,400 |
| Private | Surface | Less than 100 | $13,825 | $22,440 | $33,672 |
| Private | Surface | 100 to 500 | $25,990 | $34,414 | $44,293 |
| Private | Surface | 500 to 1,000 | $31,117 | $49,160 | $70,681 |
| Private | Surface | 1,000 to 3,300 | $51,733 | $71,512 | $94,466 |
| Private | Surface | 3,300 to 10,000 | $99,840 | $143,310 | $189,180 |
| Private | Surface | 10,000 to 50,000 | $320,010 | $376,680 | $441,640 |
| Private | Surface | 50,000 to 100,000 | $455,230 | $580,310 | $722,250 |
| Private | Surface | 100,000 to 1,000,000 | $3,070,400 | $3,677,400 | $4,323,600 |
| Public | Ground | Less than 100 | $12,509 | $15,804 | $19,872 |
| Public | Ground | 100 to 500 | $24,659 | $27,579 | $30,985 |
| Public | Ground | 500 to 1,000 | $33,895 | $37,684 | $42,053 |
| Public | Ground | 1,000 to 3,300 | $60,164 | $65,292 | $71,266 |
| Public | Ground | 3,300 to 10,000 | $124,420 | $138,050 | $153,510 |
| Public | Ground | 10,000 to 50,000 | $310,720 | $332,940 | $359,380 |
| Public | Ground | 50,000 to 100,000 | $572,190 | $666,560 | $767,330 |
| Public | Ground | 100,000 to 1,000,000 | $1,839,100 | $2,243,500 | $2,696,400 |
| Public | Surface | Less than 100 | $14,608 | $23,242 | $34,898 |
| Public | Surface | 100 to 500 | $31,258 | $38,394 | $46,282 |
| Public | Surface | 500 to 1,000 | $44,745 | $54,166 | $64,710 |
| Public | Surface | 1,000 to 3,300 | $80,587 | $89,394 | $100,290 |
| Public | Surface | 3,300 to 10,000 | $174,280 | $192,360 | $211,670 |
| Public | Surface | 10,000 to 50,000 | $390,180 | $413,650 | $440,960 |
| Public | Surface | 50,000 to 100,000 | $558,040 | $617,230 | $680,550 |
| Public | Surface | 100,000 to 1,000,000 | $1,955,300 | $2,180,000 | $2,409,300 |

Abbreviations: CWS – Community Water System.

**Table C-10: Mean Annualized Cost per CWSs that Treat or Change Water Source, Option 1a (PFOA and PFOS MCLs of 4 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | 5th Percentile | Mean | 95th Percentile |
|---|---|---|---|---|---|
| Private | Ground | Less than 100 | $13,797 | $15,360 | $17,165 |
| Private | Ground | 100 to 500 | $22,620 | $24,958 | $27,881 |
| Private | Ground | 500 to 1,000 | $30,091 | $35,340 | $41,144 |
| Private | Ground | 1,000 to 3,300 | $47,736 | $55,900 | $64,492 |
| Private | Ground | 3,300 to 10,000 | $95,732 | $121,890 | $150,170 |
| Private | Ground | 10,000 to 50,000 | $234,880 | $273,690 | $318,220 |
| Private | Ground | 50,000 to 100,000 | $380,760 | $554,250 | $763,320 |
| Private | Ground | 100,000 to 1,000,000 | $602,820 | $873,550 | $1,260,600 |
| Private | Surface | Less than 100 | $13,825 | $22,417 | $32,893 |
| Private | Surface | 100 to 500 | $25,929 | $34,364 | $44,729 |
| Private | Surface | 500 to 1,000 | $31,760 | $49,023 | $68,984 |
| Private | Surface | 1,000 to 3,300 | $51,733 | $71,315 | $94,466 |
| Private | Surface | 3,300 to 10,000 | $100,280 | $142,600 | $187,850 |
| Private | Surface | 10,000 to 50,000 | $312,310 | $368,670 | $432,680 |
| Private | Surface | 50,000 to 100,000 | $446,710 | $571,210 | $718,700 |
| Private | Surface | 100,000 to 1,000,000 | $2,945,100 | $3,548,000 | $4,185,100 |
| Public | Ground | Less than 100 | $12,508 | $15,786 | $19,872 |
| Public | Ground | 100 to 500 | $24,647 | $27,529 | $30,749 |
| Public | Ground | 500 to 1,000 | $33,905 | $37,582 | $41,824 |
| Public | Ground | 1,000 to 3,300 | $59,904 | $65,018 | $71,258 |
| Public | Ground | 3,300 to 10,000 | $123,730 | $137,210 | $152,030 |
| Public | Ground | 10,000 to 50,000 | $303,220 | $325,520 | $351,740 |
| Public | Ground | 50,000 to 100,000 | $560,950 | $650,410 | $750,540 |
| Public | Ground | 100,000 to 1,000,000 | $1,709,000 | $2,109,700 | $2,556,100 |
| Public | Surface | Less than 100 | $14,707 | $23,217 | $34,389 |
| Public | Surface | 100 to 500 | $31,284 | $38,328 | $46,405 |
| Public | Surface | 500 to 1,000 | $45,319 | $54,047 | $64,642 |
| Public | Surface | 1,000 to 3,300 | $80,343 | $89,200 | $99,333 |
| Public | Surface | 3,300 to 10,000 | $174,620 | $191,760 | $211,100 |
| Public | Surface | 10,000 to 50,000 | $384,370 | $407,370 | $432,800 |
| Public | Surface | 50,000 to 100,000 | $549,840 | $605,030 | $661,580 |
| Public | Surface | 100,000 to 1,000,000 | $1,894,700 | $2,117,600 | $2,346,500 |

Abbreviations: CWS – Community Water System.

**Table C-11: Mean Annualized Cost per CWSs that Treat or Change Water Source, Option 1b (PFOA and PFOS MCLs of 5.0 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | 5th Percentile | Mean | 95th Percentile |
|---|---|---|---|---|---|
| Private | Ground | Less than 100 | $13,628 | $15,348 | $17,285 |
| Private | Ground | 100 to 500 | $22,264 | $24,902 | $28,287 |
| Private | Ground | 500 to 1,000 | $29,179 | $34,987 | $41,682 |
| Private | Ground | 1,000 to 3,300 | $46,419 | $55,271 | $65,374 |
| Private | Ground | 3,300 to 10,000 | $92,947 | $119,610 | $151,040 |
| Private | Ground | 10,000 to 50,000 | $212,950 | $253,590 | $298,520 |
| Private | Ground | 50,000 to 100,000 | $322,410 | $483,190 | $682,510 |
| Private | Ground | 100,000 to 1,000,000 | $481,610 | $720,550 | $1,054,200 |
| Private | Surface | Less than 100 | $13,299 | $22,383 | $35,730 |
| Private | Surface | 100 to 500 | $24,251 | $34,417 | $46,479 |
| Private | Surface | 500 to 1,000 | $29,347 | $48,679 | $73,251 |
| Private | Surface | 1,000 to 3,300 | $48,169 | $70,702 | $96,783 |
| Private | Surface | 3,300 to 10,000 | $92,104 | $140,100 | $195,870 |
| Private | Surface | 10,000 to 50,000 | $296,000 | $354,490 | $422,720 |
| Private | Surface | 50,000 to 100,000 | $422,310 | $569,950 | $744,160 |
| Private | Surface | 100,000 to 1,000,000 | $2,692,900 | $3,294,000 | $3,963,200 |
| Public | Ground | Less than 100 | $11,802 | $15,778 | $20,539 |
| Public | Ground | 100 to 500 | $24,239 | $27,445 | $30,997 |
| Public | Ground | 500 to 1,000 | $33,307 | $37,342 | $42,096 |
| Public | Ground | 1,000 to 3,300 | $58,301 | $64,247 | $70,591 |
| Public | Ground | 3,300 to 10,000 | $119,090 | $133,890 | $149,780 |
| Public | Ground | 10,000 to 50,000 | $291,670 | $313,770 | $341,640 |
| Public | Ground | 50,000 to 100,000 | $528,450 | $626,110 | $737,620 |
| Public | Ground | 100,000 to 1,000,000 | $1,578,200 | $1,986,000 | $2,443,400 |
| Public | Surface | Less than 100 | $13,946 | $23,116 | $35,821 |
| Public | Surface | 100 to 500 | $30,195 | $38,103 | $47,319 |
| Public | Surface | 500 to 1,000 | $43,413 | $53,838 | $65,474 |
| Public | Surface | 1,000 to 3,300 | $77,609 | $88,477 | $100,280 |
| Public | Surface | 3,300 to 10,000 | $171,080 | $190,810 | $211,650 |
| Public | Surface | 10,000 to 50,000 | $371,540 | $395,540 | $422,410 |
| Public | Surface | 50,000 to 100,000 | $513,520 | $569,380 | $632,290 |
| Public | Surface | 100,000 to 1,000,000 | $1,758,500 | $1,984,400 | $2,231,100 |

Abbreviations: CWS – Community Water System.

**Table C-12: Mean Annualized Cost per CWSs that Treat or Change Water Source, Option 1c (PFOA and PFOS MCLs of 10.0 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | 5th Percentile | Mean | 95th Percentile |
|---|---|---|---|---|---|
| Private | Ground | Less than 100 | $12,623 | $15,266 | $18,265 |
| Private | Ground | 100 to 500 | $20,928 | $24,867 | $29,633 |
| Private | Ground | 500 to 1,000 | $25,195 | $34,328 | $45,727 |
| Private | Ground | 1,000 to 3,300 | $39,923 | $53,253 | $69,516 |
| Private | Ground | 3,300 to 10,000 | $67,601 | $111,670 | $160,040 |
| Private | Ground | 10,000 to 50,000 | $149,440 | $190,110 | $236,170 |
| Private | Ground | 50,000 to 100,000 | $138,770 | $250,590 | $413,130 |
| Private | Ground | 100,000 to 1,000,000 | $181,810 | $335,330 | $556,430 |
| Private | Surface | Less than 100 | $11,312 | $21,631 | $48,766 |
| Private | Surface | 100 to 500 | $19,433 | $34,132 | $54,990 |
| Private | Surface | 500 to 1,000 | $0 | $45,387 | $87,847 |
| Private | Surface | 1,000 to 3,300 | $31,944 | $67,316 | $119,200 |
| Private | Surface | 3,300 to 10,000 | $0 | $126,060 | $232,900 |
| Private | Surface | 10,000 to 50,000 | $219,550 | $286,960 | $371,720 |
| Private | Surface | 50,000 to 100,000 | $357,660 | $546,630 | $798,650 |
| Private | Surface | 100,000 to 1,000,000 | $1,811,000 | $2,375,100 | $3,006,700 |
| Public | Ground | Less than 100 | $9,959 | $15,815 | $24,391 |
| Public | Ground | 100 to 500 | $22,245 | $27,144 | $32,751 |
| Public | Ground | 500 to 1,000 | $29,548 | $36,349 | $43,505 |
| Public | Ground | 1,000 to 3,300 | $54,295 | $61,836 | $70,426 |
| Public | Ground | 3,300 to 10,000 | $104,700 | $125,700 | $148,080 |
| Public | Ground | 10,000 to 50,000 | $248,310 | $274,750 | $301,260 |
| Public | Ground | 50,000 to 100,000 | $428,340 | $557,010 | $696,310 |
| Public | Ground | 100,000 to 1,000,000 | $1,272,400 | $1,737,100 | $2,343,700 |
| Public | Surface | Less than 100 | $11,050 | $21,773 | $47,885 |
| Public | Surface | 100 to 500 | $25,066 | $37,813 | $55,612 |
| Public | Surface | 500 to 1,000 | $34,959 | $53,196 | $74,908 |
| Public | Surface | 1,000 to 3,300 | $69,223 | $86,744 | $106,090 |
| Public | Surface | 3,300 to 10,000 | $157,500 | $186,670 | $220,730 |
| Public | Surface | 10,000 to 50,000 | $338,060 | $367,130 | $399,760 |
| Public | Surface | 50,000 to 100,000 | $391,500 | $461,120 | $536,130 |
| Public | Surface | 100,000 to 1,000,000 | $1,406,600 | $1,610,100 | $1,842,900 |

Abbreviations: CWS – Community Water System.

## *C.1.4 Mean Annual Cost for Non-Transient Non-Community Water Systems that Treat or Change Water Source*

**Table C-13: Mean Annualized Cost per NTNCWSs that Treat or Change Water Source, Proposed Option (PFOA and PFOS MCLs of 4.0 ppt and HI of 1.0) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | 5th Percentile | Mean | 95th Percentile |
|---|---|---|---|---|---|
| Private | Ground | Less than 100 | $14,944 | $16,802 | $19,106 |
| Private | Ground | 100 to 500 | $22,289 | $25,430 | $28,973 |
| Private | Ground | 500 to 1,000 | $26,994 | $33,645 | $41,449 |
| Private | Ground | 1,000 to 3,300 | $41,545 | $53,745 | $68,213 |
| Private | Ground | 3,300 to 10,000 | $40,954 | $116,000 | $182,440 |
| Private | Ground | 10,000 to 50,000 | $0 | $73,652 | $450,020 |
| Private | Surface | Less than 100 | $12,304 | $22,749 | $38,986 |
| Private | Surface | 100 to 500 | $19,960 | $35,121 | $58,014 |
| Private | Surface | 500 to 1,000 | $23,099 | $48,140 | $91,951 |
| Private | Surface | 1,000 to 3,300 | $35,604 | $72,650 | $126,920 |
| Private | Surface | 3,300 to 10,000 | $0 | $146,250 | $287,490 |
| Private | Surface | 10,000 to 50,000 | $48,432 | $251,710 | $501,260 |
| Private | Surface | 100,000 to 1,000,000 | $0 | $238,530 | $2,044,000 |
| Public | Ground | Less than 100 | $13,147 | $16,806 | $20,754 |
| Public | Ground | 100 to 500 | $23,273 | $26,988 | $31,412 |
| Public | Ground | 500 to 1,000 | $29,074 | $34,958 | $41,922 |
| Public | Ground | 1,000 to 3,300 | $46,306 | $59,460 | $74,131 |
| Public | Ground | 3,300 to 10,000 | $0 | $115,160 | $236,120 |
| Public | Ground | 10,000 to 50,000 | $201,020 | $386,810 | $638,040 |
| Public | Surface | Less than 100 | $11,006 | $22,625 | $54,345 |
| Public | Surface | 100 to 500 | $19,067 | $36,564 | $70,084 |
| Public | Surface | 500 to 1,000 | $0 | $40,721 | $123,550 |
| Public | Surface | 1,000 to 3,300 | $0 | $87,328 | $162,990 |
| Public | Surface | 3,300 to 10,000 | $0 | $137,840 | $297,070 |
| Public | Surface | 10,000 to 50,000 | $0 | $325,460 | $827,950 |
| Public | Surface | 50,000 to 100,000 | $0 | $81,787 | $506,000 |

Abbreviations: NTNCWS – Non-Transient, Non-Community Water Systems.

**Table C-14: Mean Annualized Cost per NTNCWSs that Treat or Change Water Source, Option 1a (PFOA and PFOS MCLs of 4 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | 5th Percentile | Mean | 95th Percentile |
|---|---|---|---|---|---|
| Private | Ground | Less than 100 | $14,755 | $16,765 | $19,090 |
| Private | Ground | 100 to 500 | $22,386 | $25,372 | $29,041 |
| Private | Ground | 500 to 1,000 | $26,642 | $33,558 | $41,519 |
| Private | Ground | 1,000 to 3,300 | $41,261 | $53,550 | $68,193 |
| Private | Ground | 3,300 to 10,000 | $38,732 | $115,590 | $183,890 |
| Private | Ground | 10,000 to 50,000 | $0 | $72,962 | $450,020 |
| Private | Surface | Less than 100 | $12,212 | $22,713 | $38,986 |
| Private | Surface | 100 to 500 | $20,047 | $35,037 | $58,014 |
| Private | Surface | 500 to 1,000 | $22,725 | $47,930 | $91,951 |
| Private | Surface | 1,000 to 3,300 | $35,604 | $72,214 | $120,710 |
| Private | Surface | 3,300 to 10,000 | $0 | $145,010 | $283,220 |
| Private | Surface | 10,000 to 50,000 | $46,976 | $245,720 | $497,570 |
| Private | Surface | 100,000 to 1,000,000 | $0 | $235,400 | $2,044,000 |
| Public | Ground | Less than 100 | $13,147 | $16,775 | $20,754 |
| Public | Ground | 100 to 500 | $23,291 | $26,946 | $31,412 |
| Public | Ground | 500 to 1,000 | $28,669 | $34,876 | $42,260 |
| Public | Ground | 1,000 to 3,300 | $45,327 | $59,252 | $74,131 |
| Public | Ground | 3,300 to 10,000 | $0 | $114,760 | $236,120 |
| Public | Ground | 10,000 to 50,000 | $202,700 | $378,980 | $638,040 |
| Public | Surface | Less than 100 | $11,006 | $22,602 | $54,345 |
| Public | Surface | 100 to 500 | $18,746 | $36,491 | $70,084 |
| Public | Surface | 500 to 1,000 | $0 | $40,562 | $118,960 |
| Public | Surface | 1,000 to 3,300 | $0 | $86,982 | $163,570 |
| Public | Surface | 3,300 to 10,000 | $0 | $136,790 | $294,960 |
| Public | Surface | 10,000 to 50,000 | $0 | $322,080 | $869,420 |
| Public | Surface | 50,000 to 100,000 | $0 | $80,434 | $506,000 |

Abbreviations: NTNCWS – Non-Transient, Non-Community Water Systems.

**Table C-15: Mean Annualized Cost per NTNCWSs that Treat or Change Water Source, Option 1b (PFOA and PFOS MCLs of 5.0 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | 5th Percentile | Mean | 95th Percentile |
|---|---|---|---|---|---|
| Private | Ground | Less than 100 | $14,574 | $16,753 | $19,228 |
| Private | Ground | 100 to 500 | $21,694 | $25,274 | $29,239 |
| Private | Ground | 500 to 1,000 | $25,841 | $33,159 | $42,008 |
| Private | Ground | 1,000 to 3,300 | $38,717 | $53,029 | $70,227 |
| Private | Ground | 3,300 to 10,000 | $0 | $107,710 | $184,870 |
| Private | Ground | 10,000 to 50,000 | $0 | $56,633 | $450,020 |
| Private | Surface | Less than 100 | $11,736 | $22,512 | $44,040 |
| Private | Surface | 100 to 500 | $18,147 | $34,672 | $61,094 |
| Private | Surface | 500 to 1,000 | $0 | $45,520 | $101,190 |
| Private | Surface | 1,000 to 3,300 | $0 | $69,878 | $137,120 |
| Private | Surface | 3,300 to 10,000 | $0 | $134,110 | $288,170 |
| Private | Surface | 10,000 to 50,000 | $0 | $224,800 | $480,670 |
| Private | Surface | 100,000 to 1,000,000 | $0 | $162,070 | $1,051,400 |
| Public | Ground | Less than 100 | $12,677 | $16,754 | $21,459 |
| Public | Ground | 100 to 500 | $22,399 | $26,878 | $31,692 |
| Public | Ground | 500 to 1,000 | $28,044 | $34,737 | $43,256 |
| Public | Ground | 1,000 to 3,300 | $44,274 | $58,753 | $75,683 |
| Public | Ground | 3,300 to 10,000 | $0 | $100,990 | $234,660 |
| Public | Ground | 10,000 to 50,000 | $170,360 | $360,500 | $599,940 |
| Public | Surface | Less than 100 | $0 | $21,337 | $56,764 |
| Public | Surface | 100 to 500 | $0 | $34,996 | $72,257 |
| Public | Surface | 500 to 1,000 | $0 | $34,438 | $106,300 |
| Public | Surface | 1,000 to 3,300 | $0 | $79,410 | $163,840 |
| Public | Surface | 3,300 to 10,000 | $0 | $117,080 | $281,100 |
| Public | Surface | 10,000 to 50,000 | $0 | $264,010 | $804,430 |
| Public | Surface | 50,000 to 100,000 | $0 | $57,368 | $485,750 |

Abbreviations: NTNCWS – Non-Transient, Non-Community Water Systems.

**Table C-16: Mean Annualized Cost per NTNCWSs that Treat or Change Water Source, Option 1c (PFOA and PFOS MCLs of 10.0 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | 5th Percentile | Mean | 95th Percentile |
|---|---|---|---|---|---|
| Private | Ground | Less than 100 | $13,443 | $16,618 | $20,349 |
| Private | Ground | 100 to 500 | $19,735 | $24,953 | $31,471 |
| Private | Ground | 500 to 1,000 | $22,088 | $32,706 | $48,603 |
| Private | Ground | 1,000 to 3,300 | $29,695 | $50,688 | $80,990 |
| Private | Ground | 3,300 to 10,000 | $0 | $66,598 | $178,520 |
| Private | Ground | 10,000 to 50,000 | $0 | $22,172 | $163,500 |
| Private | Surface | Less than 100 | $0 | $19,528 | $55,631 |
| Private | Surface | 100 to 500 | $0 | $29,873 | $81,076 |
| Private | Surface | 500 to 1,000 | $0 | $28,629 | $106,660 |
| Private | Surface | 1,000 to 3,300 | $0 | $46,594 | $150,160 |
| Private | Surface | 3,300 to 10,000 | $0 | $84,427 | $298,160 |
| Private | Surface | 10,000 to 50,000 | $0 | $150,420 | $439,000 |
| Private | Surface | 100,000 to 1,000,000 | $0 | $34,439 | $0 |
| Public | Ground | Less than 100 | $10,234 | $16,663 | $25,514 |
| Public | Ground | 100 to 500 | $19,918 | $26,542 | $35,205 |
| Public | Ground | 500 to 1,000 | $24,337 | $34,172 | $48,183 |
| Public | Ground | 1,000 to 3,300 | $34,816 | $56,918 | $88,928 |
| Public | Ground | 3,300 to 10,000 | $0 | $50,638 | $192,610 |
| Public | Ground | 10,000 to 50,000 | $0 | $268,350 | $591,950 |
| Public | Surface | Less than 100 | $0 | $12,436 | $39,864 |
| Public | Surface | 100 to 500 | $0 | $23,895 | $79,534 |
| Public | Surface | 500 to 1,000 | $0 | $15,610 | $83,872 |
| Public | Surface | 1,000 to 3,300 | $0 | $45,908 | $156,730 |
| Public | Surface | 3,300 to 10,000 | $0 | $57,878 | $252,450 |
| Public | Surface | 10,000 to 50,000 | $0 | $112,850 | $543,790 |
| Public | Surface | 50,000 to 100,000 | $0 | $10,060 | $0 |

Abbreviations: NTNCWS – Non-Transient, Non-Community Water Systems.

## C.1.5 Distribution of Small Community Water System Costs

**Table C-17: Distribution of Annualized Cost for Small CWSs, Proposed Option (PFOA and PFOS MCLs of 4.0 ppt and HI of 1.0) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | Annualized Cost Per CWS | | | | |
|---|---|---|---|---|---|---|---|
| | | | 10th Percentile | 25th Percentile | 50th Percentile | 75th Percentile | 90th Percentile |
| Private | Ground | Less than 100 | $159 | $159 | $159 | $330 | $2,993 |
| Private | Ground | 100 to 500 | $193 | $193 | $211 | $553 | $3,542 |
| Private | Ground | 500 to 1,000 | $185 | $185 | $316 | $812 | $4,452 |
| Private | Ground | 1,000 to 3,300 | $193 | $193 | $361 | $1,224 | $6,684 |
| Private | Ground | 3,300 to 10,000 | $320 | $368 | $852 | $2,436 | $12,812 |
| Private | Surface | Less than 100 | $257 | $257 | $258 | $610 | $3,585 |
| Private | Surface | 100 to 500 | $297 | $297 | $304 | $972 | $4,468 |
| Private | Surface | 500 to 1,000 | $280 | $280 | $318 | $1,171 | $5,468 |
| Private | Surface | 1,000 to 3,300 | $267 | $267 | $393 | $1,339 | $6,547 |
| Private | Surface | 3,300 to 10,000 | $332 | $334 | $644 | $2,246 | $13,966 |
| Public | Ground | Less than 100 | $159 | $159 | $159 | $343 | $2,996 |
| Public | Ground | 100 to 500 | $193 | $193 | $212 | $565 | $3,603 |
| Public | Ground | 500 to 1,000 | $185 | $185 | $313 | $731 | $4,386 |
| Public | Ground | 1,000 to 3,300 | $193 | $193 | $359 | $1,107 | $6,288 |
| Public | Ground | 3,300 to 10,000 | $320 | $544 | $876 | $2,541 | $13,311 |
| Public | Surface | Less than 100 | $257 | $257 | $259 | $650 | $3,683 |
| Public | Surface | 100 to 500 | $297 | $297 | $299 | $803 | $4,499 |
| Public | Surface | 500 to 1,000 | $280 | $280 | $308 | $1,175 | $5,493 |
| Public | Surface | 1,000 to 3,300 | $267 | $267 | $365 | $1,206 | $6,942 |
| Public | Surface | 3,300 to 10,000 | $332 | $332 | $594 | $1,833 | $13,241 |

Abbreviations: CWS – Community Water System.

**Table C-18: Distribution of Annualized Cost for Small CWSs, Option 1a (PFOA and PFOS MCLs of 4 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | Annualized Cost Per CWS | | | | |
|---|---|---|---|---|---|---|---|
| | | | 10th Percentile | 25th Percentile | 50th Percentile | 75th Percentile | 90th Percentile |
| Private | Ground | Less than 100 | $159 | $159 | $159 | $307 | $2,946 |
| Private | Ground | 100 to 500 | $193 | $193 | $210 | $462 | $3,212 |
| Private | Ground | 500 to 1,000 | $185 | $185 | $316 | $685 | $3,920 |
| Private | Ground | 1,000 to 3,300 | $193 | $193 | $360 | $995 | $5,527 |
| Private | Ground | 3,300 to 10,000 | $320 | $368 | $847 | $2,288 | $10,697 |
| Private | Surface | Less than 100 | $257 | $257 | $258 | $493 | $3,131 |
| Private | Surface | 100 to 500 | $297 | $297 | $303 | $629 | $3,342 |
| Private | Surface | 500 to 1,000 | $280 | $280 | $316 | $796 | $3,808 |
| Private | Surface | 1,000 to 3,300 | $267 | $267 | $392 | $842 | $4,199 |
| Private | Surface | 3,300 to 10,000 | $332 | $334 | $622 | $1,898 | $9,849 |
| Public | Ground | Less than 100 | $159 | $159 | $159 | $310 | $2,938 |
| Public | Ground | 100 to 500 | $193 | $193 | $212 | $450 | $3,209 |
| Public | Ground | 500 to 1,000 | $185 | $185 | $313 | $607 | $3,759 |
| Public | Ground | 1,000 to 3,300 | $193 | $193 | $359 | $931 | $5,375 |
| Public | Ground | 3,300 to 10,000 | $320 | $544 | $871 | $2,436 | $11,874 |
| Public | Surface | Less than 100 | $257 | $257 | $259 | $521 | $3,190 |
| Public | Surface | 100 to 500 | $297 | $297 | $299 | $607 | $3,277 |
| Public | Surface | 500 to 1,000 | $280 | $280 | $307 | $697 | $3,442 |
| Public | Surface | 1,000 to 3,300 | $267 | $267 | $364 | $773 | $3,698 |
| Public | Surface | 3,300 to 10,000 | $332 | $332 | $594 | $1,456 | $5,735 |

Abbreviations: CWS – Community Water System.

**Table C-19: Distribution of Annualized Cost for Small CWSs, Option 1b (PFOA and PFOS MCLs of 5.0 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | Annualized Cost Per CWS | | | | |
|---|---|---|---|---|---|---|---|
| | | | 10th Percentile | 25th Percentile | 50th Percentile | 75th Percentile | 90th Percentile |
| Private | Ground | Less than 100 | $159 | $159 | $159 | $278 | $2,705 |
| Private | Ground | 100 to 500 | $193 | $193 | $211 | $382 | $2,898 |
| Private | Ground | 500 to 1,000 | $185 | $185 | $311 | $540 | $3,119 |
| Private | Ground | 1,000 to 3,300 | $193 | $193 | $359 | $709 | $3,802 |
| Private | Ground | 3,300 to 10,000 | $320 | $367 | $818 | $1,829 | $5,966 |
| Private | Surface | Less than 100 | $257 | $257 | $258 | $444 | $2,726 |
| Private | Surface | 100 to 500 | $297 | $297 | $303 | $551 | $2,999 |
| Private | Surface | 500 to 1,000 | $280 | $280 | $315 | $605 | $3,121 |
| Private | Surface | 1,000 to 3,300 | $267 | $267 | $391 | $659 | $3,185 |
| Private | Surface | 3,300 to 10,000 | $332 | $334 | $605 | $1,418 | $5,278 |
| Public | Ground | Less than 100 | $159 | $159 | $159 | $279 | $2,661 |
| Public | Ground | 100 to 500 | $193 | $193 | $212 | $375 | $2,920 |
| Public | Ground | 500 to 1,000 | $185 | $185 | $310 | $480 | $3,078 |
| Public | Ground | 1,000 to 3,300 | $193 | $193 | $358 | $666 | $3,734 |
| Public | Ground | 3,300 to 10,000 | $320 | $531 | $857 | $1,879 | $6,569 |
| Public | Surface | Less than 100 | $257 | $257 | $259 | $450 | $2,800 |
| Public | Surface | 100 to 500 | $297 | $297 | $299 | $531 | $3,002 |
| Public | Surface | 500 to 1,000 | $280 | $280 | $306 | $564 | $3,071 |
| Public | Surface | 1,000 to 3,300 | $267 | $267 | $362 | $622 | $3,152 |
| Public | Surface | 3,300 to 10,000 | $332 | $332 | $593 | $1,103 | $3,749 |

Abbreviations: CWS – Community Water System.

**Table C-20: Distribution of Annualized Cost for Small CWSs, Option 1c (PFOA and PFOS MCLs of 10.0 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | Annualized Cost Per CWS | | | | |
|---|---|---|---|---|---|---|---|
| | | | 10th Percentile | 25th Percentile | 50th Percentile | 75th Percentile | 90th Percentile |
| Private | Ground | Less than 100 | $159 | $159 | $159 | $276 | $389 |
| Private | Ground | 100 to 500 | $193 | $193 | $211 | $358 | $660 |
| Private | Ground | 500 to 1,000 | $185 | $185 | $310 | $460 | $928 |
| Private | Ground | 1,000 to 3,300 | $193 | $193 | $358 | $576 | $1,311 |
| Private | Ground | 3,300 to 10,000 | $320 | $366 | $747 | $1,394 | $2,877 |
| Private | Surface | Less than 100 | $257 | $257 | $258 | $431 | $610 |
| Private | Surface | 100 to 500 | $297 | $297 | $302 | $496 | $967 |
| Private | Surface | 500 to 1,000 | $280 | $280 | $313 | $516 | $1,276 |
| Private | Surface | 1,000 to 3,300 | $267 | $267 | $389 | $515 | $1,194 |
| Private | Surface | 3,300 to 10,000 | $332 | $334 | $594 | $1,071 | $2,608 |
| Public | Ground | Less than 100 | $159 | $159 | $159 | $276 | $406 |
| Public | Ground | 100 to 500 | $193 | $193 | $211 | $358 | $671 |
| Public | Ground | 500 to 1,000 | $185 | $185 | $309 | $387 | $806 |
| Public | Ground | 1,000 to 3,300 | $193 | $193 | $358 | $554 | $1,254 |
| Public | Ground | 3,300 to 10,000 | $320 | $528 | $848 | $1,434 | $3,041 |
| Public | Surface | Less than 100 | $257 | $257 | $258 | $432 | $664 |
| Public | Surface | 100 to 500 | $297 | $297 | $299 | $494 | $942 |
| Public | Surface | 500 to 1,000 | $280 | $280 | $303 | $515 | $1,038 |
| Public | Surface | 1,000 to 3,300 | $267 | $267 | $358 | $499 | $1,126 |
| Public | Surface | 3,300 to 10,000 | $332 | $332 | $547 | $894 | $2,097 |

Abbreviations: CWS – Community Water System.

## C.1.6 Distribution of Small Non-Community Non-Transient Water System Costs

**Table C-21: Distribution of Annualized Cost for Small NTNCWSs, Proposed Option (PFOA and PFOS MCLs of 4.0 ppt and HI of 1.0) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | Annualized Cost Per NTNCWS | | | | |
|---|---|---|---|---|---|---|---|
| | | | 10th Percentile | 25th Percentile | 50th Percentile | 75th Percentile | 90th Percentile |
| Private | Ground | Less than 100 | $155 | $159 | $162 | $374 | $3,011 |
| Private | Ground | 100 to 500 | $160 | $193 | $201 | $471 | $3,142 |
| Private | Ground | 500 to 1,000 | $156 | $185 | $205 | $529 | $3,342 |
| Private | Ground | 1,000 to 3,300 | $169 | $193 | $293 | $831 | $4,322 |
| Private | Ground | 3,300 to 10,000 | $320 | $320 | $489 | $1,667 | $8,428 |
| Private | Surface | Less than 100 | $257 | $257 | $269 | $575 | $3,283 |
| Private | Surface | 100 to 500 | $297 | $297 | $375 | $784 | $3,809 |
| Private | Surface | 500 to 1,000 | $280 | $280 | $471 | $1,220 | $5,953 |
| Private | Surface | 1,000 to 3,300 | $267 | $267 | $389 | $1,395 | $5,981 |
| Private | Surface | 3,300 to 10,000 | $339 | $575 | $1,167 | $3,890 | $23,117 |
| Public | Ground | Less than 100 | $159 | $159 | $161 | $367 | $3,012 |
| Public | Ground | 100 to 500 | $193 | $193 | $196 | $424 | $3,094 |
| Public | Ground | 500 to 1,000 | $185 | $185 | $188 | $440 | $3,112 |
| Public | Ground | 1,000 to 3,300 | $193 | $193 | $251 | $661 | $3,777 |
| Public | Ground | 3,300 to 10,000 | $320 | $344 | $600 | $1,340 | $14,323 |
| Public | Surface | Less than 100 | $257 | $257 | $271 | $665 | $3,202 |
| Public | Surface | 100 to 500 | $297 | $297 | $324 | $799 | $3,784 |
| Public | Surface | 500 to 1,000 | $280 | $280 | $309 | $1,023 | $4,630 |
| Public | Surface | 1,000 to 3,300 | $267 | $268 | $477 | $1,380 | $7,205 |
| Public | Surface | 3,300 to 10,000 | $332 | $366 | $753 | $2,133 | $29,501 |

Abbreviations: NTNCWS – Non-Transient Non-Community Water System.

**Table C-22: Distribution of Annualized Cost for Small NTNCWSs, Option 1a (PFOA and PFOS MCLs of 4.0 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | Annualized Cost Per NTNCWS | | | | |
|---|---|---|---|---|---|---|---|
| | | | 10th Percentile | 25th Percentile | 50th Percentile | 75th Percentile | 90th Percentile |
| Private | Ground | Less than 100 | $155 | $159 | $162 | $373 | $3,008 |
| Private | Ground | 100 to 500 | $160 | $193 | $201 | $469 | $3,133 |
| Private | Ground | 500 to 1,000 | $156 | $185 | $205 | $525 | $3,327 |
| Private | Ground | 1,000 to 3,300 | $169 | $193 | $292 | $826 | $4,270 |
| Private | Ground | 3,300 to 10,000 | $320 | $320 | $488 | $1,663 | $8,336 |
| Private | Surface | Less than 100 | $257 | $257 | $268 | $574 | $3,277 |
| Private | Surface | 100 to 500 | $297 | $297 | $375 | $782 | $3,798 |
| Private | Surface | 500 to 1,000 | $280 | $280 | $470 | $1,213 | $5,897 |
| Private | Surface | 1,000 to 3,300 | $267 | $267 | $389 | $1,390 | $5,912 |
| Private | Surface | 3,300 to 10,000 | $339 | $574 | $1,163 | $3,833 | $22,435 |
| Public | Ground | Less than 100 | $159 | $159 | $161 | $367 | $3,006 |
| Public | Ground | 100 to 500 | $193 | $193 | $196 | $424 | $3,089 |
| Public | Ground | 500 to 1,000 | $185 | $185 | $188 | $439 | $3,103 |
| Public | Ground | 1,000 to 3,300 | $193 | $193 | $251 | $658 | $3,747 |
| Public | Ground | 3,300 to 10,000 | $320 | $344 | $600 | $1,335 | $14,199 |
| Public | Surface | Less than 100 | $257 | $257 | $271 | $664 | $3,197 |
| Public | Surface | 100 to 500 | $297 | $297 | $324 | $796 | $3,769 |
| Public | Surface | 500 to 1,000 | $280 | $280 | $309 | $1,021 | $4,615 |
| Public | Surface | 1,000 to 3,300 | $267 | $268 | $477 | $1,371 | $7,120 |
| Public | Surface | 3,300 to 10,000 | $332 | $365 | $751 | $2,119 | $28,949 |

Abbreviations: NTNCWS – Non-Transient Non-Community Water System.

**Table C-23: Distribution of Annualized Cost for Small NTNCWSs, Option 1b (PFOA and PFOS MCLs of 5.0 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | Annualized Cost Per NTNCWS | | | | |
|---|---|---|---|---|---|---|---|
| | | | 10th Percentile | 25th Percentile | 50th Percentile | 75th Percentile | 90th Percentile |
| Private | Ground | Less than 100 | $155 | $159 | $162 | $304 | $2,781 |
| Private | Ground | 100 to 500 | $160 | $193 | $200 | $378 | $2,842 |
| Private | Ground | 500 to 1,000 | $156 | $185 | $204 | $391 | $2,917 |
| Private | Ground | 1,000 to 3,300 | $169 | $193 | $288 | $605 | $3,177 |
| Private | Ground | 3,300 to 10,000 | $320 | $320 | $480 | $1,350 | $4,849 |
| Private | Surface | Less than 100 | $257 | $257 | $268 | $484 | $2,745 |
| Private | Surface | 100 to 500 | $297 | $297 | $373 | $616 | $3,046 |
| Private | Surface | 500 to 1,000 | $280 | $280 | $460 | $890 | $3,957 |
| Private | Surface | 1,000 to 3,300 | $267 | $267 | $384 | $1,081 | $3,814 |
| Private | Surface | 3,300 to 10,000 | $339 | $568 | $1,078 | $3,191 | $13,604 |
| Public | Ground | Less than 100 | $159 | $159 | $161 | $306 | $2,716 |
| Public | Ground | 100 to 500 | $193 | $193 | $196 | $359 | $2,792 |
| Public | Ground | 500 to 1,000 | $185 | $185 | $188 | $354 | $2,824 |
| Public | Ground | 1,000 to 3,300 | $193 | $193 | $249 | $482 | $2,968 |
| Public | Ground | 3,300 to 10,000 | $320 | $344 | $593 | $1,059 | $7,723 |
| Public | Surface | Less than 100 | $257 | $257 | $271 | $503 | $2,442 |
| Public | Surface | 100 to 500 | $297 | $297 | $323 | $615 | $2,836 |
| Public | Surface | 500 to 1,000 | $280 | $280 | $307 | $765 | $3,223 |
| Public | Surface | 1,000 to 3,300 | $267 | $268 | $465 | $1,062 | $4,291 |
| Public | Surface | 3,300 to 10,000 | $332 | $364 | $707 | $1,782 | $17,685 |

Abbreviations: NTNCWS – Non-Transient Non-Community Water System.

**Table C-24: Distribution of Annualized Cost for Small NTNCWSs, Option 1c (PFOA and PFOS MCLs of 10.0 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | Annualized Cost Per NTNCWS | | | | |
|---|---|---|---|---|---|---|---|
| | | | 10th Percentile | 25th Percentile | 50th Percentile | 75th Percentile | 90th Percentile |
| Private | Ground | Less than 100 | $155 | $159 | $162 | $276 | $587 |
| Private | Ground | 100 to 500 | $160 | $193 | $200 | $331 | $706 |
| Private | Ground | 500 to 1,000 | $156 | $185 | $203 | $342 | $804 |
| Private | Ground | 1,000 to 3,300 | $169 | $193 | $281 | $478 | $1,146 |
| Private | Ground | 3,300 to 10,000 | $320 | $320 | $477 | $974 | $2,114 |
| Private | Surface | Less than 100 | $257 | $257 | $268 | $438 | $774 |
| Private | Surface | 100 to 500 | $297 | $297 | $370 | $547 | $1,110 |
| Private | Surface | 500 to 1,000 | $280 | $280 | $450 | $645 | $1,583 |
| Private | Surface | 1,000 to 3,300 | $267 | $267 | $380 | $753 | $1,804 |
| Private | Surface | 3,300 to 10,000 | $339 | $551 | $963 | $2,336 | $4,662 |
| Public | Ground | Less than 100 | $159 | $159 | $161 | $276 | $559 |
| Public | Ground | 100 to 500 | $193 | $193 | $196 | $325 | $632 |
| Public | Ground | 500 to 1,000 | $185 | $185 | $188 | $313 | $649 |
| Public | Ground | 1,000 to 3,300 | $193 | $193 | $245 | $371 | $946 |
| Public | Ground | 3,300 to 10,000 | $320 | $344 | $586 | $850 | $1,797 |
| Public | Surface | Less than 100 | $257 | $257 | $271 | $435 | $787 |
| Public | Surface | 100 to 500 | $297 | $297 | $323 | $514 | $1,056 |
| Public | Surface | 500 to 1,000 | $280 | $280 | $305 | $504 | $1,361 |
| Public | Surface | 1,000 to 3,300 | $267 | $268 | $445 | $748 | $1,755 |
| Public | Surface | 3,300 to 10,000 | $332 | $364 | $641 | $1,319 | $3,910 |

Abbreviations: NTNCWS – Non-Transient Non-Community Water System.

## C.1.7 Distribution of Small Community Water System Costs that Treat or Change Water Source

**Table C-25: Distribution of Annualized Cost for Small CWSs that Treat or Change Water Source, Proposed Option (PFOA and PFOS MCLs of 4.0 ppt and HI of 1.0) (Commercial Cost of Capital)**

| Ownership | Source Water | Population Served Size Category | Annualized Cost Per CWS | | | | |
|---|---|---|---|---|---|---|---|
| | | | 10th Percentile | 25th Percentile | 50th Percentile | 75th Percentile | 90th Percentile |
| Private | Ground | Less than 100 | $8,242 | $8,683 | $9,301 | $11,346 | $27,138 |
| Private | Ground | 100 to 500 | $12,388 | $13,573 | $15,824 | $22,255 | $41,253 |
| Private | Ground | 500 to 1,000 | $18,503 | $20,456 | $24,163 | $35,680 | $62,893 |
| Private | Ground | 1,000 to 3,300 | $25,828 | $31,113 | $41,075 | $62,626 | $101,440 |
| Private | Ground | 3,300 to 10,000 | $42,808 | $61,678 | $104,750 | $148,750 | $200,140 |
| Private | Surface | Less than 100 | $11,017 | $11,659 | $12,692 | $17,258 | $38,601 |
| Private | Surface | 100 to 500 | $15,480 | $17,234 | $20,195 | $28,916 | $62,180 |
| Private | Surface | 500 to 1,000 | $21,658 | $24,401 | $28,921 | $44,857 | $80,445 |
| Private | Surface | 1,000 to 3,300 | $28,556 | $35,544 | $47,013 | $71,191 | $116,060 |
| Private | Surface | 3,300 to 10,000 | $47,538 | $65,132 | $105,250 | $161,590 | $222,040 |
| Public | Ground | Less than 100 | $8,513 | $9,037 | $9,724 | $12,272 | $28,057 |
| Public | Ground | 100 to 500 | $13,841 | $15,669 | $18,696 | $24,900 | $45,429 |
| Public | Ground | 500 to 1,000 | $20,264 | $22,802 | $27,529 | $37,874 | $63,959 |
| Public | Ground | 1,000 to 3,300 | $29,277 | $36,300 | $49,322 | $79,479 | $116,780 |
| Public | Ground | 3,300 to 10,000 | $47,826 | $69,046 | $120,390 | $175,150 | $242,740 |
| Public | Surface | Less than 100 | $11,478 | $12,340 | $13,568 | $18,255 | $38,665 |
| Public | Surface | 100 to 500 | $17,641 | $20,038 | $24,264 | $33,456 | $69,933 |
| Public | Surface | 500 to 1,000 | $25,435 | $29,535 | $35,977 | $49,550 | $98,337 |
| Public | Surface | 1,000 to 3,300 | $36,552 | $45,699 | $60,955 | $108,180 | $158,060 |
| Public | Surface | 3,300 to 10,000 | $61,341 | $109,550 | $157,880 | $223,440 | $315,330 |

Abbreviations: CWS – Community Water System.

**Table C-26: Distribution of Annualized Cost for Small CWSs that Treat or Change Water Source, Option 1a (PFOA and PFOS MCLs of 4.0 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | Annualized Cost Per CWS | | | | |
|---|---|---|---|---|---|---|---|
| | | | 10th Percentile | 25th Percentile | 50th Percentile | 75th Percentile | 90th Percentile |
| Private | Ground | Less than 100 | $8,241 | $8,683 | $9,300 | $11,327 | $27,122 |
| Private | Ground | 100 to 500 | $12,388 | $13,571 | $15,813 | $22,150 | $41,135 |
| Private | Ground | 500 to 1,000 | $18,495 | $20,435 | $24,093 | $35,472 | $62,521 |
| Private | Ground | 1,000 to 3,300 | $25,792 | $31,035 | $40,863 | $62,207 | $100,980 |
| Private | Ground | 3,300 to 10,000 | $42,645 | $61,280 | $104,060 | $147,920 | $198,890 |
| Private | Surface | Less than 100 | $11,017 | $11,659 | $12,690 | $17,222 | $38,422 |
| Private | Surface | 100 to 500 | $15,480 | $17,229 | $20,182 | $28,840 | $62,034 |
| Private | Surface | 500 to 1,000 | $21,656 | $24,391 | $28,876 | $44,625 | $80,068 |
| Private | Surface | 1,000 to 3,300 | $28,551 | $35,499 | $46,932 | $70,801 | $115,570 |
| Private | Surface | 3,300 to 10,000 | $47,559 | $64,780 | $104,660 | $160,580 | $220,770 |
| Public | Ground | Less than 100 | $8,512 | $9,037 | $9,723 | $12,242 | $28,005 |
| Public | Ground | 100 to 500 | $13,840 | $15,663 | $18,681 | $24,805 | $45,299 |
| Public | Ground | 500 to 1,000 | $20,250 | $22,778 | $27,458 | $37,693 | $63,747 |
| Public | Ground | 1,000 to 3,300 | $29,229 | $36,204 | $49,100 | $78,996 | $116,420 |
| Public | Ground | 3,300 to 10,000 | $47,688 | $68,318 | $119,840 | $173,990 | $241,120 |
| Public | Surface | Less than 100 | $11,473 | $12,336 | $13,563 | $18,180 | $38,580 |
| Public | Surface | 100 to 500 | $17,638 | $20,030 | $24,244 | $33,353 | $69,691 |
| Public | Surface | 500 to 1,000 | $25,416 | $29,510 | $35,935 | $49,329 | $97,973 |
| Public | Surface | 1,000 to 3,300 | $36,514 | $45,642 | $60,830 | $107,860 | $157,780 |
| Public | Surface | 3,300 to 10,000 | $61,146 | $109,170 | $157,500 | $222,660 | $314,150 |

Abbreviations: CWS – Community Water System.

**Table C-27: Distribution of Annualized Cost for Small CWSs that Treat or Change Water Source, Option 1b (PFOA and PFOS MCLs of 5.0 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | Annualized Cost Per CWS | | | | |
|---|---|---|---|---|---|---|---|
| | | | 10th Percentile | 25th Percentile | 50th Percentile | 75th Percentile | 90th Percentile |
| Private | Ground | Less than 100 | $8,243 | $8,684 | $9,299 | $11,315 | $27,068 |
| Private | Ground | 100 to 500 | $12,404 | $13,592 | $15,814 | $22,000 | $41,107 |
| Private | Ground | 500 to 1,000 | $18,457 | $20,361 | $23,896 | $34,884 | $61,286 |
| Private | Ground | 1,000 to 3,300 | $25,648 | $30,705 | $40,201 | $61,181 | $98,083 |
| Private | Ground | 3,300 to 10,000 | $41,805 | $59,107 | $99,511 | $143,270 | $192,070 |
| Private | Surface | Less than 100 | $11,024 | $11,617 | $12,659 | $17,347 | $36,341 |
| Private | Surface | 100 to 500 | $15,445 | $17,190 | $20,104 | $28,731 | $60,478 |
| Private | Surface | 500 to 1,000 | $22,051 | $24,239 | $28,622 | $43,537 | $73,417 |
| Private | Surface | 1,000 to 3,300 | $29,009 | $35,094 | $45,915 | $69,367 | $108,070 |
| Private | Surface | 3,300 to 10,000 | $49,697 | $62,806 | $99,489 | $153,560 | $208,260 |
| Public | Ground | Less than 100 | $8,513 | $9,035 | $9,721 | $12,311 | $27,622 |
| Public | Ground | 100 to 500 | $13,869 | $15,683 | $18,655 | $24,690 | $45,364 |
| Public | Ground | 500 to 1,000 | $20,235 | $22,712 | $27,257 | $37,317 | $63,297 |
| Public | Ground | 1,000 to 3,300 | $29,104 | $35,900 | $48,432 | $77,739 | $115,360 |
| Public | Ground | 3,300 to 10,000 | $46,991 | $65,063 | $117,300 | $169,370 | $235,640 |
| Public | Surface | Less than 100 | $11,510 | $12,312 | $13,534 | $18,227 | $36,911 |
| Public | Surface | 100 to 500 | $17,579 | $19,934 | $24,072 | $32,931 | $67,725 |
| Public | Surface | 500 to 1,000 | $25,309 | $29,420 | $35,748 | $49,163 | $94,752 |
| Public | Surface | 1,000 to 3,300 | $36,310 | $45,398 | $60,422 | $106,750 | $156,470 |
| Public | Surface | 3,300 to 10,000 | $60,592 | $107,090 | $156,240 | $221,180 | $314,330 |

Abbreviations: CWS – Community Water System.

**Table C-28: Distribution of Annualized Cost for Small CWSs that Treat or Change Water Source, Option 1c (PFOA and PFOS MCLs of 10.0 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | Annualized Cost Per CWS | | | | |
|---|---|---|---|---|---|---|---|
| | | | 10th Percentile | 25th Percentile | 50th Percentile | 75th Percentile | 90th Percentile |
| Private | Ground | Less than 100 | $8,246 | $8,685 | $9,296 | $11,309 | $26,576 |
| Private | Ground | 100 to 500 | $12,443 | $13,644 | $15,814 | $21,811 | $42,334 |
| Private | Ground | 500 to 1,000 | $18,167 | $20,056 | $23,343 | $33,375 | $55,838 |
| Private | Ground | 1,000 to 3,300 | $25,043 | $29,561 | $38,032 | $57,040 | $86,431 |
| Private | Ground | 3,300 to 10,000 | $46,598 | $54,349 | $80,681 | $121,300 | $160,810 |
| Private | Surface | Less than 100 | $11,874 | $11,996 | $12,704 | $16,406 | $29,507 |
| Private | Surface | 100 to 500 | $15,695 | $16,927 | $19,498 | $28,151 | $49,859 |
| Private | Surface | 500 to 1,000 | $25,697 | $25,938 | $27,971 | $36,375 | $59,476 |
| Private | Surface | 1,000 to 3,300 | $36,662 | $37,534 | $43,464 | $59,249 | $88,349 |
| Private | Surface | 3,300 to 10,000 | $67,604 | $68,920 | $83,604 | $117,100 | $171,040 |
| Public | Ground | Less than 100 | $8,484 | $8,978 | $9,675 | $12,569 | $25,391 |
| Public | Ground | 100 to 500 | $13,874 | $15,675 | $18,507 | $24,307 | $44,767 |
| Public | Ground | 500 to 1,000 | $19,996 | $22,340 | $26,368 | $35,849 | $59,638 |
| Public | Ground | 1,000 to 3,300 | $28,623 | $34,810 | $46,314 | $73,135 | $110,780 |
| Public | Ground | 3,300 to 10,000 | $45,527 | $59,221 | $107,720 | $157,310 | $219,500 |
| Public | Surface | Less than 100 | $12,720 | $12,814 | $13,541 | $16,792 | $29,851 |
| Public | Surface | 100 to 500 | $17,401 | $19,634 | $23,454 | $32,686 | $58,677 |
| Public | Surface | 500 to 1,000 | $24,877 | $28,671 | $34,581 | $48,272 | $79,172 |
| Public | Surface | 1,000 to 3,300 | $34,856 | $44,117 | $58,833 | $100,210 | $147,770 |
| Public | Surface | 3,300 to 10,000 | $59,278 | $98,619 | $150,840 | $215,500 | $308,880 |

Abbreviations: CWS – Community Water System.

## *C.1.8 Distribution of Small Non-Community Water Non-Transient System Costs that Treat or Change Water Source*

**Table C-29: Distribution of Annualized Cost for Small NTNCWSs that Treat or Change Water Source, Proposed Option (PFOA and PFOS MCLs of 4.0 ppt and HI of 1.0) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | Annualized Cost Per NTNCWS | | | | |
|---|---|---|---|---|---|---|---|
| | | | 10th Percentile | 25th Percentile | 50th Percentile | 75th Percentile | 90th Percentile |
| Private | Ground | Less than 100 | $8,151 | $8,652 | $9,402 | $13,927 | $29,307 |
| Private | Ground | 100 to 500 | $12,366 | $13,514 | $15,869 | $22,370 | $43,434 |
| Private | Ground | 500 to 1,000 | $18,336 | $20,363 | $23,726 | $32,058 | $56,838 |
| Private | Ground | 1,000 to 3,300 | $25,223 | $30,622 | $39,135 | $56,911 | $88,201 |
| Private | Ground | 3,300 to 10,000 | $68,153 | $70,086 | $84,488 | $109,320 | $145,570 |
| Private | Surface | Less than 100 | $11,004 | $11,389 | $12,714 | $18,294 | $34,841 |
| Private | Surface | 100 to 500 | $16,242 | $17,512 | $20,804 | $31,341 | $53,902 |
| Private | Surface | 500 to 1,000 | $27,455 | $27,751 | $30,531 | $40,657 | $67,812 |
| Private | Surface | 1,000 to 3,300 | $36,257 | $37,665 | $45,202 | $65,710 | $101,980 |
| Private | Surface | 3,300 to 10,000 | $78,055 | $79,016 | $94,687 | $136,070 | $213,890 |
| Public | Ground | Less than 100 | $8,391 | $8,962 | $9,798 | $14,498 | $31,389 |
| Public | Ground | 100 to 500 | $13,771 | $15,456 | $18,566 | $24,145 | $45,771 |
| Public | Ground | 500 to 1,000 | $20,454 | $22,936 | $26,097 | $33,347 | $57,315 |
| Public | Ground | 1,000 to 3,300 | $29,309 | $35,505 | $44,022 | $64,724 | $100,390 |
| Public | Ground | 3,300 to 10,000 | $82,369 | $82,494 | $87,770 | $102,890 | $144,070 |
| Public | Surface | Less than 100 | $13,233 | $13,292 | $14,048 | $18,239 | $31,632 |
| Public | Surface | 100 to 500 | $19,511 | $19,896 | $22,515 | $31,137 | $51,418 |
| Public | Surface | 500 to 1,000 | $34,025 | $34,025 | $34,464 | $37,435 | $55,439 |
| Public | Surface | 1,000 to 3,300 | $50,739 | $51,412 | $58,817 | $76,914 | $113,290 |
| Public | Surface | 3,300 to 10,000 | $94,800 | $94,963 | $101,130 | $119,070 | $165,810 |

Abbreviations: NTNCWS – Non-Transient Non-Community Water System.

**Table C-30: Distribution of Annualized Cost for Small NTNCWSs that Treat or Change Water Source, Option 1a (PFOA and PFOS MCLs of 4.0 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | Annualized Cost Per NTNCWS | | | | |
|---|---|---|---|---|---|---|---|
| | | | 10th Percentile | 25th Percentile | 50th Percentile | 75th Percentile | 90th Percentile |
| Private | Ground | Less than 100 | $8,151 | $8,651 | $9,400 | $13,862 | $29,201 |
| Private | Ground | 100 to 500 | $12,365 | $13,512 | $15,856 | $22,258 | $43,245 |
| Private | Ground | 500 to 1,000 | $18,332 | $20,349 | $23,689 | $31,923 | $56,483 |
| Private | Ground | 1,000 to 3,300 | $25,193 | $30,542 | $39,029 | $56,643 | $87,732 |
| Private | Ground | 3,300 to 10,000 | $68,040 | $69,972 | $84,199 | $108,800 | $145,070 |
| Private | Surface | Less than 100 | $10,999 | $11,381 | $12,704 | $18,261 | $34,774 |
| Private | Surface | 100 to 500 | $16,240 | $17,498 | $20,769 | $31,252 | $53,635 |
| Private | Surface | 500 to 1,000 | $27,406 | $27,699 | $30,447 | $40,557 | $67,438 |
| Private | Surface | 1,000 to 3,300 | $36,244 | $37,639 | $45,074 | $65,228 | $101,290 |
| Private | Surface | 3,300 to 10,000 | $77,908 | $78,795 | $94,100 | $134,480 | $211,810 |
| Public | Ground | Less than 100 | $8,390 | $8,961 | $9,796 | $14,433 | $31,194 |
| Public | Ground | 100 to 500 | $13,769 | $15,452 | $18,554 | $24,100 | $45,656 |
| Public | Ground | 500 to 1,000 | $20,448 | $22,921 | $26,072 | $33,251 | $57,021 |
| Public | Ground | 1,000 to 3,300 | $29,264 | $35,443 | $43,904 | $64,387 | $99,974 |
| Public | Ground | 3,300 to 10,000 | $82,239 | $82,352 | $87,613 | $102,430 | $143,460 |
| Public | Surface | Less than 100 | $13,238 | $13,296 | $14,061 | $18,231 | $31,586 |
| Public | Surface | 100 to 500 | $19,511 | $19,893 | $22,504 | $31,063 | $51,281 |
| Public | Surface | 500 to 1,000 | $33,894 | $33,894 | $34,338 | $37,251 | $55,138 |
| Public | Surface | 1,000 to 3,300 | $50,602 | $51,259 | $58,474 | $76,432 | $112,550 |
| Public | Surface | 3,300 to 10,000 | $94,451 | $94,612 | $100,620 | $118,000 | $163,920 |

Abbreviations: NTNCWS – Non-Transient Non-Community Water System.

**Table C-31: Distribution of Annualized Cost for Small NTNCWSs that Treat or Change Water Source, Option 1b (PFOA and PFOS MCLs of 5.0 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | Annualized Cost Per NTNCWS | | | | |
|---|---|---|---|---|---|---|---|
| | | | 10th Percentile | 25th Percentile | 50th Percentile | 75th Percentile | 90th Percentile |
| Private | Ground | Less than 100 | $8,154 | $8,652 | $9,399 | $13,780 | $29,332 |
| Private | Ground | 100 to 500 | $12,370 | $13,514 | $15,827 | $22,103 | $43,086 |
| Private | Ground | 500 to 1,000 | $18,126 | $20,127 | $23,360 | $31,478 | $54,595 |
| Private | Ground | 1,000 to 3,300 | $25,002 | $30,024 | $38,197 | $55,500 | $83,953 |
| Private | Ground | 3,300 to 10,000 | $70,785 | $71,520 | $79,719 | $97,765 | $131,930 |
| Private | Surface | Less than 100 | $11,217 | $11,461 | $12,609 | $18,004 | $32,108 |
| Private | Surface | 100 to 500 | $16,937 | $17,750 | $20,640 | $30,245 | $50,656 |
| Private | Surface | 500 to 1,000 | $28,890 | $28,976 | $30,699 | $37,838 | $62,611 |
| Private | Surface | 1,000 to 3,300 | $39,132 | $39,774 | $44,641 | $60,545 | $95,018 |
| Private | Surface | 3,300 to 10,000 | $82,605 | $82,822 | $91,849 | $119,600 | $188,480 |
| Public | Ground | Less than 100 | $8,385 | $8,952 | $9,800 | $14,386 | $30,867 |
| Public | Ground | 100 to 500 | $13,759 | $15,442 | $18,494 | $23,999 | $45,449 |
| Public | Ground | 500 to 1,000 | $20,357 | $22,801 | $25,939 | $33,147 | $55,606 |
| Public | Ground | 1,000 to 3,300 | $28,855 | $34,887 | $43,242 | $62,864 | $95,930 |
| Public | Ground | 3,300 to 10,000 | $78,626 | $78,695 | $80,908 | $89,118 | $120,970 |
| Public | Surface | Less than 100 | $13,635 | $13,653 | $14,102 | $16,892 | $28,898 |
| Public | Surface | 100 to 500 | $20,649 | $20,804 | $22,536 | $29,155 | $48,972 |
| Public | Surface | 500 to 1,000 | $30,515 | $30,515 | $30,653 | $32,028 | $43,871 |
| Public | Surface | 1,000 to 3,300 | $51,409 | $51,669 | $55,832 | $67,481 | $98,713 |
| Public | Surface | 3,300 to 10,000 | $87,944 | $88,024 | $91,161 | $101,240 | $134,750 |

Abbreviations: NTNCWS – Non-Transient Non-Community Water System.

**Table C-32: Distribution of Annualized Cost for Small NTNCWSs that Treat or Change Water Source, Option 1c (PFOA and PFOS MCLs of 10.0 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | Annualized Cost Per NTNCWS | | | | |
|---|---|---|---|---|---|---|---|
| | | | 10th Percentile | 25th Percentile | 50th Percentile | 75th Percentile | 90th Percentile |
| Private | Ground | Less than 100 | $8,158 | $8,642 | $9,394 | $13,498 | $29,755 |
| Private | Ground | 100 to 500 | $12,351 | $13,479 | $15,684 | $21,714 | $42,285 |
| Private | Ground | 500 to 1,000 | $18,233 | $19,774 | $22,724 | $30,351 | $45,974 |
| Private | Ground | 1,000 to 3,300 | $28,443 | $29,839 | $35,451 | $48,171 | $68,049 |
| Private | Ground | 3,300 to 10,000 | $54,781 | $54,819 | $55,576 | $58,802 | $73,180 |
| Private | Surface | Less than 100 | $12,831 | $12,842 | $13,162 | $15,351 | $26,237 |
| Private | Surface | 100 to 500 | $19,558 | $19,604 | $20,335 | $24,123 | $39,400 |
| Private | Surface | 500 to 1,000 | $24,041 | $24,041 | $24,165 | $24,977 | $33,683 |
| Private | Surface | 1,000 to 3,300 | $36,481 | $36,509 | $37,094 | $39,732 | $54,838 |
| Private | Surface | 3,300 to 10,000 | $69,885 | $69,885 | $70,472 | $74,324 | $100,370 |
| Public | Ground | Less than 100 | $8,375 | $8,883 | $9,779 | $13,988 | $27,831 |
| Public | Ground | 100 to 500 | $13,670 | $15,313 | $18,162 | $23,729 | $42,742 |
| Public | Ground | 500 to 1,000 | $20,347 | $22,160 | $25,161 | $32,310 | $47,559 |
| Public | Ground | 1,000 to 3,300 | $32,900 | $34,495 | $40,468 | $55,548 | $78,082 |
| Public | Ground | 3,300 to 10,000 | $46,464 | $46,464 | $46,535 | $47,197 | $54,139 |
| Public | Surface | Less than 100 | $10,362 | $10,362 | $10,385 | $10,678 | $14,112 |
| Public | Surface | 100 to 500 | $18,747 | $18,747 | $18,963 | $20,109 | $28,531 |
| Public | Surface | 500 to 1,000 | $15,568 | $15,568 | $15,570 | $15,646 | $17,328 |
| Public | Surface | 1,000 to 3,300 | $37,082 | $37,082 | $37,527 | $39,003 | $48,527 |
| Public | Surface | 3,300 to 10,000 | $49,931 | $49,931 | $50,141 | $51,539 | $59,786 |

Abbreviations: NTNCWS – Non-Transient Non-Community Water System.

# C.2 Household-Level Cost Details

Section C.2 provides estimates of household costs by primary source water, ownership, and system size category. Costs are provided for all CWSs as well as for only CWSs that must treat or change water source to comply with the regulatory option.

## *C.2.1 Household Costs for all Community Water Systems*

**Table C-33: Mean Annualized Cost per Household, Proposed Option (PFOA and PFOS MCLs of 4.0 ppt and HI of 1.0) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | 5th Percentile | Mean | 95th Percentile |
|---|---|---|---|---|---|
| Private | Ground | Less than 100 | $41 | $59 | $82 |
| Private | Ground | 100 to 500 | $23 | $33 | $49 |
| Private | Ground | 500 to 1,000 | $7 | $10 | $15 |
| Private | Ground | 1,000 to 3,300 | $4 | $7 | $10 |
| Private | Ground | 3,300 to 10,000 | $3 | $5 | $7 |
| Private | Ground | 10,000 to 50,000 | $8 | $9 | $11 |
| Private | Ground | 50,000 to 100,000 | $5 | $8 | $11 |
| Private | Ground | 100,000 to 1,000,000 | $4 | $6 | $8 |
| Private | Surface | Less than 100 | $38 | $66 | $105 |
| Private | Surface | 100 to 500 | $18 | $32 | $61 |
| Private | Surface | 500 to 1,000 | $6 | $11 | $23 |
| Private | Surface | 1,000 to 3,300 | $3 | $6 | $12 |
| Private | Surface | 3,300 to 10,000 | $2 | $4 | $8 |
| Private | Surface | 10,000 to 50,000 | $6 | $7 | $9 |
| Private | Surface | 50,000 to 100,000 | $4 | $5 | $7 |
| Private | Surface | 100,000 to 1,000,000 | $10 | $12 | $14 |
| Public | Ground | Less than 100 | $49 | $73 | $106 |
| Public | Ground | 100 to 500 | $19 | $28 | $43 |
| Public | Ground | 500 to 1,000 | $5 | $8 | $11 |
| Public | Ground | 1,000 to 3,300 | $3 | $5 | $7 |
| Public | Ground | 3,300 to 10,000 | $7 | $11 | $15 |
| Public | Ground | 10,000 to 50,000 | $8 | $8 | $9 |
| Public | Ground | 50,000 to 100,000 | $5 | $7 | $8 |
| Public | Ground | 100,000 to 1,000,000 | $7 | $8 | $10 |
| Public | Surface | Less than 100 | $54 | $95 | $155 |
| Public | Surface | 100 to 500 | $19 | $31 | $55 |
| Public | Surface | 500 to 1,000 | $5 | $9 | $18 |
| Public | Surface | 1,000 to 3,300 | $3 | $5 | $10 |
| Public | Surface | 3,300 to 10,000 | $7 | $11 | $19 |
| Public | Surface | 10,000 to 50,000 | $7 | $8 | $9 |
| Public | Surface | 50,000 to 100,000 | $5 | $6 | $6 |
| Public | Surface | 100,000 to 1,000,000 | $8 | $9 | $10 |

Abbreviations: CWS – Community Water System.

**Table C-34: Mean Annualized Cost per Household, Option 1a (PFOA and PFOS MCLs of 4.0 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | 5th Percentile | Mean | 95th Percentile |
|---|---|---|---|---|---|
| Private | Ground | Less than 100 | $41 | $59 | $82 |
| Private | Ground | 100 to 500 | $23 | $33 | $49 |
| Private | Ground | 500 to 1,000 | $7 | $10 | $15 |
| Private | Ground | 1,000 to 3,300 | $4 | $6 | $9 |
| Private | Ground | 3,300 to 10,000 | $3 | $5 | $7 |
| Private | Ground | 10,000 to 50,000 | $7 | $9 | $11 |
| Private | Ground | 50,000 to 100,000 | $4 | $7 | $10 |
| Private | Ground | 100,000 to 1,000,000 | $3 | $5 | $8 |
| Private | Surface | Less than 100 | $38 | $66 | $103 |
| Private | Surface | 100 to 500 | $18 | $32 | $61 |
| Private | Surface | 500 to 1,000 | $5 | $11 | $22 |
| Private | Surface | 1,000 to 3,300 | $3 | $6 | $12 |
| Private | Surface | 3,300 to 10,000 | $2 | $4 | $8 |
| Private | Surface | 10,000 to 50,000 | $5 | $7 | $9 |
| Private | Surface | 50,000 to 100,000 | $4 | $5 | $7 |
| Private | Surface | 100,000 to 1,000,000 | $9 | $11 | $13 |
| Public | Ground | Less than 100 | $49 | $72 | $106 |
| Public | Ground | 100 to 500 | $19 | $28 | $43 |
| Public | Ground | 500 to 1,000 | $5 | $8 | $11 |
| Public | Ground | 1,000 to 3,300 | $3 | $5 | $7 |
| Public | Ground | 3,300 to 10,000 | $7 | $11 | $15 |
| Public | Ground | 10,000 to 50,000 | $7 | $8 | $9 |
| Public | Ground | 50,000 to 100,000 | $5 | $6 | $8 |
| Public | Ground | 100,000 to 1,000,000 | $6 | $8 | $10 |
| Public | Surface | Less than 100 | $53 | $95 | $155 |
| Public | Surface | 100 to 500 | $19 | $30 | $54 |
| Public | Surface | 500 to 1,000 | $5 | $9 | $18 |
| Public | Surface | 1,000 to 3,300 | $3 | $5 | $10 |
| Public | Surface | 3,300 to 10,000 | $7 | $11 | $19 |
| Public | Surface | 10,000 to 50,000 | $7 | $8 | $9 |
| Public | Surface | 50,000 to 100,000 | $5 | $5 | $6 |
| Public | Surface | 100,000 to 1,000,000 | $7 | $8 | $9 |

Abbreviations: CWS – Community Water System.

**Table C-35: Mean Annualized Cost per Household, Option 1b (PFOA and PFOS MCLs of 5.0 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | 5th Percentile | Mean | 95th Percentile |
|---|---|---|---|---|---|
| Private | Ground | Less than 100 | $33 | $47 | $66 |
| Private | Ground | 100 to 500 | $18 | $26 | $38 |
| Private | Ground | 500 to 1,000 | $5 | $8 | $12 |
| Private | Ground | 1,000 to 3,300 | $3 | $5 | $7 |
| Private | Ground | 3,300 to 10,000 | $2 | $4 | $6 |
| Private | Ground | 10,000 to 50,000 | $6 | $7 | $8 |
| Private | Ground | 50,000 to 100,000 | $3 | $5 | $8 |
| Private | Ground | 100,000 to 1,000,000 | $2 | $4 | $6 |
| Private | Surface | Less than 100 | $30 | $53 | $87 |
| Private | Surface | 100 to 500 | $14 | $25 | $47 |
| Private | Surface | 500 to 1,000 | $4 | $9 | $18 |
| Private | Surface | 1,000 to 3,300 | $2 | $4 | $9 |
| Private | Surface | 3,300 to 10,000 | $1 | $3 | $6 |
| Private | Surface | 10,000 to 50,000 | $4 | $6 | $7 |
| Private | Surface | 50,000 to 100,000 | $3 | $4 | $6 |
| Private | Surface | 100,000 to 1,000,000 | $8 | $9 | $11 |
| Public | Ground | Less than 100 | $37 | $58 | $86 |
| Public | Ground | 100 to 500 | $15 | $22 | $35 |
| Public | Ground | 500 to 1,000 | $4 | $6 | $9 |
| Public | Ground | 1,000 to 3,300 | $3 | $4 | $6 |
| Public | Ground | 3,300 to 10,000 | $5 | $8 | $12 |
| Public | Ground | 10,000 to 50,000 | $6 | $7 | $7 |
| Public | Ground | 50,000 to 100,000 | $4 | $5 | $6 |
| Public | Ground | 100,000 to 1,000,000 | $5 | $7 | $8 |
| Public | Surface | Less than 100 | $44 | $77 | $130 |
| Public | Surface | 100 to 500 | $15 | $24 | $42 |
| Public | Surface | 500 to 1,000 | $4 | $7 | $15 |
| Public | Surface | 1,000 to 3,300 | $2 | $4 | $6 |
| Public | Surface | 3,300 to 10,000 | $5 | $9 | $14 |
| Public | Surface | 10,000 to 50,000 | $6 | $6 | $7 |
| Public | Surface | 50,000 to 100,000 | $3 | $4 | $5 |
| Public | Surface | 100,000 to 1,000,000 | $6 | $7 | $8 |

Abbreviations: CWS – Community Water System.

**Table C-36: Mean Annualized Cost per Household, Option 1c (PFOA and PFOS MCLs of 10.0 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | 5th Percentile | Mean | 95th Percentile |
|---|---|---|---|---|---|
| Private | Ground | Less than 100 | $18 | $24 | $33 |
| Private | Ground | 100 to 500 | $9 | $13 | $18 |
| Private | Ground | 500 to 1,000 | $2 | $4 | $6 |
| Private | Ground | 1,000 to 3,300 | $1 | $2 | $3 |
| Private | Ground | 3,300 to 10,000 | $1 | $2 | $3 |
| Private | Ground | 10,000 to 50,000 | $2 | $3 | $4 |
| Private | Ground | 50,000 to 100,000 | $1 | $2 | $3 |
| Private | Ground | 100,000 to 1,000,000 | $1 | $1 | $2 |
| Private | Surface | Less than 100 | $18 | $28 | $45 |
| Private | Surface | 100 to 500 | $8 | $13 | $18 |
| Private | Surface | 500 to 1,000 | $2 | $4 | $7 |
| Private | Surface | 1,000 to 3,300 | $1 | $2 | $3 |
| Private | Surface | 3,300 to 10,000 | $0 | $1 | $3 |
| Private | Surface | 10,000 to 50,000 | $2 | $2 | $3 |
| Private | Surface | 50,000 to 100,000 | $1 | $2 | $3 |
| Private | Surface | 100,000 to 1,000,000 | $4 | $5 | $6 |
| Public | Ground | Less than 100 | $20 | $30 | $44 |
| Public | Ground | 100 to 500 | $7 | $11 | $15 |
| Public | Ground | 500 to 1,000 | $2 | $3 | $4 |
| Public | Ground | 1,000 to 3,300 | $1 | $2 | $3 |
| Public | Ground | 3,300 to 10,000 | $2 | $4 | $5 |
| Public | Ground | 10,000 to 50,000 | $3 | $3 | $3 |
| Public | Ground | 50,000 to 100,000 | $2 | $2 | $3 |
| Public | Ground | 100,000 to 1,000,000 | $2 | $3 | $4 |
| Public | Surface | Less than 100 | $24 | $39 | $66 |
| Public | Surface | 100 to 500 | $8 | $12 | $17 |
| Public | Surface | 500 to 1,000 | $2 | $3 | $4 |
| Public | Surface | 1,000 to 3,300 | $1 | $2 | $2 |
| Public | Surface | 3,300 to 10,000 | $2 | $3 | $5 |
| Public | Surface | 10,000 to 50,000 | $2 | $3 | $3 |
| Public | Surface | 50,000 to 100,000 | $1 | $2 | $2 |
| Public | Surface | 100,000 to 1,000,000 | $2 | $3 | $3 |

Abbreviations: CWS – Community Water System.

## C.2.2 Household Costs for Community Water Systems that Treat or Change Water Source

**Table C-37: Mean Annualized Cost per Household in CWSs that Treat or Change Water Source, Proposed Option (PFOA and PFOS MCLs of 4.0 ppt and HI of 1.0) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | 5th Percentile | Mean | 95th Percentile |
|---|---|---|---|---|---|
| Private | Ground | Less than 100 | $677 | $677 | $677 |
| Private | Ground | 100 to 500 | $392 | $392 | $392 |
| Private | Ground | 500 to 1,000 | $123 | $123 | $123 |
| Private | Ground | 1,000 to 3,300 | $76 | $76 | $76 |
| Private | Ground | 3,300 to 10,000 | $52 | $52 | $52 |
| Private | Ground | 10,000 to 50,000 | $32 | $32 | $32 |
| Private | Ground | 50,000 to 100,000 | $25 | $25 | $25 |
| Private | Ground | 100,000 to 1,000,000 | $12 | $12 | $12 |
| Private | Surface | Less than 100 | $798 | $798 | $798 |
| Private | Surface | 100 to 500 | $389 | $389 | $389 |
| Private | Surface | 500 to 1,000 | $141 | $141 | $141 |
| Private | Surface | 1,000 to 3,300 | $76 | $76 | $76 |
| Private | Surface | 3,300 to 10,000 | $53 | $53 | $53 |
| Private | Surface | 10,000 to 50,000 | $33 | $33 | $33 |
| Private | Surface | 50,000 to 100,000 | $21 | $21 | $21 |
| Private | Surface | 100,000 to 1,000,000 | $25 | $25 | $25 |
| Public | Ground | Less than 100 | $835 | $835 | $835 |
| Public | Ground | 100 to 500 | $341 | $341 | $341 |
| Public | Ground | 500 to 1,000 | $94 | $94 | $94 |
| Public | Ground | 1,000 to 3,300 | $63 | $63 | $63 |
| Public | Ground | 3,300 to 10,000 | $118 | $118 | $118 |
| Public | Ground | 10,000 to 50,000 | $31 | $31 | $31 |
| Public | Ground | 50,000 to 100,000 | $23 | $23 | $23 |
| Public | Ground | 100,000 to 1,000,000 | $24 | $24 | $24 |
| Public | Surface | Less than 100 | $1,131 | $1,131 | $1,131 |
| Public | Surface | 100 to 500 | $392 | $392 | $392 |
| Public | Surface | 500 to 1,000 | $117 | $117 | $117 |
| Public | Surface | 1,000 to 3,300 | $73 | $73 | $73 |
| Public | Surface | 3,300 to 10,000 | $149 | $149 | $149 |
| Public | Surface | 10,000 to 50,000 | $39 | $39 | $39 |
| Public | Surface | 50,000 to 100,000 | $24 | $24 | $24 |
| Public | Surface | 100,000 to 1,000,000 | $30 | $30 | $30 |

Abbreviations: CWS – Community Water System.

**Table C-38: Mean Annualized Cost per Household in CWSs that Treat or Change Water Source, Option 1a (PFOA and PFOS MCLs of 4.0 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | 5th Percentile | Mean | 95th Percentile |
|---|---|---|---|---|---|
| Private | Ground | Less than 100 | $676 | $676 | $676 |
| Private | Ground | 100 to 500 | $391 | $391 | $391 |
| Private | Ground | 500 to 1,000 | $122 | $122 | $122 |
| Private | Ground | 1,000 to 3,300 | $76 | $76 | $76 |
| Private | Ground | 3,300 to 10,000 | $52 | $52 | $52 |
| Private | Ground | 10,000 to 50,000 | $30 | $30 | $30 |
| Private | Ground | 50,000 to 100,000 | $21 | $21 | $21 |
| Private | Ground | 100,000 to 1,000,000 | $12 | $12 | $12 |
| Private | Surface | Less than 100 | $797 | $797 | $797 |
| Private | Surface | 100 to 500 | $388 | $388 | $388 |
| Private | Surface | 500 to 1,000 | $140 | $140 | $140 |
| Private | Surface | 1,000 to 3,300 | $76 | $76 | $76 |
| Private | Surface | 3,300 to 10,000 | $53 | $53 | $53 |
| Private | Surface | 10,000 to 50,000 | $32 | $32 | $32 |
| Private | Surface | 50,000 to 100,000 | $20 | $20 | $20 |
| Private | Surface | 100,000 to 1,000,000 | $24 | $24 | $24 |
| Public | Ground | Less than 100 | $834 | $834 | $834 |
| Public | Ground | 100 to 500 | $341 | $341 | $341 |
| Public | Ground | 500 to 1,000 | $94 | $94 | $94 |
| Public | Ground | 1,000 to 3,300 | $62 | $62 | $62 |
| Public | Ground | 3,300 to 10,000 | $117 | $117 | $117 |
| Public | Ground | 10,000 to 50,000 | $30 | $30 | $30 |
| Public | Ground | 50,000 to 100,000 | $22 | $22 | $22 |
| Public | Ground | 100,000 to 1,000,000 | $23 | $23 | $23 |
| Public | Surface | Less than 100 | $1,129 | $1,129 | $1,129 |
| Public | Surface | 100 to 500 | $391 | $391 | $391 |
| Public | Surface | 500 to 1,000 | $117 | $117 | $117 |
| Public | Surface | 1,000 to 3,300 | $73 | $73 | $73 |
| Public | Surface | 3,300 to 10,000 | $148 | $148 | $148 |
| Public | Surface | 10,000 to 50,000 | $39 | $39 | $39 |
| Public | Surface | 50,000 to 100,000 | $24 | $24 | $24 |
| Public | Surface | 100,000 to 1,000,000 | $30 | $30 | $30 |

Abbreviations: CWS – Community Water System.

**Table C-39: Mean Annualized Cost per Household in CWSs that Treat or Change Water Source, Option 1b (PFOA and PFOS MCLs of 5.0 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | 5th Percentile | Mean | 95th Percentile |
|---|---|---|---|---|---|
| Private | Ground | Less than 100 | $674 | $674 | $674 |
| Private | Ground | 100 to 500 | $389 | $389 | $389 |
| Private | Ground | 500 to 1,000 | $121 | $121 | $121 |
| Private | Ground | 1,000 to 3,300 | $75 | $75 | $75 |
| Private | Ground | 3,300 to 10,000 | $51 | $51 | $51 |
| Private | Ground | 10,000 to 50,000 | $28 | $28 | $28 |
| Private | Ground | 50,000 to 100,000 | $19 | $19 | $19 |
| Private | Ground | 100,000 to 1,000,000 | $10 | $10 | $10 |
| Private | Surface | Less than 100 | $794 | $794 | $794 |
| Private | Surface | 100 to 500 | $387 | $387 | $387 |
| Private | Surface | 500 to 1,000 | $139 | $139 | $139 |
| Private | Surface | 1,000 to 3,300 | $76 | $76 | $76 |
| Private | Surface | 3,300 to 10,000 | $52 | $52 | $52 |
| Private | Surface | 10,000 to 50,000 | $31 | $31 | $31 |
| Private | Surface | 50,000 to 100,000 | $20 | $20 | $20 |
| Private | Surface | 100,000 to 1,000,000 | $22 | $22 | $22 |
| Public | Ground | Less than 100 | $830 | $830 | $830 |
| Public | Ground | 100 to 500 | $339 | $339 | $339 |
| Public | Ground | 500 to 1,000 | $94 | $94 | $94 |
| Public | Ground | 1,000 to 3,300 | $62 | $62 | $62 |
| Public | Ground | 3,300 to 10,000 | $114 | $114 | $114 |
| Public | Ground | 10,000 to 50,000 | $29 | $29 | $29 |
| Public | Ground | 50,000 to 100,000 | $21 | $21 | $21 |
| Public | Ground | 100,000 to 1,000,000 | $22 | $22 | $22 |
| Public | Surface | Less than 100 | $1,147 | $1,147 | $1,147 |
| Public | Surface | 100 to 500 | $387 | $387 | $387 |
| Public | Surface | 500 to 1,000 | $116 | $116 | $116 |
| Public | Surface | 1,000 to 3,300 | $73 | $73 | $73 |
| Public | Surface | 3,300 to 10,000 | $147 | $147 | $147 |
| Public | Surface | 10,000 to 50,000 | $37 | $37 | $37 |
| Public | Surface | 50,000 to 100,000 | $22 | $22 | $22 |
| Public | Surface | 100,000 to 1,000,000 | $28 | $28 | $28 |

Abbreviations: CWS – Community Water System.

**Table C-40: Mean Annualized Cost per Household in CWSs that Treat or Change Water Source, Option 1c (PFOA and PFOS MCLs of 10.0 ppt) (Commercial Cost of Capital, $2021)**

| Ownership | Source Water | Population Served Size Category | 5th Percentile | Mean | 95th Percentile |
|---|---|---|---|---|---|
| Private | Ground | Less than 100 | $661 | $661 | $661 |
| Private | Ground | 100 to 500 | $386 | $386 | $386 |
| Private | Ground | 500 to 1,000 | $119 | $119 | $119 |
| Private | Ground | 1,000 to 3,300 | $72 | $72 | $72 |
| Private | Ground | 3,300 to 10,000 | $47 | $47 | $47 |
| Private | Ground | 10,000 to 50,000 | $20 | $20 | $20 |
| Private | Ground | 50,000 to 100,000 | $10 | $10 | $10 |
| Private | Ground | 100,000 to 1,000,000 | $5 | $5 | $5 |
| Private | Surface | Less than 100 | $766 | $766 | $766 |
| Private | Surface | 100 to 500 | $381 | $381 | $381 |
| Private | Surface | 500 to 1,000 | $130 | $130 | $130 |
| Private | Surface | 1,000 to 3,300 | $72 | $72 | $72 |
| Private | Surface | 3,300 to 10,000 | $48 | $48 | $48 |
| Private | Surface | 10,000 to 50,000 | $24 | $24 | $24 |
| Private | Surface | 50,000 to 100,000 | $19 | $19 | $19 |
| Private | Surface | 100,000 to 1,000,000 | $16 | $16 | $16 |
| Public | Ground | Less than 100 | $823 | $823 | $823 |
| Public | Ground | 100 to 500 | $334 | $334 | $334 |
| Public | Ground | 500 to 1,000 | $91 | $91 | $91 |
| Public | Ground | 1,000 to 3,300 | $59 | $59 | $59 |
| Public | Ground | 3,300 to 10,000 | $107 | $107 | $107 |
| Public | Ground | 10,000 to 50,000 | $25 | $25 | $25 |
| Public | Ground | 50,000 to 100,000 | $19 | $19 | $19 |
| Public | Ground | 100,000 to 1,000,000 | $18 | $18 | $18 |
| Public | Surface | Less than 100 | $1,107 | $1,107 | $1,107 |
| Public | Surface | 100 to 500 | $381 | $381 | $381 |
| Public | Surface | 500 to 1,000 | $114 | $114 | $114 |
| Public | Surface | 1,000 to 3,300 | $72 | $72 | $72 |
| Public | Surface | 3,300 to 10,000 | $144 | $144 | $144 |
| Public | Surface | 10,000 to 50,000 | $34 | $34 | $34 |
| Public | Surface | 50,000 to 100,000 | $18 | $18 | $18 |
| Public | Surface | 100,000 to 1,000,000 | $24 | $24 | $24 |

Abbreviations: CWS – Community Water System.

# Appendix D. PFOA and PFOS Serum Concentration-Birth Weight Relationship

This appendix describes the methods used to estimate relationships between birth weight (BW) and serum per- and polyfluoroalkyl substances (PFAS) based on available studies. EPA used these relationships to estimate incremental changes in birth weight associated with reduced exposure to PFAS, namely perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS).

## D.1 Weight of Evidence of Birth Weight Effects

In the Health Effects Support Document (HESD) for PFOA (U.S. EPA, 2016b), EPA characterized the evidence for PFOA effects on birth weight as "plausible" based on human and animal study data, and four of the five endpoints used for derivation of an RfD were lowered fetal weights in rodents. The HESD for PFOS (U.S. EPA, 2016a) indicated that, despite considerable uncertainty, the available human data "suggest an association of prenatal serum PFOS with deficits in mean birth weight and with LBW [low birth weight]." The Agency for Toxic Substances and Disease Registry (ATSDR, 2018) listed reduced birth weight as one of the endpoints for which the available evidence "suggested" a relationship between human PFAS exposure and effect. Negri et al. (2017), considering both toxicological and epidemiological evidence, concluded that a causal relationship between PFOA and PFOS exposure and reduced birth weight was "likely". The most recent syntheses of evidence, EPA's *Toxicity Assessments and Proposed Maximum Contaminant Level Goals for PFOA and PFOS in Drinking Water*, found clear evidence of an association between PFOA and PFOS and birth weight in both toxicological and epidemiological studies (U.S. EPA, 2023a; U.S. EPA, 2023b). Based on these findings, EPA's Office of Ground Water and Drinking Water (OGWDW) derived exposure-response estimates for both compounds.

## D.2 Review of Available Meta-Analyses

EPA's OGWDW reviewed literature identified in the EPA Office of Water, Office of Science and Technology (OW/OST) literature reviews on the relationship between PFAS and birth weight to identify previous estimates of serum PFAS-birth weight relationships. Many epidemiological studies and several meta-analyses of existing studies have identified associations between perfluorinated compound exposure and indices of fetal growth (primarily reduced birth weight) (ATSDR, 2018; Johnson et al., 2014; Verner et al., 2015; Negri et al., 2017; Steenland et al., 2018; Dzierlenga, Crawford, et al., 2020). Most studies of the relationship between maternal serum PFOA and birth weight reported negative (i.e., inverse) relationships, while the evidence for PFOS was more variable, as described below. Note that EPA's review was based primarily on secondary sources; OGWDW did not conduct a systematic literature search or independent risk of bias (ROB) analyses for any identified systematic reviews and meta-analyses. Rather, EPA relied on previous authors who have analyzed the literature using different protocols related to literature relevance, study quality, and ROB. However, OW/OST has evaluated epidemiological literature for PFOA/PFOS as part of a systematic review to update the 2016 HESDs for PFOS and PFOA.

The five studies considered by EPA/OST for PFOA report the following slope estimates (in birth weight g per ng/mL serum): -4.9 (Sagiv et al., 2018), -20.7 (Govarts et al., 2016 The five studies considered by EPA/OST for PFOA report the following slope estimates (in birth weight g per ng/mL serum): -4.9 (Sagiv et al., 2018), -20.7 (Govarts et al., 2016), -41.0 (Wikström et al., 2019), -45.0 (Starling et al., 2017), and -45.2 (Chu et al., 2020). Compare these estimates to the selected slope estimate from Negri et al. (2017) of -12.8 g per ng/mL. The four studies considered by EPA/OST for PFOS report the following slope estimates (in birth weight g per ng/mL serum): -1.1 (Sagiv et al., 2018), -5.5 (Starling et al., 2017), -8.4 (Wikström et al., 2019), and -11.0 (Chu et al., 2020). Compare these estimates to the selected exposure-response function from Dzierlenga, Crawford, et al. (2020) of -3.2 g per ng/mL. Wikström et al., 2019), -45.0 (Starling et al., 2017), and -45.2 (Chu et al., 2020). Compare these estimates to the selected slope estimate from Negri et al. (2017) of -12.8 g per ng/mL. The four studies considered by EPA/OST for PFOS report the following slope estimates (in birth weight g per ng/mL serum): -1.1 (Sagiv et al., 2018), -5.5 (Starling et al., 2017), -8.4 (Wikström et al., 2019), and -11.0 (Chu et al., 2020). Compare these estimates to the selected exposure-response function from Dzierlenga, Crawford, et al. (2020) of -3.2 g per ng/mL.

EPA reviewed six of the identified meta-analyses of PFAS-low birth weight relationships in detail. One study, Monroy et al. (2008), presented regression results for body weight versus maternal PFOA and PFOS concentrations, but the reported slope factors[4] were not adjusted for other covariates. Because of this it was not pursued further. Two of the analyses (Johnson et al., 2014; Negri et al., 2017) used well-documented systematic review and ROB procedures to identify relevant studies in the literature. The three other studies did not document ROB protocols and study quality evaluation criteria (Verner et al., 2015; Dzierlenga, Crawford, et al., 2020; Steenland et al., 2018). However, as discussed below, there was extensive overlap in the data sets addressed in the various meta-analyses. Two of the meta-analyses included exposure-response modeling for both PFOS and PFOA (Verner et al., 2015; Negri et al., 2017), while one study addressed only PFOS (Dzierlenga, Crawford, et al., 2020) and the remaining two addressed only PFOA (Johnson et al., 2014; Steenland et al., 2018).

There was relative conformity in the publications evaluated and ultimately selected for use in the meta-analyses especially amongst the most recent ones, as later authors tended to include all the studies evaluated in previous studies, adding newer results that had become available (Table D-1):

- Johnson et al. (2014) conducted random effects meta-analysis based on data from nine studies (including 4,149 births) published between 2007 and 2012. The authors requested individual data on PFOA and covariates (variables other than PFAS exposure that may predict study outcomes) from all authors of the primary studies used in their studies. In cases where data were available, Johnson et al. (2014) used random effects methods to estimate covariate-adjusted linear regression coefficients and used these values as inputs to their meta-analysis. They found that including or excluding studies likely to have high ROB resulted in only small effects on estimated slope factors for PFOA-birth weight relationships.

[4] When referring to a "slope factor" in this document, EPA is discussing a measure of association between PFAS serum and BW.

- Verner et al. (2015) included data from all the studies identified by Johnson et al. (2014), with the exception of results from two studies: Fromme et al. (2010) and Kim et al. (2011). Verner et al. (2015) excluded these studies because they were based on 50 or fewer participants.

- Negri et al. (2017) included all the data sets identified by Johnson et al. (2014) plus five newer data sets (Table D-1). Negri et al. (2017) also included data from an older study (Monroy et al., 2008) that Johnson et al. (2014) omitted because "BW [birth weight] is not the dependent model variable."

- Steenland et al. (2018) based their analyses of PFOA-birth weight effects on results from the same studies in the Negri et al. (2017) meta-analysis (except for one study, Monroy et al. (2008) plus 10 additional recent epidemiological studies (Table D-1). However, Steenland et al. (2018) did not conduct a formal ROB evaluation to exclude these studies based on design or analysis flaws, as was done in prior meta-analyses by Johnson et al. (2014) and Negri et al. (2017).[5] Dzierlenga, Crawford, et al. (2020) included PFOS-birth weight data from all the studies identified by Verner et al. (2015), with the exception of results from Fei et al. (2007), and an additional 22 studies, many of which overlap with studies evaluated in Steenland et al. (2018). Although Dzierlenga, Crawford, et al. (2020) did not conduct formal ROB evaluations, the authors examined some study design aspects by characterizing studies with respect to certain characteristics that might influence results and evaluating those characteristics in meta-regression analyses.

[5] Steenland et al. (2018) noted that ROB analyses have advantages in identifying biases, but stated that "using a quantitative score of bias as a basis to exclude studies ultimately includes subjective components."

**Table D-1: Data Sources for PFOA/PFOS Meta-Analyses of Birth Weight Effects**

| Study | PFOA/PFOS-BW Relationship Studies Included in Meta-Analyses for Effects on BW | | | | | |
|---|---|---|---|---|---|---|
| | **Johnson et al. (2014)** | **Verner et al. (2015)** | **Negri et al. (2017)** | **Steenland et al. (2018)** | **Dzierlenga (2020)** | **EPA/OST Review (PFOA/PFOS) (2021)[a]** |
| Apelberg et al. (2007) | X | X* | X* | X | X | X |
| Fei et al. (2007) | X | X* | X* | X | | X |
| Hamm et al. (2010) | X | X* | X* | X | X | X |
| Washino et al. (2009) | X | X* | X* | X | X | X |
| Fromme et al. (2010) | X | | X | X | | |
| Kim et al. (2011) | X | | X | X | | |
| Whitworth et al. (2012) | X | X* | X* | X | X | X |
| Maisonet et al. (2012) | X | X* | X* | X | X | X |
| Chen et al. (2012) | X | X* | X* | X | X | X |
| Darrow et al. (2013) | | | X | X | X | X |
| Bach et al. (2016) | | | X* | X | X | X |
| Lenters et al. (2016) | | | X* | X | X | X |
| Monroy et al. (2008) | | | X* | | X | X |
| Robledo et al. (2015) [m, f] | | | X* | X | X | X |
| Wu et al. (2012) | | | | X | | X |
| Savitz et al. (2012) | | | | X** | | X |
| Callan et al. (2016) | | | | X | X | X |
| Govarts et al. (2016) | | | | | X | X[d] |
| Kwon et al. (2016) | | | | | X | X |
| Lee et al. (2016) | | | | X | X | X |
| Wang et al. (2016) | | | | X | X | X |
| Minatoya et al. (2017) | | | | X | | X |
| Shi et al. (2017) | | | | X | X | X |
| Manzano-Salgado et al. (2017) | | | | X | X | X |
| Chen et al. (2017) | | | | X | X | X |
| Starling et al. (2017) | | | | X | X | X[d] |
| Sagiv et al. (2018) | | | | X | X | X[d] |
| Ashley-Martin et al. (2017) | | | | | X | X |
| Lauritzen et al. (2017)[m, f] | | | | | X | X |
| M. Li et al. (2017) | | | | | X | X |
| Lind et al. (2017)[m, f] | | | | | X | X |
| Valvi et al. (2017) | | | | | X | X |
| Cao et al. (2018) | | | | | X | X |

**Table D-1: Data Sources for PFOA/PFOS Meta-Analyses of Birth Weight Effects**

| Study | PFOA/PFOS-BW Relationship Studies Included in Meta-Analyses for Effects on BW | | | | | |
|---|---|---|---|---|---|---|
| | **Johnson et al. (2014)** | **Verner et al. (2015)** | **Negri et al. (2017)** | **Steenland et al. (2018)** | **Dzierlenga (2020)** | **EPA/OST Review (PFOA/PFOS) (2021)[a]** |
| Meng et al. (2018) | | | | | X | X |
| Marks et al. (2019) | | | | | X | X |
| Workman et al. (2019) | | | | | | X |
| Xu et al. (2019) | | | | | | X |
| Bell et al. (2018) | | | | | | X |
| Louis et al. (2018) | | | | | | X |
| Gao et al. (2019) | | | | | | X |
| Chu et al. (2020) | | | | | | X[d] |
| Hjermitslev et al. (2020) | | | | | | X |
| Kashino et al. (2020) | | | | | | X |
| Wikström et al. (2020) | | | | | | X[d] |

Abbreviations: BW – birth weight; EPA/OST– U.S. Environmental Protection Agency Office of Science and Technology; PFOA – perfluorooctanoic acid; PFOS – perfluorooctane sulfonic acid.

Notes:

[a]EPA/OST evaluation of study quality reflected in blue (high confidence), green (medium confidence) or pink (low confidence) cell shading. EPA/OST literature review focused on literature published between 2000 and 2020. Studies in this field reflect the studies EPA reviewed to select those that were used for modeling.

* Indicates a data set used for PFOS, as well as PFOA meta-analysis.

** Indicates a data set included only in sensitivity analysis.

[m, f] Indicates results presented only stratified by sex or location [e.g., Lauritzen et al. (2017)].

[d] Indicates studies used by EPA/OST for derivation of point of departures (PODs).

The authors used different techniques to evaluate sources of variability in the meta-analyses. As expected, random effects models generated results with lower heterogeneity (as measured by the proportion of between-study variance in the data sets) than fixed effects models. Each of the meta-analyses reported sensitivity analyses, stratified analyses, or leave-one-out results (influence analyses) to explore the relative contributions of individual or groups of studies to the quantitative pooled estimates of PFOA and PFOS effects on birth weight.

Johnson et al. (2014) reported a pooled beta across nine included studies of -18.9 g (95%CI: -29.8, -7.9) for PFOA per each 1 ng/mL. Johnson et al. (2014) used well-documented meta-analytical methods: random effects models with inverse variance weighting. In addition, Johnson et al. (2014) conducted analyses omitting several small studies with relatively high ROB, as well as one that included a large study (Savitz et al., 2012) that modeled maternal serum levels based on historical exposures, rather than measured exposures. Johnson et al. (2014) found that inclusion or exclusion of high-ROB studies and studies based on modeled serum levels resulted in only a small effect on the estimated slope factor for PFOA-birth weight relationships (Johnson et al. (2014) reported a pooled beta across nine included studies of -18.9 g (95%CI: -29.8, -7.9) for PFOA per each 1 ng/mL. Johnson et al. (2014) used well-documented meta-analytical methods: random effects models with inverse variance weighting. In addition, Johnson et al. (2014) conducted analyses omitting several small studies with relatively high ROB, as well as one that included a large study (Savitz et al., 2012) that modeled maternal serum levels based on historical exposures, rather than measured exposures. Johnson et al. (2014) found that inclusion or exclusion of high-ROB studies and studies based on modeled serum levels resulted in only a small effect on the estimated slope factor for PFOA-birth weight relationships (Figure D-1).[6]

Verner et al. (2015) reported a pooled beta across seven included studies of –5.00 g (95% CI: -8.92, -1.09) for PFOS and -14.72 g (95% CI: -21.66, -7.78) for PFOA each per each 1 ng/mL. In addition, Verner et al. (2015) also investigated the potential impact of changing glomerular filtration rate (GFR), an index of kidney function, on PFAS-birth weight relationships. They based their analysis on the fact that maternal GFR and blood volume are known to change across the three trimesters of pregnancy in such a way that the assumed independent effect of GFR on birth weight, coupled with changes in PFAS excretion rates, could account for part of the birth weight reduction found in the epidemiological studies of PFAS exposure. In addition to a standard meta-analysis, they simulated PFOA/PFOS levels in a hypothetical population, using a pharmacologically based pharmacokinetic (PBPK) model, and evaluated the impact of changes in GFR on PFAS-associated changes in birth weight across trimesters. The results of the conventional meta-analysis for the overall effects of PFAS on birth weight were similar to those derived by Johnson et al. (2014) (Figure D-1). Verner et al. (2015) concluded, however, that a portion of the observed association may be attributable to confounding by GFR , with the effect of GFR increasing across trimesters. This suggested that studies which have not controlled for GFR might overestimate the impact of prenatal exposure to PFAS on fetal growth.

[6] Note that this finding may not apply to all meta-analyses, especially if they did not use the exact studies and same ROB methods as those employed in Johnson et al. (2014).

All of the simulations employed different assumptions related to variability in PFOA/PFOS levels and the strength of GFR impacts on birth weight. The simulated estimated relationships between PFOA/PFOS and birth weight remained negative for all sample collection times, except for the initial sampling time (at conception).

Negri et al. (2017) reported a pooled beta across eight included studies of -0.92 g (95% CI: -3.4, 1.6) for PFOS and twelve included studies of -12.8 g (95% CI: -23.2, -2.4) for PFOA each per each 1 ng/mL. Negri et al. (2017) conducted random effects meta-analyses based on 14 studies. In addition to the main analysis, Negri et al. (2017) conducted a sensitivity analysis related to model form (fixed versus random effects), degree of adjustment (full, defined as adjustment for infant sex, gestational age, maternal age, pre-pregnancy body mass index, education, parity, and smoking, versus partial, which includes only some of these covariates), and location of populations (America, Asia, and Europe). They also ran separate analyses for studies in which the time of blood sampling varied (1st and 2nd trimester, 3rd trimester, and cord blood), to further investigate the potential impacts of time of blood sampling as a proxy for changes in GFR. Negri et al. (2017) found that the degree of adjustment had relatively little effect on the magnitude of estimated slopes for PFOA and PFOS. The pooled PFOA/PFOS effect estimates (i.e., beta coefficients) for studies in which sampling occurred late in pregnancy reported birth weight decreases larger magnitude than for those where sampling occurred in the first two trimesters, but the results were quite uncertain due to the small numbers of studies with late-term sampling.

Steenland et al. (2018) reported a pooled beta across twenty-four included studies of -10.5 g (95% CI: -16.7, -4.4) for PFOA per each 1 ng/mL. Steenland et al. (2018) conducted a random effects meta-analysis based on 24 studies. In addition, they estimated PFOA slope factors separately for studies of maternal and cord blood and for studies where PFOA serum levels were measured in the first trimester versus any time later in pregnancy (Figure D-1). The slope factor from the main analysis was significantly negative and similar in magnitude to that derived by Negri et al. (2017). Coefficients for maternal blood were slightly smaller in magnitude than in studies where cord blood was sampled, but still negative. The coefficient for the nine data sets where blood PFOA was measured during the first trimester was small in magnitude (-3.3 g per ng/mL), but not significant.

The most recent meta-analysis from Dzierlenga, Crawford, et al. (2020) reported a pooled beta across thirty-two included studies of -3.2 g (95% confidence interval: -5.1, -1.3) for PFOS per each 1 ng/mL. The study conducted a random effects meta-analysis based on 32 results from 29 studies. The authors of the analysis estimated a slope of −3.2 g birth weight per ng PFOS/mL (95% confidence interval: −5.1, −1.3) with significant moderate heterogeneity (I2 = 58%). Sensitivity analyses suggested that the results are sensitive to timing of blood samples. Among those with blood measurements before or early in pregnancy, however, PFOS was inversely associated with birth weight (−1.35, 95% confidence interval: −2.33, −0.37), and for the later pregnancy group, the association was −7.17 (95% confidence interval: −10.93, −3.41).

| Study | Estimate | Mean (g per ng/mL) | Lower CI | Upper CI | Number of Studies | Heterogeneity I2 | p-value |
|---|---|---|---|---|---|---|---|
| Johnson et al. (2014) | PFOA - Main | -18.9 | -29.8 | -7.9 | 9 | 38 | 0.12 |
| | PFOA - High ROB study included | -15.4 | -26.5 | -4.3 | 10 | 72 | 0 |
| Verner et al. (2015) | PFOA - Main | -14.7 | -21.7 | -7.8 | 7 | - | >0.05 |
| | PFOA - Adjusted for GFR | -7.9 | -9.4 | -6.4 | 7 | - | - |
| Negri et al. (2017) | PFOA - Main | -12.8 | -23.2 | -2.4 | 12 | 52.9 | 0.016 |
| | PFOA - First/second trimester | -10.5 | -23.6 | 2.6 | 6 | - | - |
| | PFOA - Third trimester | -20 | -52.1 | 12.1 | 2 | - | - |
| | PFOA - Cord Blood | -35.3 | -101 | 30.7 | 4 | - | - |
| Steenland et al. (2018) | PFOA - Main | -10.5 | -16.7 | -4.4 | 24 | 63 | <0.0001 |
| | PFOA - First Trimester | -3.3 | -9.6 | 3 | 7 | 68 | <0.0001 |
| | PFOA - Second/Third trimester | -17.8 | -25 | -10.6 | 17 | 29 | 0.13 |
| | PFOA - Include Savitz (2012) | -1 | -2.4 | 0.4 | 25 | - | - |
| Verner et al. (2015) | PFOS - Main | -5 | -8.9 | -1.09 | 7 | - | <0.05 |
| | PFOS - Adjusted for GFR | -1.5 | -1.8 | -1.1 | 7 | - | - |
| Negri et al. (2017) | PFOS - Main | -0.92 | -3.4 | 1.6 | 8 | 74.3 | <0.001 |
| | PFOS - First/second trimester | 0.6 | -1.4 | 2.5 | 5 | - | - |
| | PFOS - Third trimester | -4 | -16.3 | 8.2 | 2 | - | - |
| | PFOS - Cord Blood | -11.3 | -17.4 | -5.2 | 1 | - | - |
| Dzierlenga et al. (2020) | PFOS - Main | -3.2 | -5.1 | -1.3 | 32 | 58 | 0 |
| | PFOS - Before or early in pregnancy | -1.35 | -2.33 | -0.37 | 10 | 5 | 0.4 |
| | PFOS - Later pregnancy | -7.17 | -10.39 | -3.41 | 22 | 55 | 0.001 |

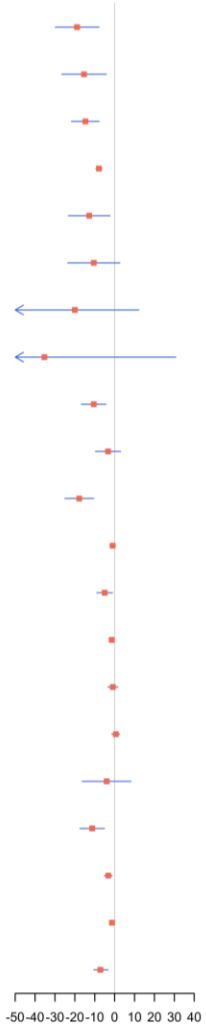



**Figure D-1: Results and Confidence Limits from PFOA, PFOS Meta-Analyses: Changes in BW (grams) per Change in Serum PFAS Levels (ng/mL)**

## D.3 Exposure-Response Functions Based on Epidemiological Studies

EPA selected the exposure-response result for PFOA from the main analysis reported by Steenland et al. (2018) for use in the risk assessment from exposure to PFOA and benefits analysis of reducing PFOA in PWS even though this study did not use a systematic ROB analysis of the studies included in the meta-analysis. Although Negri et al. (2017) employed a systematic ROB analysis for the studies included in the meta-analysis and showed moderate heterogeneity among studies ($I^2$ = 38%)[7], EPA did not select it because the study is less recent and includes fewer studies than Steenland et al. (2018). The Agency selected the main (random effects) analysis from Steenland et al. (2018) because it is the most recent meta-analysis on PFOA-birth weight and included the largest number of studies. The pooled beta estimate for PFOA effects on birth weight in Steenland et al. (2018) is -10.5 g (95% confidence interval: -16.7; -4.4) birth weight per ng serum PFOA/mL based on 24. The Agency also uses the 95% confidence limits of -16.7 and -4.4 g birth weight per ng PFOA/mL as lower and upper bound slope estimates for a sensitivity analysis. The pooled mean estimate (g birth weight per ng PFOA/mL) for all studies is in the midrange of the results for the early, middle, and late blood sampling results (Figure D-1).

EPA selected the exposure-response result for PFOS from the most recent meta-analysis of 32 observations from 29 publications reported by Dzierlenga, Crawford, et al. (2020) for use in the risk assessment from exposure to PFOS and benefits of reducing PFOS in PWS.[8] The Agency chose the main analysis from Dzierlenga, Crawford, et al. (2020) because it considered the largest number of recent studies, the heterogeneity among studies was moderate ($I^2$ = 58%), and sensitivity analyses suggested an inverse relationship with birth weight. Additionally, sensitivity analyses suggested that the results were not particularly sensitive to timing of blood samples, consistent with the early pregnancy subgroup analysis result. Dzierlenga, Crawford, et al. (2020) also examined study quality aspects by characterizing studies with respect to certain characteristics[9] that might influence results and examining those in meta-regression analyses.

[7] $I^2$ represents the proportion of total variance in the estimated model due to inter-study variation; a value of 38 percent is considered "moderate", suggesting that the studies are not seriously inhomogeneous and that a pooled model (meta-analysis) is appropriate.

[8] Although Negri et al. (2017) also estimated an exposure-response slope for PFOS effects on BW based on eight studies, the analysis includes a slope factor derived from the Maisonet et al. (2012) study that was given as (positive) 5.77 (95% confidence limits = 2.01, 9.53). However, in the original Maisonet et al. (2012) study, the relationship between maternal PFOS and female infant BW was reported as being negative; it appears that there was a transcription error in the Negri et al. (2017) analysis.[8] An sensitivity analysis from Negri et al. (2017) that excluded the Maisonet et al. (2012) study resulted in a pooled estimate of -2.0 g BW per ng/mL PFOS, which is similar in magnitude to the estimate reported by Dzierlenga, Crawford, et al. (2020). Also, although the estimated slope factor for PFOS effects from Verner et al. (2015), based on seven studies, included the slope factor from Maisonet et al. (2012) as (negative) -5.77 g BW per ng PFOS/mL (95% confidence limits –9.53, -2.01), Dzierlenga, Crawford, et al. (2020) includes a larger number of studies, many of which were published more recently than those considered in Negri et al. (2017) and Verner et al. (2015) (32 results from 29 studies conducted from 2007 to 2019, compared to seven and eight studies considered in Negri et al., 2017 and Verner et al., 2015, respectively, that were conducted from 2007 to 2016).

[9] For example, the quality of evidence was characterized as low for the BW-PFOS associations when the timing of blood draw was before or early in pregnancy.

EPA reanalyzed the pooled estimate from this study after determining that the original Dzierlenga, Crawford, et al. (2020) pooled estimate included a duplicated estimate from Chen et al. (2017). EPA reran the analysis excluding the duplicated estimate to obtain a slope of −3.0 g birth weight per ng PFOS/mL with the same heterogeneity ($I^2$ = 58%) as the prior estimate (p-value for heterogeneity <0.001).

# Appendix E. Effects of Reduced Birth Weight on Infant Mortality

This appendix summarizes EPA's analysis of the relationship between infant mortality and birth weight. This relationship is fundamental in estimating benefits from changes in birth weight among infants whose mothers were exposed to PFOA or PFOS during or prior to pregnancy. EPA developed a cross-sectional model to quantify this relationship based on the most recent 2016/17 and 2017/18 Centers for Disease Control (CDC) Period Cohort Linked Birth-Infant Death Data files.

## E.1 Birth Weight-Mortality Relationship

Low birth weight (LBW), defined as weight at birth <2,500 grams, is recognized as a significant predictor of infant mortality (McCormick, 1985; World Health Organization, 2014).
The majority of infants born with LBW are premature, but other gestational factors such as maternal hypertensive disorders and anemia can result in full-term infants who are born at LBW (Joyce et al., 2012). Many of the top 10 causes of infant mortality are factors associated with preterm birth, including LBW (Jacob, 2016). Advances in U.S. prenatal and neonatal care and successes in public health initiatives, such as those designed to decrease maternal smoking, have increased LBW survival rates and reduced the prevalence of LBW infants (Callaghan et al., 2017; Singh et al., 2019). To quantify potential mortality impacts from changes in infant birth weight resulting from changes in maternal PFOA and PFOS exposure via drinking water, robust data supporting a relationship between incremental changes in infant birth weight and mortality risk are needed.

A number of epidemiological studies in the U.S. have reported relationships between birth weight and mortality. However, most of these studies evaluate relationships between infant mortality and birth weight above or below various birth weight thresholds (e.g., McIntire et al., 1999; Lau et al., 2013). EPA identified only two studies that show statistically significant relationships between incremental changes in birth weight and infant mortality that can be leveraged for PFOS/PFOA health impact modeling: Ma et al. (2010) and Almond et al. (2005).

Ma et al. (2010) used 2001 National Center for Health Statistics/National Vital Statistics System (NCHS/NVSS) linked birth/infant death data for singleton and multiple birth infants among subpopulations defined by sex and race/ethnicity to estimate a regression model assessing the associations between 14 key birth outcome measures, including birth weight, and infant mortality. They found notable variation in the relationship between birth weight and mortality across race/ethnicity subpopulations, with odds ratios for best-fit birth weight-mortality models ranging from 0.8-1 per 100 gram (g) birth weight change. Almond et al. (2005) used 1989-1991 NCHS linked birth/infant death data for multiple birth infants to analyze relationships between birth weight and infant mortality within birth weight ranges. For their preferred model, they reported coefficients in deaths per 1,000 births per 1 g increase in birth weight that range from -0.420 to -0.002.

However, the data used in these studies (Almond et al., 2005 and Ma et al., 2010) are old (1989-1991 and 2001, respectively). Given the significant decline in infant mortality over the last 30 years (discussed in Section E.2 below), and changes in other maternal and birth characteristics

that are likely to influence infant mortality (e.g., average maternal age and rates of maternal smoking), the birth weight-mortality relationship estimates from Almond et al. (2005) and Ma et al. (2010) are likely to overestimate benefits of birth weight changes. Moreover, Almond et al. (2005) focused on multiple birth infants to analyze relationships between birth weight and infant mortality.

LBW is determined by two main processes: duration of gestation and rate of fetal growth (Institute of Medicine, 1985; Quah, 2016). Thus, infants can be LBW because they are born preterm or are born small for gestational age, which is a proxy for intrauterine growth retardation. Researchers have found that birth weight and gestational age are closely associated but not perfectly correlated (e.g., Kiely et al., 1994; Mathews, 2013). A study by Almond et al. (2005) found that gestational age is an important determinant of birth weight as it explains over half of the overall variance in birth weight among a pooled sample of twins. Moreover, multiple studies suggest that, when available, both birth weight and gestational age should be included when predicting infant mortality odds (Almond et al., 2005; Ma et al., 2010; Ray et al., 2017). Cole et al. (2010) developed a logistic regression model showing that gestational age and birth weight z-score[10] were the strongest predictors of survival among very preterm infants. Ma et al. (2010) predicted infant mortality by combining birth weight and gestational age variables to distinguish between the two major causes of LBW. Ray et al. (2017) used modified Poisson regression to show that singleton infants who are born preterm and small for gestational age have a higher risk of neonatal death than infants born preterm alone.

The CDC indicated that the mortality rate among multiples is very high for reasons that are often unrelated to birth weight and recommended that a model based on singletons may provide a more representative relationship between birth weight and infant mortality (Communication with Horon, 2020). Studies of birth weight-specific infant mortality among singletons and multiples suggest that, due to differences in intrauterine growth restriction, prematurity rates, and zygosity, analyses that examine perinatal outcomes should be stratified by plurality (Russell et al., 2003; Cooke, 2010). Furthermore, singleton infants represent the majority of U.S. births (96% of infants born in 2016 and 2017). Following CDC's recommendations, EPA developed cross-sectional models to estimate a relationship between birth weight at four distinct gestational age categories and infant mortality based on the most recently available 2016-2018 NCHS/NVSS data and focusing on singleton infants. To identify variation in the birth weight-mortality relationship across race/ethnicity subpopulations, EPA estimated separate relationships for non-Hispanic Black, non-Hispanic White, and Hispanic subpopulations.

In developing the singleton models, EPA used similar variables and partitioning techniques as detailed in Ma et al. (2010). Specifically, EPA developed separate models for different race/ethnicity categories and interacted birth weight with gestational age. Ma et al. (2010) found that key predictors of infant mortality include birth weight, Apgar score,[11] and gestational age. Ma et al. (2010) developed multivariate logistic regression models for gender- and race-specific subpopulations[12] to assess associations of various combinations of birth weight, gestational age,

[10] Z-scores describe how far from the mean a given data point is.

[11] Apgar score refers to a metric indicating the health of a newborn. The score, which ranges from 0 to 10, is based on skin color, heart rate, reflexes, muscle tone, and breathing rate/effort.

[12] Separate models were fit for non-Hispanic white girls, non-Hispanic white boys, non-Hispanic black girls, non-Hispanic black boys, Mexican girls, and Mexican boys.

fetal growth rate, and Apgar scores with four mortality outcomes (infant mortality, early neonatal, late neonatal, and post-neonatal mortality). In addition to these covariates, Ma et al. (2010) automatically selected covariates such as parental characteristics (e.g., maternal age and education), maternal risk factors (e.g., smoking), and child characteristics (e.g., birth order) based on predictive power. Ma et al. (2010) showed that the baseline rates of each birth outcome differ by both race/ethnicity and postnatal period. Model results indicated that birth weight is a stronger predictor of infant mortality among the non-Hispanic Black subpopulation compared to the non-Hispanic White and Hispanic subpopulations.

## E.2 Basis for Updated Birth Weight-Mortality Relationship

There has been a notable decline in U.S. infant mortality rates during the two decades since analyses reported in Ma et al. (2010) and Almond et al. (2005). In the last 30 years, overall infant mortality rates have declined steadily (ICF, 2020).[13] The infant mortality rate in 2018 was 5.67 per 1,000 live births, while the infant mortality rate in 1991 was 8.6 per 1,000 live births. Except for infants born with birth weight lower than 500 grams, for whom mortality rates have not changed considerably, mortality rates for infants with birth weight greater than 500 grams are decreasing and converging on a low rate.[14]

Given a decline in infant mortality in the birth weight categories lower than 1,500 g, a unit change in birth weight is likely to produce less of an impact on the probability of mortality in 2016-2018 compared to 1989-1991 (the years evaluated in Almond et al., 2005) or 2001 (the year evaluated in Ma et al., 2010). Despite recent declines in U.S. infant mortality, disparities in infant mortality experience continue to exist across race/ethnicity subpopulations (Osterman et al., 2015). Recent research indicates that infant mortality is consistently highest among Black infants (both Hispanic and non-Hispanic), while non-Hispanic White and Hispanic White infants have the lowest mortality rates (Rice et al., 2017; Rowley et al., 2012; Collins Jr et al., 2009).

In addition to the decline in infant mortality in LBW categories, other maternal and birth characteristics that are likely to influence infant mortality have evolved over time. Almond et al. (2005) provided sample means for birth and maternal characteristics for singletons based on the 1989 NCHS/NVSS Linked Natality-Mortality Detail file. EPA provides similar statistics for singletons from the 2016-2018 NCHS/NVSS Period/Cohort Linked Birth-Infant Death Data Files[15] that demonstrate how birth and mortality characteristics have changed over time. Table E-1 shows a subset of the 1989 sample means among singletons born to non-Hispanic Black and non-Hispanic White mothers from Almond et al. (2005) Table II and the same statistics derived from the 2016-2018 data. The comparison shows that teen pregnancy rates, pregnancy among mothers with less than a high school education, and maternal smoking during pregnancy have decreased since 1989. While mean and median birth weight has decreased

[13] CDC publishes National Vital Statistics Reports that summarize mortality trends over time (e.g. Kochanek et al., 2019) and provides detailed tables of infant mortality trends by race and age at death in annual *Health, United States* reports (National Center for Health Statistics, 2019).

[14] EPA assembled summary statistics on infant mortality by BW category provided in the documentation for 1983-2018 Linked Infant Birth-Death Detail Files. These files are published on the online data portal by NCHS/NVSS: https://www.cdc.gov/nchs/data_access/vitalstatsonline.htm

[15] The 2016-2018 NCHS/NVSS Period/Cohort Linked Birth-Infant Death Data Files represent two separate datasets. The 2016/2017 data includes infants born in 2016 and follows their mortality experience for one year (through the end of 2017). The 2017/2018 data includes infants born in 2017 and follows their mortality experience through the end of 2018.

slightly for singleton infants, the 1-year infant mortality rate has decreased by about 42%. Possible explanations for this trend may include advancements in prenatal and postnatal care (e.g., advances in infection control practices and the use of intubation to reduce infant lung injury; Callaghan et al., 2017) as well as positive effects of public health education (e.g., reduced smoking during pregnancy; Singh et al., 2019).

In addition to a decreasing 1-year mortality rate, Table E-1 shows a decrease in the fraction of infants with congenital anomalies and a decrease in median gestational age. The decrease in gestational age is supported by analysis from Donahue et al. (2010), who found that gestational age among full-term singletons in the United States decreased by more than two days from 1990-2005.

**Table E-1: Comparison of Sample Means for Singletons between the 1989 Natality-Mortality Detail File and the combined 2016-2018 Period/Cohort Linked Birth-Infant Death Data Files**

| Variable | Sample Means[a,b,c] | |
|---|---|---|
| | 1989 | 2016-2018 (% Change) |
| Sample size | 2,655,977 | 4,212,764 |
| **Infant deaths (per 1000 live births)** | | |
| Within 1 year of birth (infant mortality) | 8.46 | 4.94 (-42%) |
| Within 28 days (neonatal) | 4.99 | 2.94 (-41%) |
| 28 days to 1 year (postneonatal) | 3.49 | 2.00 (-43%) |
| **Fraction of dead with birth weight < 2500 g** | | |
| Infant mortality | 0.570 | 0.592 (+4%) |
| Within 24-hour mortality | 0.890 | 0.285 (-68%) |
| Neonatal mortality | 0.760 | 0.463 (-39%) |
| Postneonatal mortality | 0.300 | 0.129 (-57%) |
| **Infant birth weight (g)** | | |
| Mean | 3,369 | 3,313 (-2%) |
| Median | 3,402 | 3,345 (-2%) |
| 5th percentile | 2,410 | 2,390 (-1%) |
| Fraction LBW (<2500 g) | 0.061 | 0.065 (+7%) |
| **Gestational age (in weeks)** | | |
| Mean | 39 | 39 (0%) |
| Median | 40 | 39 (-3%) |
| 5th percentile | 35 | 35 (0%) |
| **Characteristics of birth** | | |
| 5-minute Apgar score (0–10) | 8.97 | 8.79 (-2%) |
| Fraction male | 0.512 | 0.512 (0%) |
| Fraction congenital anomaly[d] | 0.019 | 0.001 (-93%) |
| **Mother's demographic characteristics** | | |
| Fraction Black | 0.195 | 0.193 (-1%) |

**Table E-1: Comparison of Sample Means for Singletons between the 1989 Natality-Mortality Detail File and the combined 2016-2018 Period/Cohort Linked Birth-Infant Death Data Files**

| Variable | Sample Means[a,b,c] | |
|---|---|---|
| | 1989 | 2016-2018 (% Change) |
| Fraction high school dropout | 0.184 | 0.085 (-54%) |
| Fraction college graduate | 0.187 | 0.451 (+141%) |
| Age | 26.3 | 28.6 (+9%) |
| Fraction teenager | 0.129 | 0.049 (-62%) |
| Fraction 30+ | 0.289 | 0.444 (+54%) |
| Fraction married | 0.736 | 0.595 (-19%) |
| **Mother's risk factors** | | |
| Number of prenatal visits | 11.2 | 11.5 (+3%) |
| Fraction smoke during pregnancy | 0.212 | 0.100 (-53%) |

Abbreviations BW – birth weight; LBW – low birth weight.
Notes:
[a]The data are restricted to non-Hispanic Black and White mothers born in the United States, as reported in Almond et al. (2005) Table II.
[b]The 1989 data summary in Almond et al. (2005) included anemia of mother, assisted ventilation (<30 minutes) and assisted ventilation (>= 30 minutes), which are not included in the 2016-2018 NCHS/NVSS dataset. The 2016-2018 NCHS/NVSS dataset does include assisted ventilation and assisted ventilation (6 hours), but these variables are not necessarily comparable to the assisted ventilation variables included in the 1989 NCHS/NVSS dataset. Similarly, 1989 data summary in Almond et al. (2005) included "pregnancy-associated hypertension" which is further split up into "gestational hypertension" and "hypertension eclampsia" in the 2016-2018 NCHS/NVSS dataset. Due to differences in variable definitions among the data, EPA excludes hypertension.
[c]Records with "Unknown" or "Not Stated" values not included in the 2016-2018 summary.
[d]Congenital anomalies among the 1989 and 2016-2018 data are not directly comparable due to differences in the congenital anomalies included in this metric between the datasets. The 1989 dataset includes the following congenital anomalies: Anencephalus, spina bifida/meningocele, hydrocephalus, other central nervous system anomalies, heart malformations, other circulatory/respiratory anomalies, rectal atresia/stenosis, trachea-esophageal fistula/esophageal atresia, omphalocele/gastroschisis, other gastrointestinal anomalies, malformed genitalia, renal agenesis, other urogenital anomalies, cleft lip/palate, polydactyly, club foot, diaphragmatic hernia, other musculoskeletal/integumental anomalies, down's syndrome, other chromosomal anomalies, and other congenital anomalies. The 2016-2018 dataset includes the following congenital anomalies: anencephaly, meningomyelocele/spina bifida, cyanotic congenital heart disease, congenital diaphragmatic hernia, omphalocele, gastroschisis.

The remainder of this appendix summarizes the development of regression models implemented using newer data.

# E.3 Development of the Analytical Dataset

## *E.3.1 Data Sources*

This analysis relies on Period/Cohort Linked Birth-Infant Death Data Files published by NCHS/NVSS from the 2017 period/2016 cohort and the 2018 period/2017 cohort.[16] Each dataset includes files linking all infant deaths during the period and cohort years to information from corresponding birth certificates and separate files consisting of all births occurring during the period. The data include all infants under 1 year of age in the U.S. or its territories (Centers for

[16] https://www.cdc.gov/nchs/data_access/vitalstatsonline.htm

Disease Control and Prevention, 2017f). This analysis excludes multiple birth infants. In addition to infant birth and mortality information, the data include details on maternal characteristics (e.g., mother's education, marital status, and age category), maternal risk factors (e.g., smoking status), and pregnancy and birth characteristics (e.g., gestational age, infant birth weight, presence of congenital anomalies, and birth order).

## *E.3.2 Dataset Development*

EPA combined the infant birth and death files using the SAS code examples from the user guides accompanying the datasets to create user-created cohort files, which follow the birth cohorts for an entire year to ascertain their mortality experience (Centers for Disease Control and Prevention, 2017f, 2018). At this stage, EPA also selected variables of interest for the regression analysis. These variables include maternal demographic and socioeconomic characteristics, maternal risk and risk mitigation factors, and infant birth characteristics. EPA included several variables used in Ma et al. (2010) as well as additional variables to augment the set of covariates included in the regression analyses. Variable selection was informed by literature on the leading causes of infant mortality (e.g., Ahrens et al., 2017; Mishra et al., 2018; Centers for Disease Control and Prevention, 2020a, 2020b; Ely et al., 2020).

## *E.3.3 Identification of Infant Mortality Risk Factors*

To identify infant mortality risk factors for inclusion in the regression analyses, EPA relied on multiple data sources, including key risk factors identified by the CDC and prior studies of the relationship between infant mortality and various maternal and birth characteristics. Although risks to infant mortality include conditions related to infant and maternal health, demographic and socioeconomic characteristics also contribute to infant mortality outcomes. Based on the studies EPA reviewed, infant mortality risk factors generally fall within three general categories described below:

- **Birth Characteristics:**
    - *Birth Weight and Gestational Age:* The CDC identifies preterm birth and LBW as leading causes of infant death in the United States (Ely et al., 2020). The majority of infant deaths in 2018 occurred among infants born preterm (gestational age < 37 weeks; Ely et al., 2020). Previous studies of the relationship between birth weight and infant mortality identify birth weight and gestational age as important predictors of infant mortality (e.g., Almond et al., 2005; Ma et al., 2010).
    - *Other Infant Birth Characteristics:* Studies of leading causes of infant mortality suggest that birth order plays a significant role in infant mortality outcomes. Higher birth order is linked to risk of injury and may be indicative of other socioeconomic factors (Ahrens et al., 2017; Mishra et al., 2018). Another substantive predictor of infant mortality is five-minute Apgar score (Almond et al., 2005; Ma et al., 2010). Birth defects, such as the presence of congenital anomalies, also contribute to infant mortality (Ely et al., 2020).

- **Maternal Risk and Risk Mitigation Factors:** Many causes of infant death are exacerbated by tobacco use, substance use, and stress (Centers for Disease Control and Prevention, 2020a). CDC guidance suggests that regular prenatal care visits[17] lead to detection of infant mortality risk factors (e.g., hypertension).
- **Maternal Demographic and Socioeconomic Characteristics:** Infant birth outcomes are influenced by demographic and socioeconomic factors such as maternal race/ethnicity, age, education, and marital status (Ma et al., 2010). Infant mortality rates vary for mothers of different ages, with the lowest mortality rates among mothers age 30-34 and highest mortality rates among teen mothers and mothers over 40 in 2018 (Ely et al., 2020). Singh et al. (2019) found that the risk of 1-year mortality in 2016 was 3.7 times greater for mothers with less than 12 years of education than for mothers with 16 or more years of education. Marital status also influences the risk of infant mortality—studies show that the risk of infant mortality increases when one parent is absent (Ngui et al., 2015; Alio et al., 2011). In 2018, the non-Hispanic Black subpopulation had the highest infant mortality rate at 10.8 deaths per 1,000 live births, while Hispanic and non-Hispanic White subpopulations experienced much lower rates of infant mortality (4.9 and 4.6 deaths per 1,000 births, respectively; Ely et al., 2020).

While maternal risk variables such as hypertension, diabetes, and infection lead to premature birth, LBW, and reduced motor function, birth-related factors such as Apgar score, birth weight, and gestational age likely account for these risks (Backes et al., 2011; Centers for Disease Control and Prevention, 2016c; M. Li et al., 2017). Given that birth weight impacts on infant mortality are the focus of our analysis, selected covariates do not include maternal risk factors, such as maternal hypertension, diabetes, and infection, whose mortality influence pathway is primarily through birth weight, gestational age, and Apgar score.[18]

## E.4 Development of Variables

The dependent variable (BIRTH_MORT) is a binary variable indicating whether the infant died within one year of birth. Covariates included in the regression analyses fall under three categories:

- Birth characteristics (denoted with BIRTH prefix)
- Maternal risk and risk mitigation factors (denoted with MRF prefix)
- Maternal demographic and socioeconomic characteristics (denoted with MDEM prefix)

Table E-2 provides a detailed description of all variables included in the singleton regression analysis and the corresponding variables from the NCHS/NVSS data used to develop the variables. EPA estimated different regression models for three race/ethnicity subpopulations: Non-Hispanic Black, non-Hispanic White, and Hispanic. Infants whose mothers fall into these race/ethnicity subpopulations are identified using the MRACEHISP variable from the NCHS/NVSS data.

[17] While prenatal care visits fall under the maternal risk and risk mitigation factors category, it could also be considered a maternal demographic and socioeconomic characteristic indicative of access to care.

[18] Pearson correlation tests indicated significant relationships between these variables (p-values < 5%).

The focus of EPA's analysis is the relationship between birth weight and infant mortality. However, Ma et al. (2010) noted that the practice of specifying regression models that assume that every 1-gram increase in birth weight has the same effect on infant mortality outcome (regardless of gestational age or LBW status of the infant) has been challenged.[19] Following researchers who emphasize the importance of examining birth outcomes from the perspective of combined birth weight and gestational age variables (Solis et al., 2000; Powers et al., 2006), Ma et al. (2010) found that models with birth weight-gestational age interaction variables had higher predictive power than models that only used birth weight and gestational age separately. Following best practices from the health economic literature (e.g., Solis et al., 2000; Powers et al., 2006; Ma et al., 2010), EPA interacted continuous birth weight with four gestational age category indicator variables (extremely pre-term, very pre-term, moderately pre-term, term as defined by the World Health Organization, 2018) to account for the heterogeneity in birth weight impact with respect to the gestational age of the infant. EPA expected that birth weight effects would be highest for extremely pre-term infants and lowest for full-term infants.

In addition to the set of birth weight-gestational age category interaction variables, EPA added variables for other infant birth characteristics (birth order, birth year, sex, Apgar score, congenital anomaly indicator), maternal risk and risk mitigation factors (smoker status, categorized number of prenatal care visits), and maternal demographic and socioeconomic characteristics (education, age, marital status). These variables control for additional factors beyond birth weight and gestational age that contribute to the probability of infant mortality.[20] EPA included categorized Apgar score variables based on analysis from Ma et al. (2010), who found that Apgar scores, separated into low (0-3), medium (4-6), and high (7-10) categories, were the strongest predictor of infant mortality among race/ethnicity-specific models. Further, the 2016-2018 NCHS/NVSS data show that Apgar scores are significantly higher for non-Hispanic White infants than for non-Hispanic Black infants. Ma et al. (2010) also found that the inclusion Apgar scores in models predicting infant mortality significantly improved goodness of fit. EPA also included a variable indicating whether the infant was born in 2016 or 2017 (BIRTH_YR_2016) as a control to determine whether there are any significant differences between the 2016 and 2017 NCHS/NVSS datasets that are not readily captured by other covariates.

**Table E-2: Variables Used in Singleton Mortality Regression Analysis**

| Variable | Variable Type | Variable Definition | Basis for Variable in NCHS/NVSS Dataset |
|---|---|---|---|
| **Dependent Variable** | | | |
| BIRTH_MORT | Binary | Binary variable indicating whether the infant died within one year of birth | DOD_YY |

[19] Ma et al. (2010) indicate that birth weight effects vary according to the position on the distribution of birth weight (they characterize the birth weight-mortality distribution as a reverse J-shaped distribution).

[20] EPA also explored adding additional maternal risk factor variables, including maternal hypertension, diabetes, and infection, based on CDC's identified infant mortality risk factors (see Section E.3.1.2). However, the inclusion of these variables in our models produced counterintuitive results and they were eliminated from the covariate set.

**Table E-2: Variables Used in Singleton Mortality Regression Analysis**

| Variable | Variable Type | Variable Definition | Basis for Variable in NCHS/NVSS Dataset |
|---|---|---|---|
| **Covariates** | | | |
| **Birth Weight and GA** | | | |
| BIRTH_BW_I_EXT_PRETERM | Discrete/ Continuous | Continuous BW (in grams) if gestational age is <=28 weeks (extremely preterm), 0 if otherwise | BRTHWGT, COMBGEST |
| BIRTH_BW_I_VER_PRETERM | Discrete/ Continuous | Continuous BW (in grams) if gestational age is >28 weeks and <=32 weeks (very preterm), 0 if otherwise | BRTHWGT, COMBGEST |
| BIRTH_BW_I_MOD_PRETERM | Discrete/ Continuous | BW (in grams) if gestational age is >32 weeks and <=37 weeks (moderately preterm), 0 if otherwise | BRTHWGT, COMBGEST |
| BIRTH_BW_I_TERM | Discrete/ Continuous | Continuous BW (in grams) if gestational age is >37 weeks (term), 0 if otherwise | BRTHWGT, COMBGEST |
| **Other Infant Birth Characteristics**[a] | | | |
| BIRTH_MALE | Binary | Binary variable indicating that the infant is male | SEX |
| BIRTH_CONANOM | Binary | Binary variable indicating that the infant experienced one or more of the following congenital anomalies: anencephaly, meningomyelocele/spina bifida, cyanotic congenital heart disease, congenital diaphragmatic hernia, omphalocele, gastroschisis | CA_ANEN, CA_MNSB, CA_CCHD, CA_CDH, CA_OMPH, CA_GAST |
| BIRTH_APGAR_0_3 | Binary | Binary variable indicating that the five-minute Apgar score is between 0 and 3. Five-minute Apgar score indicates the health of a newborn based on skin color, heart rate, reflexes, muscle tone, and breathing rate/effort. | APGAR5 |
| BIRTH_APGAR_4_6 | Binary | Binary variable indicating that the five-minute Apgar score is between 4 and 6. Five-minute Apgar score indicates the health of a newborn based on skin color, heart rate, reflexes, muscle tone, and breathing rate/effort. | APGAR5 |
| BIRTH_YR_2016 | Binary | Binary variable indicating whether the infant was born in 2016. If 0, the infant was born in 2017. | N/A; based on CDC dataset |
| BIRTH_BOCat1 | Binary | Binary variable indicating that the infant has one sibling (second-born) | LBO_REC |
| BIRTH_BOCat2 | Binary | Binary variable indicating that the infant has two or more siblings (third- or later-born) | LBO_REC |

**Table E-2: Variables Used in Singleton Mortality Regression Analysis**

| Variable | Variable Type | Variable Definition | Basis for Variable in NCHS/NVSS Dataset |
|---|---|---|---|
| **Maternal Risk and Risk Mitigation Factors[b,d]** | | | |
| MRF_NOPRECARE | Binary | Binary variable indicating that the mother had no prenatal care visits | PREVIS |
| MRF_1_9_PRECARE | Binary | Binary variable indicating that the mother had 1 to 9 prenatal care visits | PREVIS |
| MRF_16_ORMORE_PRECARE | Binary | Binary variable indicating that the mother had 16 or more prenatal care visits | PREVIS |
| MRF_SMOKE | Binary | Binary variable indicating that, if maternal smoking status is known, the mother was a smoker | CIG_REC |
| **Maternal Demographic and Socioeconomic Characteristics[c,d]** | | | |
| MDEM_I_NOHS | Binary | Binary variable indicating that the mother's education is known and that the mother did not graduate high school or obtain a GED | MEDUC |
| MDEM_I_COLLEGEPLUS | Binary | Binary variable indicating that the mother's education is known and that the mother attended college or higher education | MEDUC |
| MDEM_AGE_TEEN | Binary | Binary variable indicating that the mother's age is <20 | MAGER |
| MDEM_AGE_ADV_35_40 | Binary | Binary variable indicating that the mother's age is >34 and <= 40 | MAGER |
| MDEM_AGE_ADV_40plus | Binary | Binary variable indicating that the mother's age is >40 | MAGER |
| MDEM_I_MARRIED | Binary | Binary variable indicating that the mother's marital status is known and that the mother is married | DMAR |

Abbreviations: BW – birth weight; NCHS – National Center for Health Statistics; NVSS – National Vital Statistics System.
Notes:
[a]Reference categories for binary variables in the other infant birth characteristics category include female infants, infants who did not experience a congenital anomaly, infants with Apgar scores from 7 to 10, infants born in 2017, and infants who have no siblings.
[b]Reference categories for binary variables in the maternal risk and risk mitigation factors category include mothers who had 10 to 15 prenatal care visits and mothers who do not smoke.
[c]Reference categories for binary variables in the maternal demographic and socioeconomic characteristics category include mothers who went to high school but who did not attend any college, mothers aged 25 to 34, and mothers whose marital status is unknown or single.
[d]The maternal age (MDEM_AGE) variables are split into three categories to show effects associated with teen mothers, mother's aged 35 to 40, and mothers over the age of 40 with respect to the reference case of mother's aged 20 to 34. This is to reflect differences in infant mortality rates associated with different maternal age groups. In 2018, the CDC indicated that total mortality rates were highest for infants of mothers under age 20, while infants of mother's age 30-34 had the lowest mortality rates (Ely et al., 2020). Infant mortality rates increased among infants born to older mothers, especially those over age 40 (Ely et al., 2020).

Of the available singleton data, 0.8% had no race information. These records are excluded from consideration. For regression modeling, records with incomplete or missing data (specified as "Unknown" or "Not Stated" in the raw NCHS/NVSS data) for any of the covariates listed in

Table E-2 were excluded from the analytical dataset. Records with incomplete or missing covariate information account for 8.5% of the non-Hispanic Black records, 6.5% of the non-Hispanic White records, and 7.0% of the Hispanic records (for a combined total of 7.0% of all records). EPA did not attempt to fill in these data gaps using imputations or assumptions, because records with missing data constituted less than 10% of all records. The resulting sample sizes are: 981,212 for the non-Hispanic Black subpopulation, 3,644,499 for the non-Hispanic White subpopulation, 1,646,713 for the Hispanic subpopulation.

## E.5 Summary Statistics

Table E-3 presents maternal and infant characteristics of the study population, including number and proportion of the sample associated with different age ranges, gestation weeks, races and ethnicities, educational attainment, marital status, number of prenatal care visits, and whether or not the mother smoked during pregnancy. Sample statistics indicate that the majority of mothers are between ages 20 and 33, have full-term pregnancies, are non-Hispanic White, graduated high school, had more than ten prenatal care visits, and did not smoke during pregnancy.

**Table E-3: Maternal and Infant Characteristics of the Study Population**

| Description | N | Proportion (%) |
|---|---|---|
| **Age** | | |
| <20 years | 343,784 | 5.48 |
| 20-33 years | 4,606,124 | 73.43 |
| 34-39 years | 1,138,646 | 18.15 |
| 40+ years | 183,870 | 2.93 |
| **Gestation Week** | | |
| <=28 | 43,654 | 0.70 |
| >28 and <=32 | 80,408 | 1.28 |
| >32 and <=37 | 106,8585 | 17.04 |
| >37 | 5,079,777 | 80.99 |
| **Race/Ethnicity** | | |
| Non-Hispanic White | 3,644,499 | 58.10 |
| Non-Hispanic Black | 981,212 | 15.64 |
| Hispanic | 1,646,713 | 26.25 |
| **Education** | | |
| No high school or GED | 871,274 | 13.89 |
| Graduated high school | 2,963,900 | 47.25 |
| Attended college[a] | 2,437,250 | 38.86 |
| **Marital Status** | | |
| Married | 3,504,095 | 55.87 |
| Unmarried | 2,768,329 | 44.13 |
| **Number of Prenatal Care Visits[b]** | | |
| None | 100,231 | 1.60 |
| 1-9 | 1,519,825 | 24.23 |
| 10-15 | 4,066,046 | 64.82 |
| 16+ | 586,322 | 9.35 |
| **Smoking During Pregnancy** | | |
| Yes | 455,758 | 7.27 |
| No | 5,816,666 | 92.73 |
| **Apgar Score** | | |
| Apgar score between 0 and 3 | 32,518 | 0.52 |
| Apgar score between 4 and 6 | 82,762 | 1.32 |
| Apgar score between 7 and 10 | 6,157,144 | 98.16 |

Notes:
[a] Refers to mothers who obtained an associate's degree or more. Mothers who obtained some college credit but not a degree are categorized in the "Graduated high school" field.
[b] Number of prenatal care visits in the study population range from 0 to 98.

## E.6 Estimation Methods

EPA fit the logistic regression model using Stata 15.1 (StataCorp, 2013a). The model is fit to three different race/ethnicity singleton subpopulations (non-Hispanic Black, non-Hispanic White, and Hispanic)[21] as there are known disparities in the prevalence of LBW by race and ethnicity (Collins Jr et al., 2009; Rice et al., 2017; Rowley et al., 2012; Ratnasiri et al., 2018). Coefficients of non-linear regression models with a binary outcome indicate direction of the effect that covariates have on outcome probability. That is, negative coefficients indicate that the probability of mortality decreases as the covariate increases, while positive coefficients indicate that the probability of mortality increases as the covariate increases.

In this analysis, EPA reported the results of regression modeling using both odds ratios[22] and marginal effects. While the odds ratio is an effect metric commonly reported in epidemiological research, the impact of a marginal change in the covariate on the probability of the outcome (i.e., the marginal effect) is easier to interpret. The magnitude of this marginal effect depends on all estimated coefficients of the model as well as specific values of all the covariates included in the model. When estimating marginal effects, EPA used actual observed values for the covariates rather than using covariate means.[23] For non-birth weight-gestational age variables, EPA estimated marginal effects based on covariate values from all observations included in the models. For birth weight-gestational age variables, EPA estimated marginal effects based on covariate values from the subset of observations falling within each gestational age category (see N columns for sample size used for each marginal effect calculation).[24]

Section E.5 presents EPA's preferred models. These models had the best fit and offered most intuitive results, in terms of variable sign and significance. EPA estimated additional model specifications prior to the final models, including models with the infant birth weight categories used in Almond et al. (2005) and a separate continuous gestational age variable, models with different specifications for maternal age, and models with different combinations of maternal risk factors. EPA does not believe that exclusion of maternal risk factor variables creates omitted variable bias, given that their effects are accounted for using more direct newborn health state variables such as Apgar score. The additional model specifications that EPA tested prior to determining the final model form resulted in marginal effects estimates that were inconsistent with scientifically expected directionality of their effects.

[21] EPA did not develop a model for other race subpopulations because doing so for each individual race/ethnicity or combinations of all "other" races would suffer from effects of low sample size (i.e., odds ratios and marginal effects that lack significance).

22 The natural exponent of the logistic regression coefficient is a ratio of odds of the outcome when the value of the predictor variable is changed by a certain amount relative to the odds of the outcome using the baseline value of the predictor variable. The odds are the ratio of the probability that the outcome of interest occurs to the probability that the outcome of interest does not occur

[23] EPA calculated marginal effects using the "margins, dydx(*)" command in Stata (StataCorp, 2013b). EPA used the default *as observed* option.

[24] EPA estimated BW-gestational age category-specific marginal effects using subsets of data that contain infants with BW in the corresponding gestational age category to account for correlations between gestational age and other variables included in the model. For example, infants in the preterm gestational age categories have lower Apgar score on average.

# E.7 Results and Discussion

## *E.7.1 Mortality Regression Models*

Overall, the sign and significance of covariates in the regression models align with expectations based on previous literature. Table E-4 presents odds ratios and marginal effects (in terms of deaths per 1,000 births) for the non-Hispanic Black, non-Hispanic White, and Hispanic models. A marginal effect estimate represents the effect of a 1-unit change in a given covariate on the infant mortality rate per 1,000 births. Pseudo $R^2$ values are approximately 40%, which is in line with previous literature.[25] The Agency notes that the estimated models are potentially subject to omitted variable bias from other sources, such as income level, but EPA does not have adequate information to evaluate the impacts of this bias on the marginal birth weight-mortality relationship. The following subsections discuss the effects of regression model covariates on the probability of infant mortality.

### *E.7.1.1 Birth Characteristics*

The results for the birth weight-gestational age variables match literature-based expectations. In all three models, the coefficients and marginal effects for birth weight among different gestational age categories are negative and statistically significant ($p<0.01$). Negative marginal effect values for the birth weight- gestational age categories indicate that a 1-gram birth weight increase is associated with decreases in the infant mortality rate per 1,000 births, ranging from -0.20 (extremely preterm) to -0.005 (term) for the non-Hispanic Black population, from -0.12 to -0.002 for the non-Hispanic White population, and from -0.15 to -0.002 for the Hispanic population. The magnitude of birth weight marginal effect is lower in gestational age categories corresponding to longer gestation, indicating that the probability of mortality decreases as both gestational age and birth weight increase.

Determining the magnitude of the mortality probability decrease is straightforward using marginal effects. For example, using marginal effects from the non-Hispanic Black model, for extremely preterm infants a 100 g birth weight increase would translate to 20 fewer infant deaths per 1000 births in this gestational age category or a 2% decrease in the probability of mortality within one year of birth.[26] The same birth weight increase at a higher gestational age would still decrease mortality risk but to a lesser extent. A 100 g birth weight increase for a non-Hispanic Black infant in the moderately pre-term category would translate to only 1 fewer infant death per 1000 births or a 0.1% decrease in the probability of mortality within one year of birth.

Figure E-1 shows variability of marginal effects for birth weight among different gestational age categories across race/ethnicity subpopulations, with larger magnitudes estimated for the non-Hispanic Black subpopulation compared to those estimated for the non-Hispanic White subpopulation or Hispanic subpopulation, indicating that LBW increases the probability of mortality within the first year more so among non-Hispanic Black infants than among non-Hispanic White and Hispanic infants. This pattern is more pronounced for the extremely preterm infants and very preterm infants.

[25] Ma et al. (2010) reported a Pseudo $R^2$ value of approximately 27%.

[26] The implied decrease in probability of death is calculated as (100 g)*(marginal effect in terms of deaths per 1,000 births per g)/(1,000 births) and multiplied by 100 to obtain a percentage: [(100 g)*(-0.19440/1000)]*(100) = -1.94%.

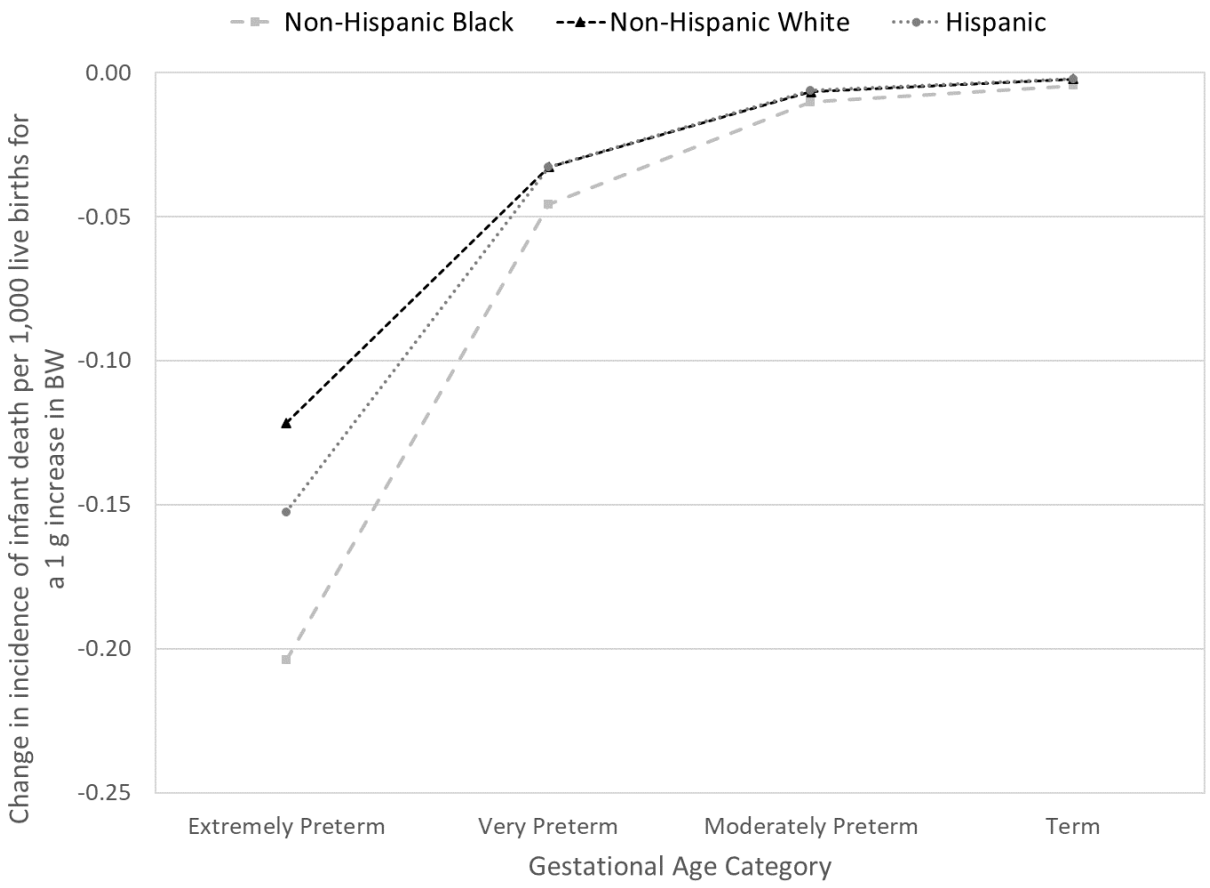



**Figure E-1: Comparison of Change in Incidence of Infant Death per 1 g Increase in Birth Weight by Gestational Age Category and Race/Ethnicity (Deaths per 1,000 Births)**

Notes: Gestational age categories defined as extremely preterm (<=28 weeks), very preterm (>28 weeks and <=32 weeks), moderately preterm (>32 weeks and <=37 weeks), and term (>37 weeks). Related covariates in the regression model include BIRTH_BW_I_EXT_PRETERM, BIRTH_BW_I_VER_PRETERM, BIRTH_BW_I_MOD_PRETERM, BIRTH_BW_I_TERM. Data based on the 2016/17 and 2017/18 CDC Period Cohort Linked Birth-Infant Death Data Files obtained from NCHS/NVSS.

For the birth order variables (BIRTH_BOCat1, BIRTH_BOCat2), the reference category is first-born children. Across all three models, odds ratios and marginal effects for these variables are large and significant ($p<0.01$). Effects for BIRTH_BOCat2 are larger than for BIRTH_BOCat1, which is consistent with research indicating that second- or later-born infants have increasingly higher probabilities of mortality compared to first-borns (Mishra et al., 2018; Ahrens et al., 2017). Coefficients and marginal effects for variables indicating male infants (BIRTH_MALE) and infants with congenital anomalies (BIRTH_CONANOM) indicate that the probability of mortality increases when the infants are male and when infants experience at least one congenital anomaly. The effect of calendar birth year was not statistically different from zero at a 5% significance level.

Marginal effects for the birth characteristics variables also vary by race/ethnicity. For example, the marginal effects for the BIRTH_BOCat1 variables indicate that, relative to first-born infants, the infant mortality rate per 1,000 births increases by 1.13, 0.90, and 0.59 for second-born non-Hispanic Black, non-Hispanic White, and Hispanic infants, respectively.[27] Compared to the non-Hispanic White and Hispanic subpopulations, 5-minute Apgar score has a stronger association with infant mortality among the non-Hispanic Black subpopulations. The marginal effects for the BIRTH_CONANOM variables indicate that, relative to infants without any congenital anomalies, the infant mortality rate per 1,000 births increases by 18.82, 8.99, and 9.66 for non-Hispanic Black, non-Hispanic White, and Hispanic infants with congenital anomalies, respectively.

### *E.7.1.2 Maternal Risk and Risk Mitigation Factors*

The probability of infant mortality varies among certain maternal risk or risk mitigation factors. The probability of infant mortality increases for mothers who smoke or mothers without a high school diploma. Maternal smoking increases the infant mortality rate per 1,000 births by 1.34, 0.47, and 0.57 for non-Hispanic Black, non-Hispanic White, and Hispanic infants, respectively. The probability of infant mortality decreases for mothers with a college education or higher. Relative to mothers with a high school education, the infant mortality rate per 1,000 births decreases by 1.29, 0.82, and 0.27 for non-Hispanic Black, non-Hispanic White, and Hispanic infants born to mothers with a college education or higher, respectively. Relative to the 10 to 15 prenatal care visit category, which is most common in the data (See Table E-3), the probability of infant mortality increases with zero visits, 1 to 9 visits, and 16 or higher visits. Marginal effects indicate that having no prenatal care visits increases the infant mortality rate per 1,000 births by 3.03, 0.95, and 0.91 for non-Hispanic Black, non-Hispanic White, and Hispanic infants, respectively.

### *E.7.1.3 Maternal Demographic and Socioeconomic Characteristics*

Results for the maternal demographic and socioeconomic characteristic variables vary by race/ethnicity and largely match EPA's expectations. The education variables serve as proxies for socioeconomic status, and results among all three models indicate that, relative to mothers with a high school diploma, the probability of infant mortality increases for mothers without a high school diploma and decreases for mothers with a college education or higher. Maternal education effects on infant mortality probability vary by race/ethnicity. For example, relative to mothers with a high school education, the infant mortality rate per 1,000 births decreases by 1.29, 0.82, and 0.27 for non-Hispanic Black, non-Hispanic White, and Hispanic infants born to mothers with a college education or higher, respectively.

The maternal age variables align with available infant mortality statistics showing the highest infant mortality rates when mothers are under age 20 and elevated rates when mothers are over 40 (Ely et al., 2020). Compared to mothers aged 20 to 34 years, probability of infant mortality is higher for mothers younger than 20 years, lower for mothers aged 35 to 40 years, and higher for mothers older than 40 years. Relative to infants born to mothers aged 20 to 34 years, infants born to mothers younger than 20 years experience 0.79, 0.61, and 0.68 additional infant deaths per

[27] The implied decrease in probability of death is calculated as (marginal effect in terms of deaths per 1,000 births)/(1,000 births) and multiplied by 100 to obtain a percentage. Example calculation using the marginal effects for BIRTH_BOCat1 from the non-Hispanic Black model: (1.19100/1000)*(100) = 0.119%.

1,000 births in non-Hispanic Black, non-Hispanic White, and Hispanic subpopulations, respectively. The decreased death probability for mothers aged 35 to 40 might be capturing effects of the financial stability of mothers in this age group.

Negative and significant coefficients and marginal effects among all models for the mother's marital status variable, MDEM_I_MARRIED, indicate that the risk of infant mortality decreases among infants with two parents, consistent with studies indicating that paternal involvement reduces the probability of infant mortality (Ngui et al., 2015; Alio et al., 2011). Compared to infants born to mothers who are not married or mothers whose marital status is unknown, infants born to married mothers experience 0.35, 0.51, and 0.30 fewer deaths per 1,000 births for non-Hispanic Black, non-Hispanic White, and Hispanic subpopulations, respectively.

**Table E-4: Odds Ratios and Marginal Effects for the Non-Hispanic Black, Non-Hispanic White, and Hispanic Mortality Regression Models**

| Variable | Odds Ratios (95% CI)[a,b] | | | Marginal Effects (Deaths per 1,000 Births (95% CI)[a,c] | | |
|---|---|---|---|---|---|---|
| | Black | White | Hispanic | Black | White | Hispanic |
| BIRTH_BW_I_EXT_PRETERM | 0.99817 (0.99802, 0.99832) | 0.99866 (0.99855, 0.99878) | 0.99835 (0.99817, 0.99853) | -0.20400 (-0.21910, -0.18890) | -0.12160 (-0.13080, -0.11240) | -0.15260 (-0.1677, -0.13750) |
| BIRTH_BW_I_VER_PRETERM | 0.99816 (0.99804, 0.99827) | 0.9985 (0.99842, 0.99858) | 0.99846 (0.99835, 0.99858) | -0.04580 (-0.04820, -0.04340) | -0.03290 (-0.03430, -0.03140) | -0.03290 (-0.0351, -0.03070) |
| BIRTH_BW_I_MOD_PRETERM | 0.99852 (0.99846, 0.99857) | 0.99867 (0.99863, 0.99872) | 0.99856 (0.99849, 0.99862) | -0.01030 (-0.01080, -0.00985) | -0.00677 (-0.00702, -0.00652) | -0.00626 (-0.00659, -0.00592) |
| BIRTH_BW_I_TERM | 0.99856 (0.99851, 0.99860) | 0.99865 (0.99861, 0.99868) | 0.99849 (0.99844, 0.99855) | -0.00453 (-0.00472, -0.00434) | -0.00228 (-0.00236, -0.00221) | -0.00219 (-0.00229, -0.00208) |
| BIRTH_BOCat1 | 1.20078 (1.12406, 1.28272) | 1.37498 (1.30875, 1.44458) | 1.23256 (1.14005, 1.33256) | 1.13170 (0.72263, 1.54080) | 0.90320 (0.76267, 1.04370) | 0.59091 (0.37013, 0.81170) |
| BIRTH_BOCat2 | 1.43158 (1.34271, 1.52634) | 1.66176 (1.57927, 1.74859) | 1.36704 (1.26426, 1.47818) | 2.21920 (1.81950, 2.61890) | 1.44050 (1.29450, 1.58650) | 0.88360 (0.66192, 1.10530) |
| BIRTH_APGAR_0_3 | 19.89802 (18.35772, 21.56734) | 43.36705 (40.67038, 46.24253) | 45.87636 (41.39996, 50.83677) | 18.49800 (17.92800, 19.06800) | 10.69200 (10.46100, 10.92300) | 10.81300 (10.466, 11.15900) |
| BIRTH_APGAR_4_6 | 3.8631 (3.54196, 4.21336) | 5.92239 (5.54208, 6.32880) | 6.86084 (6.16310, 7.63750) | 8.35950 (7.79370, 8.92530) | 5.04500 (4.83850, 5.25150) | 5.44270 (5.1129, 5.7726) |
| BIRTH_MALE | 1.28589 (1.22265, 1.35240) | 1.29367 (1.24351, 1.34583) | 1.19405 (1.12581, 1.26643) | 1.55530 (1.24280, 1.86790) | 0.73028 (0.61753, 0.84304) | 0.50123 (0.33447, 0.66798) |
| BIRTH_CONANOM | 20.95317 (16.73647, 26.23226) | 23.81106 (21.33609, 26.57338) | 30.45195 (25.31381, 36.63302) | 18.81800 (17.39300, 20.24300) | 8.99150 (8.65400, 9.32900) | 9.65470 (9.096, 10.21300) |
| BIRTH_YR_2016 | 1.04910 (0.99784, 1.10298) | 1.01725 (0.97816, 1.05791) | 0.97538 (0.91965, 1.03449) | 0.29646 (-0.01339, 0.60632) | 0.04852 (-0.06265, 0.15968) | -0.07045 (-0.23671, 0.09582) |
| MRF_NOPRECARE | 1.63300 (1.46647, 1.81844) | 1.39979 (1.24374, 1.5754) | 1.37859 (1.19240, 1.59383) | 3.03350 (2.36630, 3.70070) | 0.95389 (0.61828, 1.28950) | 0.90736 (0.49675, 1.31800) |

**Table E-4: Odds Ratios and Marginal Effects for the Non-Hispanic Black, Non-Hispanic White, and Hispanic Mortality Regression Models**

| Variable | Odds Ratios (95% CI)[a,b] | | | Marginal Effects (Deaths per 1,000 Births (95% CI)[a,c] | | |
|---|---|---|---|---|---|---|
| | Black | White | Hispanic | Black | White | Hispanic |
| MRF_1_9_PRECARE | 1.37775 (1.29674, 1.46382) | 1.34652 (1.28399, 1.41209) | 1.17236 (1.09445, 1.25582) | 1.98210 (1.60560, 2.35870) | 0.84385 (0.70831, 0.97940) | 0.44942 (0.25471, 0.64414) |
| MRF_16_ORMORE_PRECARE | 1.12520 (1.00220, 1.26329) | 1.12394 (1.04280, 1.21139) | 1.35485 (1.20490, 1.52345) | 0.72964 (0.013350, 1.44590) | 0.33139 (0.11875, 0.54403) | 0.85827 (0.52611, 1.19040) |
| MRF_SMOKE | 1.24139 (1.13425, 1.35866) | 1.17977 (1.11549, 1.24776) | 1.22117 (1.02459, 1.45549) | 1.33750 (0.77763, 1.89740) | 0.46889 (0.30933, 0.62846) | 0.56471 (0.06794, 1.06150) |
| MDEM_I_NOHS | 1.05467 (0.97987, 1.13519) | 1.10367 (1.03289, 1.17930) | 1.02742 (0.95914, 1.10056) | 0.32924 (-0.12598, 0.78447) | 0.27977 (0.09167, 0.46788) | 0.07644 (-0.11791, 0.27079) |
| MDEM_I_COLLEGEPLUS | 0.81232 (0.75874, 0.86969) | 0.7478 (0.71366, 0.78357) | 0.90822 (0.83434, 0.98863) | -1.28570 (-1.70930, -0.86211) | -0.82429 (-0.95807, -0.6905) | -0.27208 (-0.51214, -0.03202) |
| MDEM_AGE_TEEN | 1.13705 (1.02800, 1.25767) | 1.24116 (1.13208, 1.36077) | 1.27144 (1.13883, 1.41948) | 0.79446 (0.17048, 1.41840) | 0.61279 (0.35157, 0.87402) | 0.67869 (0.36668, 0.99071) |
| MDEM_AGE_ADV_35_40 | 0.90639 (0.83721, 0.98130) | 0.85079 (0.80231, 0.90220) | 0.95193 (0.87380, 1.03704) | -0.60792 (-1.0992, -0.11665) | -0.45831 (-0.62493, -0.29170) | -0.13923 (-0.38131, 0.10286) |
| MDEM_AGE_ADV_40plus | 1.37377 (1.17433, 1.60708) | 0.96251 (0.83754, 1.10613) | 1.2633 (1.07379, 1.48624) | 1.96430 (0.99358, 2.93490) | -0.10838 (-0.50285, 0.28609) | 0.66055 (0.20117, 1.11990) |
| MDEM_I_MARRIED | 0.94432 (0.88719, 1.00513) | 0.83555 (0.79827, 0.87458) | 0.89883 (0.84382, 0.95743) | -0.35439 (-0.74074, 0.03196) | -0.50957 (-0.63965, -0.37949) | -0.30144 (-0.48028, -0.12260) |
| # Model Observations | 981,212 | 3,644,499 | 1,646,713 | | | |
| Pseudo $R^2$ | 0.389 | 0.357 | 0.416 | | | |

Abbreviations: CI – confidence intervals.
Notes:
[a]Confidence intervals and significance testing do not include adjustments for multiple comparisons.
[b]Logistic regression models and ORs estimated using the "logit" likelihood function in Stata 15.1.
[c]Marginal effects estimated using the "margins, dydx(*)" command in Stata 15.1 with the default observed option. For non-BW-GA variables, EPA estimated marginal effects based on covariate values from all observations in the models. For BW-GA variables, EPA estimated marginal effects based on covariate values from the subset of observations falling within each GA category (see Supplementary Table 3).

**Table E-4: Odds Ratios and Marginal Effects for the Non-Hispanic Black, Non-Hispanic White, and Hispanic Mortality Regression Models**

| Variable | Odds Ratios (95% CI)[a,b] | | | Marginal Effects (Deaths per 1,000 Births (95% CI)[a,c] | | |
|---|---|---|---|---|---|---|
| | Black | White | Hispanic | Black | White | Hispanic |
| BIRTH_BW_I_EXT_PRETERM | 0.99817 (0.99802, 0.99832) | 0.99866 (0.99855, 0.99878) | 0.99835 (0.99817, 0.99853) | -0.20400 (-0.21910, -0.18890) | -0.12160 (-0.13080, -0.11240) | -0.15260 (-0.1677, -0.13750) |
| BIRTH_BW_I_VER_PRETERM | 0.99816 (0.99804, 0.99827) | 0.9985 (0.99842, 0.99858) | 0.99846 (0.99835, 0.99858) | -0.04580 (-0.04820, -0.04340) | -0.03290 (-0.03430, -0.03140) | -0.03290 (-0.0351, -0.03070) |
| BIRTH_BW_I_MOD_PRETERM | 0.99852 (0.99846, 0.99857) | 0.99867 (0.99863, 0.99872) | 0.99856 (0.99849, 0.99862) | -0.01030 (-0.01080, -0.00985) | -0.00677 (-0.00702, -0.00652) | -0.00626 (-0.00659, -0.00592) |
| BIRTH_BW_I_TERM | 0.99856 (0.99851, 0.99860) | 0.99865 (0.99861, 0.99868) | 0.99849 (0.99844, 0.99855) | -0.00453 (-0.00472, -0.00434) | -0.00228 (-0.00236, -0.00221) | -0.00219 (-0.00229, -0.00208) |
| BIRTH_BOCat1 | 1.20078 (1.12406, 1.28272) | 1.37498 (1.30875, 1.44458) | 1.23256 (1.14005, 1.33256) | 1.13170 (0.72263, 1.54080) | 0.90320 (0.76267, 1.04370) | 0.59091 (0.37013, 0.81170) |
| BIRTH_BOCat2 | 1.43158 (1.34271, 1.52634) | 1.66176 (1.57927, 1.74859) | 1.36704 (1.26426, 1.47818) | 2.21920 (1.81950, 2.61890) | 1.44050 (1.29450, 1.58650) | 0.88360 (0.66192, 1.10530) |
| BIRTH_APGAR_0_3 | 19.89802 (18.35772, 21.56734) | 43.36705 (40.67038, 46.24253) | 45.87636 (41.39996, 50.83677) | 18.49800 (17.92800, 19.06800) | 10.69200 (10.46100, 10.92300) | 10.81300 (10.466, 11.15900) |
| BIRTH_APGAR_4_6 | 3.8631 (3.54196, 4.21336) | 5.92239 (5.54208, 6.32880) | 6.86084 (6.16310, 7.63750) | 8.35950 (7.79370, 8.92530) | 5.04500 (4.83850, 5.25150) | 5.44270 (5.1129, 5.7726) |
| BIRTH_MALE | 1.28589 (1.22265, 1.35240) | 1.29367 (1.24351, 1.34583) | 1.19405 (1.12581, 1.26643) | 1.55530 (1.24280, 1.86790) | 0.73028 (0.61753, 0.84304) | 0.50123 (0.33447, 0.66798) |
| BIRTH_CONANOM | 20.95317 (16.73647, 26.23226) | 23.81106 (21.33609, 26.57338) | 30.45195 (25.31381, 36.63302) | 18.81800 (17.39300, 20.24300) | 8.99150 (8.65400, 9.32900) | 9.65470 (9.096, 10.21300) |
| BIRTH_YR_2016 | 1.04910 (0.99784, 1.10298) | 1.01725 (0.97816, 1.05791) | 0.97538 (0.91965, 1.03449) | 0.29646 (-0.01339, 0.60632) | 0.04852 (-0.06265, 0.15968) | -0.07045 (-0.23671, 0.09582) |
| MRF_NOPRECARE | 1.63300 (1.46647, 1.81844) | 1.39979 (1.24374, 1.5754) | 1.37859 (1.19240, 1.59383) | 3.03350 (2.36630, 3.70070) | 0.95389 (0.61828, 1.28950) | 0.90736 (0.49675, 1.31800) |

**Table E-4: Odds Ratios and Marginal Effects for the Non-Hispanic Black, Non-Hispanic White, and Hispanic Mortality Regression Models**

| Variable | Odds Ratios (95% CI)[a,b] | | | Marginal Effects (Deaths per 1,000 Births (95% CI)[a,c] | | |
|---|---|---|---|---|---|---|
| | Black | White | Hispanic | Black | White | Hispanic |
| MRF_1_9_PRECARE | 1.37775 (1.29674, 1.46382) | 1.34652 (1.28399, 1.41209) | 1.17236 (1.09445, 1.25582) | 1.98210 (1.60560, 2.35870) | 0.84385 (0.70831, 0.97940) | 0.44942 (0.25471, 0.64414) |
| MRF_16_ORMORE_PRECARE | 1.12520 (1.00220, 1.26329) | 1.12394 (1.04280, 1.21139) | 1.35485 (1.20490, 1.52345) | 0.72964 (0.013350, 1.44590) | 0.33139 (0.11875, 0.54403) | 0.85827 (0.52611, 1.19040) |
| MRF_SMOKE | 1.24139 (1.13425, 1.35866) | 1.17977 (1.11549, 1.24776) | 1.22117 (1.02459, 1.45549) | 1.33750 (0.77763, 1.89740) | 0.46889 (0.30933, 0.62846) | 0.56471 (0.06794, 1.06150) |
| MDEM_I_NOHS | 1.05467 (0.97987, 1.13519) | 1.10367 (1.03289, 1.17930) | 1.02742 (0.95914, 1.10056) | 0.32924 (-0.12598, 0.78447) | 0.27977 (0.09167, 0.46788) | 0.07644 (-0.11791, 0.27079) |
| MDEM_I_COLLEGEPLUS | 0.81232 (0.75874, 0.86969) | 0.7478 (0.71366, 0.78357) | 0.90822 (0.83434, 0.98863) | -1.28570 (-1.70930, -0.86211) | -0.82429 (-0.95807, -0.6905) | -0.27208 (-0.51214, -0.03202) |
| MDEM_AGE_TEEN | 1.13705 (1.02800, 1.25767) | 1.24116 (1.13208, 1.36077) | 1.27144 (1.13883, 1.41948) | 0.79446 (0.17048, 1.41840) | 0.61279 (0.35157, 0.87402) | 0.67869 (0.36668, 0.99071) |
| MDEM_AGE_ADV_35_40 | 0.90639 (0.83721, 0.98130) | 0.85079 (0.80231, 0.90220) | 0.95193 (0.87380, 1.03704) | -0.60792 (-1.0992, -0.11665) | -0.45831 (-0.62493, -0.29170) | -0.13923 (-0.38131, 0.10286) |
| MDEM_AGE_ADV_40plus | 1.37377 (1.17433, 1.60708) | 0.96251 (0.83754, 1.10613) | 1.2633 (1.07379, 1.48624) | 1.96430 (0.99358, 2.93490) | -0.10838 (-0.50285, 0.28609) | 0.66055 (0.20117, 1.11990) |
| MDEM_I_MARRIED | 0.94432 (0.88719, 1.00513) | 0.83555 (0.79827, 0.87458) | 0.89883 (0.84382, 0.95743) | -0.35439 (-0.74074, 0.03196) | -0.50957 (-0.63965, -0.37949) | -0.30144 (-0.48028, -0.12260) |
| # Model Observations | 981,212 | 3,644,499 | 1,646,713 | | | |
| Pseudo $R^2$ | 0.389 | 0.357 | 0.416 | | | |

Abbreviations: CI – confidence intervals.
Notes:
[a]Confidence intervals and significance testing do not include adjustments for multiple comparisons.
[b]Logistic regression models and ORs estimated using the "logit" likelihood function in Stata 15.1.
[c]Marginal effects estimated using the "margins, dydx(*)" command in Stata 15.1 with the default observed option. For non-BW-GA variables, EPA estimated marginal effects based on covariate values from all observations in the models. For BW-GA variables, EPA estimated marginal effects based on covariate values from the subset of observations falling within each GA category (see Supplementary Table 3).

## *E.7.2 Comparison to Prior Studies*

EPA's evaluation of the relationship between birth weight and infant mortality differs from those used in prior literature in terms of included covariates, model specification, and sample characteristics. In terms of modeling approach, our analysis is closest to the one used by Ma et al. (2010), who also find that birth weight and GA are important predictors of infant mortality risk and that the effects of birth weight on infant mortality vary by race/ethnicity. However, methodological differences between Ma et al. (2010) and our work, summarized in Table E-5, prevent us from making direct comparisons of birth weight-infant mortality effect magnitudes. Even in the absence of methodological differences, EPA expects that results would differ from those reported by older studies due to changes in infant mortality, maternal and birth characteristics, and maternal demographic over the past 30 years (see Table E-1).

**Table E-5: Comparison of Ma et al. (2010) and the EPA Analysis**

| Analysis Component | Ma et al. (2010) | EPA |
|---|---|---|
| Year(s) of NCHS/NVSS Data | 2001 | 2016-2018 |
| Data Sample | Singletons and multiples | Singletons only |
| Race/Ethnicity Models | Non-Hispanic Black, non-Hispanic White, Mexican | Non-Hispanic Black, non-Hispanic White, Hispanic |
| Birth Weight-Gestation Specification[a] | Birth weight (100 g increment), gestational age (weeks), and birth weight x gestational age (continuous product of birth weight and gestational age) | Birth weight interacted with four gestational age categories (extremely preterm, very preterm, moderately preterm, and term) |
| Other Covariates[b] | Categorized APGAR score (low: 0-3 and medium: 4-6, with high: 7-10 as reference category), maternal age, maternal education, marital status, whether mother was born in U.S., whether father was unreported on birth certificates, prenatal care, tobacco/alcohol use during pregnancy, and birth order | Categorized Apgar score (low: 0-3 and medium: 4-6, with high: 7-10 as reference category), categorized number of prenatal care visits (None, 1-9,16+, with ,10-15 as reference category), maternal education, maternal age, marital status, smoker status, sex, presence of congenital anomalies, birth year, birth order (see Table E-2) |

Abbreviations: NCHS – National Center for Health Statistics; NVSS – National Vital Statistics System.
Notes:
[a]Although Ma et al. (2010) tested several different models, EPA focuses on one of their highest-performing model forms, Model 12, in which the interaction term between gestational age and birth weight is almost always significant.
[b]EPA notes that Ma et al. (2010) did not report coefficients for a number of maternal and birth characteristics (i.e., maternal age, maternal education, marital status, whether mother was born in U.S., whether father was unreported on birth certificates, prenatal care, tobacco/alcohol use during pregnancy, and birth order) or discussed these variables in detail.

# E.8 Limitations and Uncertainties

Table E-6 summarizes limitations and sources of uncertainty associated with the estimated relationship between infant birth weight and mortality.

**Table E-6: Limitations and Uncertainties in the Analysis of the Birth Weight-Mortality Relationship**

| Uncertainty/Assumption | Notes |
|---|---|
| Transcription errors may be present in the NCHS/NVSS dataset | Infant birth and death records are compiled based on hand-written forms and tabulated for use in the NCHS/NVSS dataset. |
| The models do not directly account for maternal socioeconomic status and other potentially important factors that contribute to LBW and infant mortality. | Though review of the infant mortality literature suggests that socioeconomic status is an indicator of infant mortality (Ma et al., 2010; Ely et al., 2020), the NCHS/NVSS does not have a variable that would account for individual socioeconomic status of the mother (e.g., household income) or even community-level socioeconomic status (e.g., median income at the county- or state-level). EPA tested a variable for hospital payment source for delivery that specifies those who use Medicaid, but model results that included this variable did not match expectations (variable coefficient was not significant for all race/ethnicity subpopulations, mixture of negative and positive coefficients depending on race/ethnicity subpopulation). Thus, the variable was excluded from our models. The maternal education, maternal age, and marital status variables serve as rough proxies for socioeconomic status in our models. Other factors, such as indicators of parental support networks (e.g., access to paid care or grandparents that live nearby) may contribute to the relationship between birth weight and infant mortality, but such information is not publicly available at the individual infant scale. |
| The analysis relies only on singleton data to develop relationships between birth weight and infant mortality. | Because singletons represent the majority of U.S. births (96% of infants born in 2016 and 2017), EPA does not expect this to be a significant limitation. In order to address this limitation, a separate model would be required because multiples are often born at smaller birth weight than singleton infants, the mortality rate among multiples is often higher than singletons for reasons often unrelated to birth weight (Horon, 2020), and the sample size of multiples in the 2016-2018 NCHS/NVSS data is likely not adequate to represent the relationship between birth weight and mortality. |
| EPA does not model birth weight-mortality impacts for infants who fall into race categories other than non-Hispanic White, non-Hispanic Black, and Hispanic | While the NCHS/NVSS data specifies additional race categories, developing models for each individual race or even a combination of all "other" races would suffer from effects of low sample size, including coefficient and marginal effects that lack significance. All combined, the "other" race/ethnicity subpopulation would have a sample size that is at least 30 percent smaller than any one of the non-Hispanic White, non-Hispanic Black, and Hispanic race/ethnicity models. |

Abbreviations: LBW – low birth weight; NCHS – National Center for Health Statistics; NVSS – National Vital Statistics System.

# Appendix F. Serum Cholesterol Dose Response Functions

This appendix describes EPA's literature review to identify studies to estimate relationships between cholesterol levels and serum per- and polyfluoroalkyl substances (PFAS) for inclusion in a meta-analysis of these relationships. This approach has been peer reviewed by EPA's Science Advisory Board; input provided by that organization has been considered in finalizing this analysis (U.S. EPA, 2022). Statistical analyses that combine the results of multiple studies, such as meta-analyses, are widely applied to investigate the dose-specific relationship between contaminant levels and associated health effects. Such analyses are suitable for economic assessments because they can improve precision and statistical power (Engels et al., 2000; Deeks, 2002; Rücker et al., 2009). This appendix also provides details on the meta-data development, results of the meta-analysis, and limitations and uncertainties associated with the estimated relationships. EPA used the estimated relationships to estimate cardiovascular disease (CVD) risk reduction associated with exposure to PFAS mediated by changes in serum cholesterol markers.

## F.1 Data Sources

EPA relied on two literature review efforts to identify potential sources of exposure-response information for the effect of PFAS on serum cholesterol, lipids, and lipoproteins: A literature review built on the one conducted by the Agency for Toxic Substances and Disease Registry (ATSDR) in the development of their Toxicological Review Public Comment Draft (ATSDR, 2018), which included literature through mid-2017.

The most recent systematic review of the newly published epidemiological literature for PFAS performed by EPA included literature from 2013 to 2020 (U.S. EPA, 2023a; U.S. EPA, 2023b). The relationships between exposure to PFAS and serum total cholesterol (TC) and high-density lipoprotein cholesterol (HDLC) identified based on these literature reviews allowed EPA to generate inputs for the Pooled Cohort Atherosclerotic Cardiovascular Disease (ASCVD) risk model (Goff et al., 2014).[28, 29]

### *F.1.1 Literature Review and Studies Identification for the Meta-Analysis*

Two reviewers independently screened references retrieved from the literature search by title and abstract, and then reviewed relevant studies in full text. EPA evaluated studies identified during the search according to the following criteria prior to inclusion in the meta-analysis to ensure validity, consistency, and applicability. Briefly, of interest were studies conducted on adults in the general population, evaluating the outcomes of TC and HDLC, and the exposures of PFOA and PFOS. Because EPA evaluates CVD risk among a general population of adults aged 40 to

[28] The ASCVD model relies on the following inputs: demographic information, smoking and diabetes status, serum TC, and HDLC.

[29] Note that EPA evaluated HDLC effects as part of a sensitivity analysis (see Appendix K). EPA did not model the effects of PFOA/PFOS changes on HDLC levels in the overall benefits analysis because evidence of an association between PFOA/PFOS and HDLC effects is uncertain (U.S. EPA, 2023a; U.S. EPA, 2023b).

89, studies performed on specific population subsets, such as occupational populations, were not considered for inclusion in the meta-analysis due to the potential for greater levels of exposure to PFOA and PFOS in these populations compared to the general population.

*Applicability:* EPA evaluated each study to determine whether it estimated the association between exposure to PFOA or PFOS (measured in serum or plasma) and a quantitative measure of TC or HDLC in general populations (age 20 and older). Of the 39 studies identified as part of the ATSDR-based literature review that provided information on the relationship between exposure to PFAS and TC and HDLC levels, 9 were general population studies. Of the 41 studies identified as part of the EPA/OST literature review that provided information on the relationship between exposure to PFAS and TC and HDLC levels, 14 were general population studies. These studies[30] were further evaluated for inclusion in the meta-analysis.

*Research methods and study details:* EPA evaluated each study to determine whether it reported numbers of participants, quantitative effect estimates (beta coefficients), measures of effect estimate variance (95% confidence intervals [CIs], standard errors [SEs], or standard deviations [SDs]). EPA retained studies with missing measures of effect estimate variance but with reported p-values for differences. For such studies, EPA used the approach in the Cochrane Handbook for Systematic Reviews (Higgins et al., 2019) to calculate SDs or SEs. Briefly, the approach estimates the SEs using the correspondence between the p-value and the t-statistic, with degrees of freedom equal to the difference between the sample size and the number of parameters in the model that provided the effect estimate. Then the SE is obtained by dividing the effect estimate by the t-statistic.

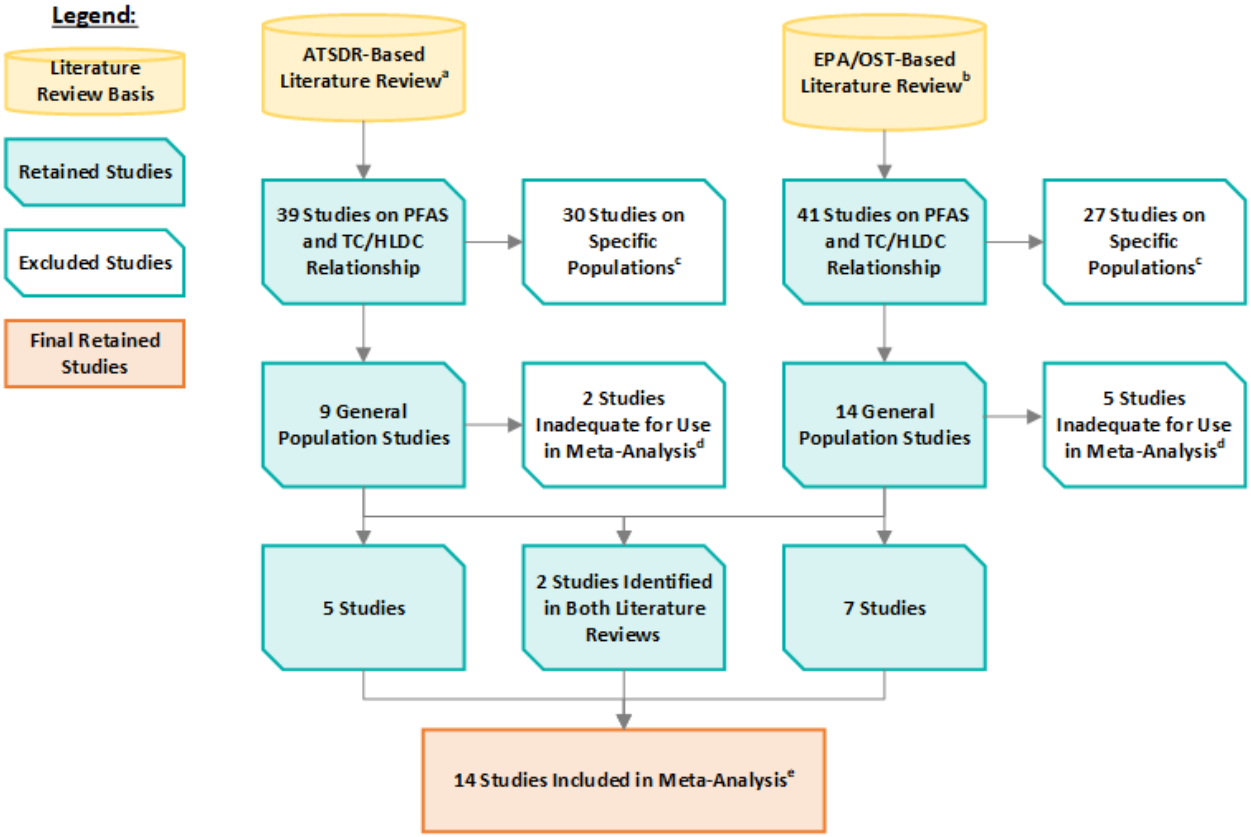
*Additional exclusion criteria:* EPA also excluded studies that reported data only for pregnant women, infants, or children. Although there is some evidence that PFAS exposure is associated with cardiometabolic impairment in children and younger adults (Rappazzo et al., 2017), EPA did not extract data from these studies because lipid levels are known to change during pregnancy from pre-pregnancy levels, and the relationships between lipid profiles at early life stages are not as well defined as they are at later life stages. Another frequent reason for study exclusion was the reporting of only relative risks or odds ratios for hypercholesteremia or hyperlipidemia; results in this form could not be used to estimate continuous exposure-response relationships.

## *F.1.2 Assessment of Study Applicability to the Meta-Analysis*

Figure F-1 presents a flow diagram of the studies reviewed as part of the ATSDR-based and EPA/OST-based literature reviews and the selection of studies retained for inclusion in the meta-analysis. Using the study inclusion criteria described in Section F.1.1, EPA retained 14 studies for use in the meta-analysis. Of these, five were identified as part of the ATSDR literature review (Château-Degat et al., 2010; Fisher et al., 2013; Fu et al., 2014; Nelson et al., 2010; Steenland et al., 2009), seven were identified from the EPA systematic review (Dong et al., 2019; Fan et al., 2020; Jain et al., 2019; Y. Li et al., 2020; C. Y. Lin et al., 2020; P.-I. D. Lin

[30] Of the general population studies identified as part of the EPA/OST literature review, five overlapped with studies identified as part of the ATSDR-based literature review.

et al., 2019; Yang et al., 2018), and two were identified in both literature reviews (He et al., 2018; Liu et al., 2018).




Notes:
ATSDR = Agency for Toxic Substances and Disease Registry, EPA = Environmental Protection Agency, OST = Office of Science and Technology, PFAS = per- and polyfluoroalkyl substances, TC = Total Cholesterol, HDLC = high-density lipoprotein cholesterol
[a]Included literature through mid-2017.
[b]Included literature published from 2016 to 2020.
[c]For example, studies based on occupational data or data only for pregnant women, infants, or children.
[d]Some studies did not include the estimates required for meta-analysis calculations. For example, certain studies did not report effect estimates or interquartile ranges.
[e]Of these studies, 8 are based on data from the United States and 6 are based on data outside of the United States.

**Figure F-1: Diagram of Literature Retained for Use in the Meta-Analysis and Data Sources.**

Table F-1 summarizes the 14 studies that were identified in the ATSDR-based and EPA literature review that EPA used to derive slope estimates for PFOA and PFOS associations with serum TC and HDLC levels.[31] Six of the studies that EPA retained for use in the meta-analysis were based on PFAS and serum lipid measurements from the U.S. general population (National Health and Nutrition Examination Survey [NHANES]) (Dong et al., 2019; Fan et al., 2020; He et al., 2018; Jain et al., 2019; Liu et al., 2018; Nelson et al., 2010); there were also general

[31] For this effort, EPA focused on PFOA and PFOS, since these are by far the most well-studied perfluorinated compounds.

population studies from Canada (Fisher et al., 2013), Sweden (Y. Li et al., 2020), Taiwan (Yang et al., 2018; C. Y. Lin et al., 2020), and Henan Province, China (Fu et al., 2014). Château-Degat et al. (2010) reported on the relationship between PFOS and serum lipids in a Canadian Inuit population. EPA also retained the results from a study of a highly exposed population in the United States (the C8 Health Project cohort) (Steenland et al., 2009) and from a study using participants in a U.S. diabetes prevention program (P.-I. D. Lin et al., 2019).

EPA excluded two general population studies identified in the ATSDR-based literature review (Eriksen et al., 2013; Seo et al., 2018) and two general population studies identified based on the agency's systematic review (Convertino et al., 2018; Huang et al., 2018) that were inadequate for use in the meta-analysis because they did not include the estimates required for meta-analysis calculations. For example, EPA excluded the studies identified in the ATSDR literature review from the meta-analysis because the authors did not report either the effect estimates (Seo et al., 2018) or interquartile ranges (Eriksen et al., 2013) needed for calculations.[32] Similarly, EPA excluded the studies identified as part of the agency's systematic review because they involved a Phase 1 controlled trial with modeled exposures in cancer patients dosed with ammonium perfluorooctanoate (Convertino et al., 2018) or reported effect estimates (Spearman correlation coefficients) that were not suitable for use in the meta-analysis (Huang et al., 2018). EPA also considered the longitudinal study by Fitz-Simon et al. (2013) of adults participating in the C8 Health Project who were not taking cholesterol-lowering medication and who were examined twice, with an average of 4.4 years between examinations. In subjects whose serum PFOA levels halved between examinations, there was a decrease of an average of 1.65% (95% confidence interval: 0.32%, 2.97%) for TC and 1.33% (−0.21%, 2.85%) for HDLC. In subjects whose serum PFOS levels halved between examinations, there were similar decreases, although larger in magnitude and variability: a decrease of an average of 3.20% (95% confidence interval: 1.63%, 4.76%) for TC and 1.28% (−0.59%, 3.12%) for HDLC. However, given the nature of the results, the effect estimates from this study were inadequate for inclusion in the meta-analysis.

[32] Efforts to contact the study authors for the missing data were unsuccessful at the time of this report.

**Table F-1: Studies Selected for Inclusion in the Meta-Analyses**

| Author and Year | Title | Cholesterol and PFAS Relationship Evaluated | | | | Medications |
|---|---|---|---|---|---|---|
| | | TC | | HDLC | | |
| | | PFOA | PFOS | PFOA | PFOS | |
| Steenland et al., 2009 [a,d] | Association of Perfluorooctanoic Acid and Perfluorooctane Sulfonate With Serum Lipids Among Adults Living Near a Chemical Plant | X | X | X | X | Participants using lipid-lowering medications were excluded |
| Château-Degat et al., 2010 [a,d] | Effects of Perfluorooctanesulfonate Exposure on Plasma Lipid Levels in the Inuit Population of Nunavik (Northern Quebec) | | X | | X | Use of lipid-lowering medication considered in statistical analysis |
| Nelson et al., 2010 [a,d] | Exposure to Polyfluoroalkyl Chemicals and Cholesterol, Body Weight, and Insulin Resistance in the General U.S. Population | X | X | X | X | Participants using lipid-lowering medications were excluded |
| Fisher et al., 2013 [a,d] | Do Perfluoroalkyl Substances Affect Metabolic Function and Plasma Lipids?—Analysis of the 2007–2009, Canadian Health Measures Survey (CHMS) Cycle 1 | X | X | X | X | Participants using lipid-lowering medications were excluded |
| Fu et al., 2014[a,d] | Associations Between Serum Concentrations of Perfluoroalkyl Acids and Serum Lipid Levels in a Chinese Population | X | X | X | X | Not taken into consideration |
| He et al., 2018[c] | PFOA is Associated with Diabetes and Metabolic Alteration in US Men: National Health and Nutrition Examination Survey 2003-2012 | X | X | X | X | Not taken into consideration |
| Liu et al., 2018[c] | Association Among Total Serum Isomers of Perfluorinated Chemicals, Glucose Homeostasis, Lipid Profiles, Serum Protein and Metabolic Syndrome in Adults: NHANES, 2013–2014 | X | X | X | X | Use of lipid-lowering medication considered in statistical analysis |

**Table F-1: Studies Selected for Inclusion in the Meta-Analyses**

| Author and Year | Title | Cholesterol and PFAS Relationship Evaluated | | | | Medications |
|---|---|---|---|---|---|---|
| | | TC | | HDLC | | |
| | | PFOA | PFOS | PFOA | PFOS | |
| Yang et al., 2018[b] | Association of Serum Levels of Perfluoroalkyl Substances (PFASs) With the Metabolic Syndrome (MetS) in Chinese Male Adults: A Cross-Sectional Study | | | X | X | Not taken into consideration |
| Dong et al., 2019[b] | Using 2003–2014 U.S. NHANES Data to Determine the Associations Between Per- and Polyfluoroalkyl Substances and Cholesterol: Trend and Implications | X | X | X | | Participants using lipid-lowering medications were excluded |
| Jain et al., 2019[b] | Roles of Gender and Obesity in Defining Correlations Between Perfluoroalkyl Substances and Lipid/Lipoproteins | X | X | X | X | Use of lipid-lowering medication considered in statistical analysis |
| P.-I. D. Lin et al., 2019[b] | Per- and Polyfluoroalkyl Substances and Blood Lipid Levels in Pre-Diabetic Adults—Longitudinal Analysis of the Diabetes Prevention Program Outcomes Study | X | X | X | X | Participants using lipid-lowering medications were excluded |
| Fan et al., 2020[b] | Serum Albumin Mediates the Effect of Multiple Per- and Polyfluoroalkyl Substances on Serum Lipid Levels | X | X | X | X | Not taken into consideration |
| Y. Li et al., 2020[b] | Associations Between Perfluoroalkyl Substances and Serum Lipids in a Swedish Adult Population With Contaminated Drinking Water | X | X | X | X | Not taken into consideration |
| C. Y. Lin et al., 2020b | The Association Between Total Serum Isomers of Per- and Polyfluoroalkyl Substances, Lipid Profiles, and the DNA Oxidative/Nitrative Stress Biomarkers in Middle-Aged Taiwanese Adults | | | X | X | Not taken into consideration |

## Table F-1: Studies Selected for Inclusion in the Meta-Analyses

| Author and Year | Title | Cholesterol and PFAS Relationship Evaluated | | | | Medications |
|---|---|---|---|---|---|---|
| | | TC | | HDLC | | |
| | | PFOA | PFOS | PFOA | PFOS | |

Abbreviations: PFAS – per-and polyfluoroalkyl substances; PFOA – perfluorooctanoic acid; PFOS – perfluorooctanesulfonic acid; TC – total cholesterol; HDLC – high-density lipoprotein cholesterol.
Notes: Study quality reflected in green (medium confidence) or pink (low confidence) cell shading.
[a]Studies identified based on ATSDR literature review.
[b]Studies identified based on EPA literature review.
[c]Studies available in both assessments.
[d]Studies available in PFOA and/or PFOS health effects support documents (U.S. EPA, 2016a, 2016b).

## F.2 Meta-Analysis

Based on the study inclusion criteria discussed in Section F.1.1, EPA included 14 studies in the meta-analysis. Of these 14 studies, 11 were used to develop exposure-response relationships for serum PFOA and TC, 13 were used to develop exposure-response relationships for serum PFOA and HDLC, 12 studies were used to develop exposure-response relationships for serum PFOS and TC, and 13 studies were used to develop exposure-response relationships for serum PFOS and HDLC (Table F-1). EPA conducted four separate meta-analyses: one analysis for each combination of chemical (PFOA or PFOS) and health outcome (TC or HDLC).

All studies were evaluated for risk of bias, selective reporting, and sensitivity as applied in developing EPA's *Toxicity Assessments and Proposed Maximum Contaminant Level Goals for PFOA and PFOS in Drinking Water* (U.S. EPA, 2023a; U.S. EPA, 2023b). Briefly, the main considerations specific to evaluating the quality of studies on serum lipids included use of medications, fasting, and potential for reverse causality. Because lipid-lowering medications strongly affect serum lipid levels, studies that did not account for the use of lipid-lowering medications by restriction, stratification, or adjustment were rated as *deficient* in the participant selection domain. For TC and HDLC measurements, fasting is not likely to introduce measurement error because the serum levels of the lipids considered change minimally after a meal (Mora, 2016). Measuring PFOS and serum lipids concurrently was considered adequate in terms of exposure assessment timing. Given the long half-life of PFOA and PFOS (Ying Li et al., 2018), current blood concentrations are expected to correlate well with past exposures. Furthermore, although reverse causation due to hypothyroidism (Dzierlenga, Allen, et al., 2020) or enterohepatic cycling of bile acids (Fragki et al., 2021) has been suggested, there is not yet clear evidence to support these reverse causal pathways.

Based on these considerations, of the 14 studies, ten were *medium confidence* in ROB evaluations, with only four deemed *low confidence* (Fu et al., 2014; He et al., 2018; Yang et al., 2018; Y. Li et al., 2020). These *low confidence* studies had deficiencies in participant selection, outcome assessment, or confounding domains. None of these studies considered use of lipid-lowering medications in the selection process or in the statistical analyses. Additional details on the ROB evaluations are available in ICF (2021).

## F.3 Extraction of Slope Values for TC and HDLC

If studies reported linear slope relationships (change in serum TC or HDLC in mg/dL per ng/mL change in serum PFOA/PFOS), EPA extracted these values, along with their confidence limits, directly as reported by the study authors. If results from multiple models with different adjustments for confounders were reported within a single study, either the most adjusted results or the main model results as presented by the study authors were selected. When studies provided results for both untransformed and log-transformed PFOA/PFOS, EPA used untransformed PFOA/PFOS to reduce bias due to back-transformations of effect estimates. For studies that provided results only for log-transformed PFOA/PFOS (five studies) or log-transformed outcomes (two studies), or log-transformed both PFOA/PFOS and outcomes (two studies), EPA approximated the results for an untransformed analysis using the approach outlined by Rodríguez-Barranco et al. (2017) and Dzierlenga, Crawford, et al. (2020). When not reported, EPA assumed that the natural logarithm was the basis of the transformation. An independent EPA reviewer evaluated the extracted slope values for quality assurance.

## F.4 Methods and Key Assumptions

The summary measure of association was a beta coefficient relating changes in TC or HDLC in mg/dL to increases in serum or plasma[33] PFOA or PFOS in ng/mL. EPA conducted random-effects meta-analyses using the DerSimonian et al. (1986) approach, which uses weights based on the inverse of the variance of the coefficient of each study plus the addition of an extra component of variance between studies. When studies reported beta coefficients by quartiles (e.g., He et al., 2018), EPA estimated a linear coefficient using a weighted linear regression of the midpoints of the quartiles and the reported beta coefficients, using the inverse of standard errors as the regression weights.

EPA assessed between-study heterogeneity using Cochran's Q test (Cochran, 1954) and the $I^2$ statistic (Higgins et al., 2003). EPA developed forest plots to display the results. EPA developed funnel plots and performed an Egger regression on the estimates of effect size to assess potential publication bias (Begg et al., 1994; Egger et al., 1997; Egger et al., 2008). Because back-transformations of effect estimates with log-transformed outcomes or exposures could introduce bias and could be a source of heterogeneity, EPA also conducted sub-analyses by type of model that provided the study-specific effect estimate (e.g., only including studies that reported linear associations [six studies] or linear-log associations [five studies]).

If publication bias was observed, EPA conduced sensitivity analyses using trim-and-fill methods (Duval et al., 2000a, 2000b) to estimate the number of missing studies and predict the impact of the hypothetical "missing" studies on the pooled effect estimate. To investigate sources of heterogeneity, EPA conducted several sensitivity analyses:

EPA evaluated the impact of using other estimation methods for the between-study variance ($tau^2$) besides the DerSimonian et al. (1986) approach, such as restricted maximum likelihood (Raudenbush, 2009) or Sidik et al. (2005).

- To assess potential impact of a single study on the overall effect estimate, EPA conducted leave-one-out meta-analyses.
- To assess potential impact of study quality on the overall effect estimate, EPA conducted sensitivity analyses excluding the four studies considered to have higher ROB.
- To assess the impact of using multiple regression coefficients from the same study (which are correlated), EPA excluded a study that contributed four effect estimates (gender- and obesity-specific) for each analysis, which also accounted for most of the weight in the overall pooled beta coefficient (Jain et al., 2019). EPA also conducted a sensitivity analysis using a single pooled estimate from the four study-specific estimates.
- EPA also assessed the impact of non-U.S or Canadian general population studies in sensitivity analyses excluding studies conducted in China (Fu et al., 2014), Taiwan (Yang et al., 2018; C. Y. Lin et al., 2020), or Sweden (Y. Li et al., 2020), the Canadian Inuit population study (Château-Degat et al., 2010), and the U.S. high-exposure community study (Steenland et al., 2009).

Six studies that EPA retained for use in the meta-analysis were based on PFAS and serum lipid measurements using data from overlapping NHANES cycles: Dong et al. (2019) used data from

[33] PFOA or PFOS concentrations is serum or plasma were treated interchangeably.

2003–2014, while He et al. (2018) used 2003–2012 data; Jain et al. (2019) used 2005–2014 data; Fan et al. (2020) used 2011–2014 data; Liu et al. (2018) used 2013–2014; and Nelson et al. (2010) used data from 2003–2004. Although the datasets and models were not exactly the same in all NHANES-based studies, to avoid estimate dependency issues due to overlapping populations in the meta-analysis, EPA also performed a sensitivity analysis including only the data from the study covering the broadest range of NHANES cycles (2003–2014) (Dong et al., 2019).

EPA performed statistical analyses using the software STATA, version 16.1 (StataCorp, 2019), with the *combine*, *meta esize*, *meta set*, *meta summarize*, *metainf*, *meta funnel*, *meta bias*, and *meta trimfill* packages (Palmer et al., 2016). Results of the meta-analyses are presented in Table F-2 and Table F-3. Overall, there is a high degree of heterogeneity when all studies are combined. Excluding Jain et al. (2019) did not significantly reduce the heterogeneity; however restricting analyses to studies reporting linear or linear-log associations did reduce heterogeneity in most cases.

## *F.4.1 Slope Estimation for PFOA*

When including the six studies reporting linear associations, there was a statistically significant positive increase in TC of 1.57 (95% confidence interval: 0.02, 3.13) mg/dL per ng/mL serum PFOA (p-value=0.048, $I^2$=87%). The association for HDLC and PFOA was positive (0.11; 95% CI: -0.22, 0.43) but not statistically significant (Table F-2, Figure F-2). Adjusting for possible publication bias through funnel plots and trim-and-fill analysis suggested the imputation of two additional studies for HDLC and PFOA with a smaller effect (-0.01, 95% confidence interval: -0.42, 0.41). For TC and PFOA, the pooled associations did not change when adjusting for possible publication bias (Figure F-3). However, methods to assess heterogeneity and publication bias have limitations in small sample-size meta-analyses, thus these results should be interpreted cautiously (von Hippel, 2015).

## Table F-2: Results for PFOA Meta-Analyses

| Group | Outcome | Number of Studies/ Number of Estimates | Beta (mg/dL per ng/mL) | 95% CIs | | p-value | Q[a] | p-value for Q | $I^2$ | $Tau^2$ |
|---|---|---|---|---|---|---|---|---|---|---|
| All Studies | TC | 11/14 | 0.003 | -0.001 | 0.006 | 0.177 | 123.68 | < 0.001 | 89.49 | 0 |
| | HDLC | 13/17 | 0.001 | -0.001 | 0.004 | 0.291 | 54.74 | < 0.001 | 70.77 | 0 |
| **Linear Models Only** | **TC** | **4** | **1.574** | **0.018** | **3.130** | **0.048** | **23.43** | **< 0.001** | **87.19** | **1.910** |
| | **HDLC** | **5** | **0.105** | **-0.219** | **0.428** | **0.526** | **14.01** | **0.007** | **71.45** | **0.069** |
| **Sensitivity Analyses** | | | | | | | | | | |
| All lower risk of bias studies | TC | 8/11 | 0.003 | -0.003 | 0.008 | 0.321 | 88.86 | < 0.001 | 88.75 | 0 |
| | HDLC | 9/13 | 0.002 | -0.002 | 0.005 | 0.290 | 28.34 | 0.005 | 57.65 | 0 |
| Exclude Jain et al. (2019) | TC | 10 | 0.004 | -0.002 | 0.010 | 0.179 | 82.04 | < 0.001 | 89.03 | 0 |
| | HDLC | 12/13 | 0.001 | -0.003 | 0.006 | 0.500 | 50.18 | < 0.001 | 76.09 | 0 |
| Exclude non-US/Canada and high exposure studies | TC | 8/11 | 0.002 | -0.003 | 0.006 | 0.496 | 55.65 | <0.001 | 82.03 | 0 |
| | HDLC | 8/11 | 0.001 | -0.003 | 0.005 | 0.647 | 26.17 | 0.004 | 61.79 | 0 |
| All studies, pooled Jain et al. (2019) | TC | 11 | 0.003 | -0.002 | 0.008 | 0.183 | 91.42 | <0.001 | 89.06 | 0 |
| | HDLC | 13/14 | 0.001 | -0.002 | 0.004 | 0.412 | 53.07 | <0.001 | 75.51 | 0 |
| All studies, no NHANES overlap | TC | 6 | 0.017 | -0.033 | 0.067 | 0.505 | 21.56 | 0.001 | 76.9 | 0.001 |
| | HDLC | 8/9 | 0.0030 | 0.0029 | 0.0031 | <0.001 | 4.12 | 0.844 | 0 | 0 |
| Linear models only, no NHANES overlap | TC | 1[b] | 1.480 | 0.180 | 2.780 | 0.026 | 0.00 | NA | NA | NA |
| | HDLC | 2 | 0.185 | -0.897 | 1.249 | 0.773 | 1.29 | 0.26 | 22.61 | 0.29 |
| Linear-log models only | TC | 3/6 | 0.002 | -0.004 | 0.007 | 0.594 | 31.56 | < 0.001 | 84.16 | 0 |
| | HDLC | 5/9 | 0.001 | -0.003 | 0.006 | 0.490 | 13.56 | 0.094 | 41.01 | 0 |
| P.-I. D. Lin et al. (2019) | TC | 1 | 1.632 | -0.841 | 2.422 | >0.05 | 0.00 | NA | NA | NA |
| | HDLC | 1 | -0.131 | -0.370 | 0.107 | >0.05 | 0.00 | NA | NA | NA |
| Dong et al. (2019) | TC | 1 | 1.480 | 0.180 | 2.780 | 0.026 | 0.00 | NA | NA | NA |
| | HDLC | 1 | -0.025 | -0.443 | 0.393 | >0.05 | 0.00 | NA | NA | NA |

Abbreviations: CI – confidence interval; HDLC – high-density lipoprotein cholesterol; TC – total cholesterol; PFOA– Perfluorooctanoic Acid.
Notes:
[a]Q statistics for heterogeneity. $Tau^2$ is the between-studies variance. $I^2$ represents the proportion of total variance in the estimated model due to inter-study variation.
[b]Data from Dong et al. (2019) Statistics for heterogeneity do not apply when only one study is used.

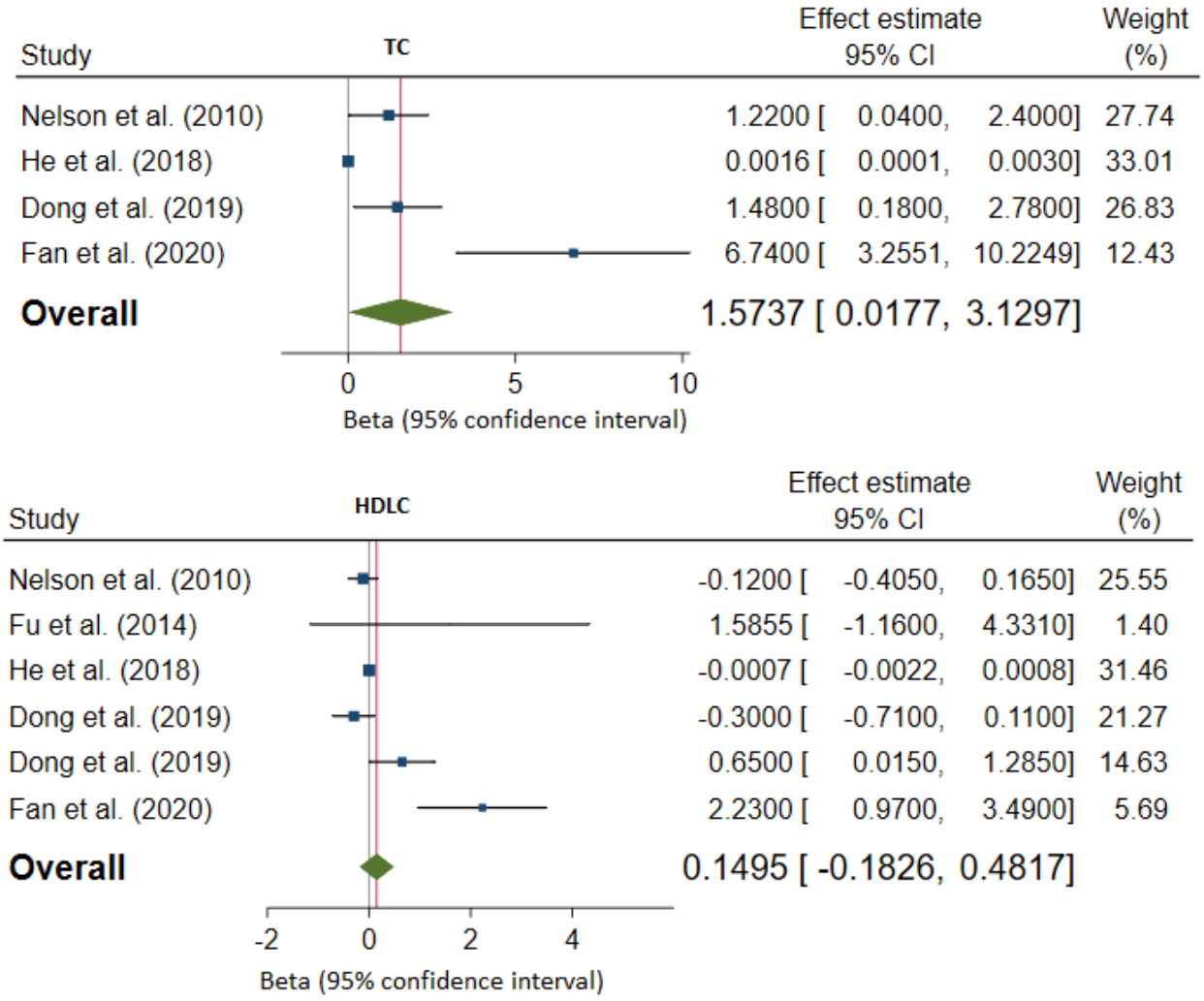



**Figure F-2: Forest Plots Showing the Beta Coefficients Relating PFOA Concentrations to TC and HDLC in Each Study Reporting Linear Associations, and Pooled Estimates After Random-Effects Meta-Analysis.**

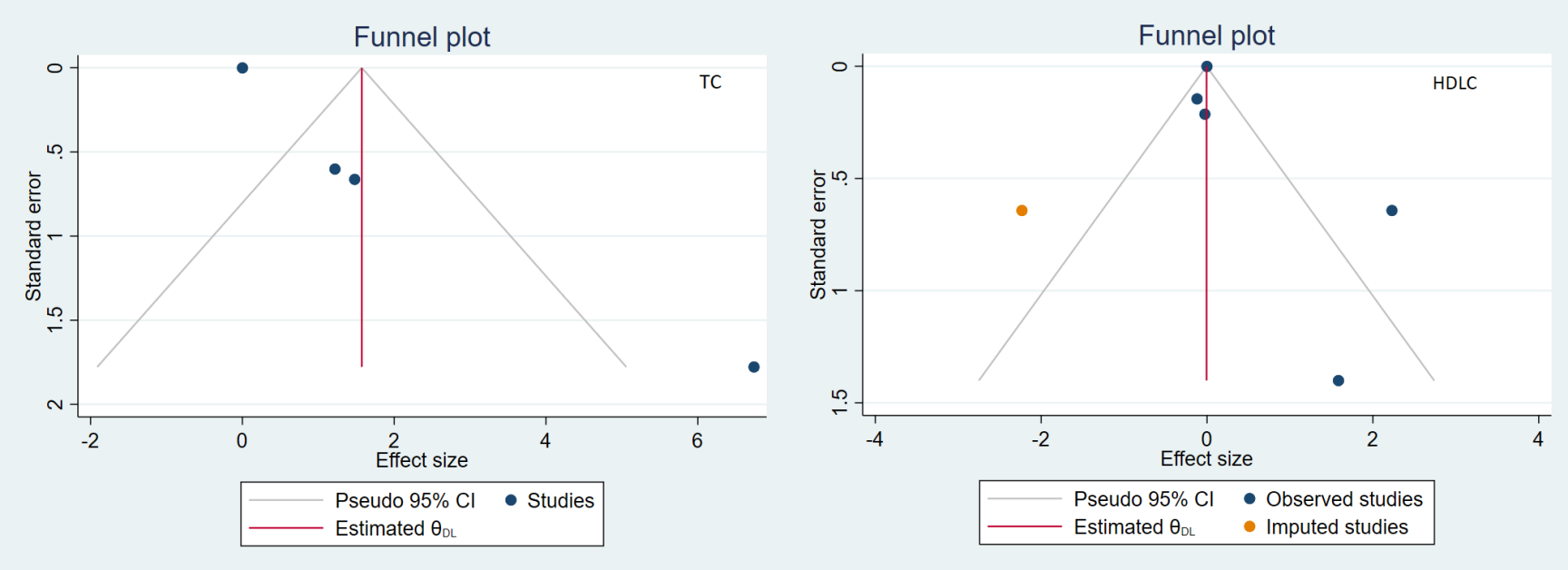



**Figure F-3: Filled-in Funnel Plots to Evaluate Publication Bias of the PFOA and TC (Left) or HDLC (Right) Association in Studies Reporting Linear Associations.**

Note: The funnel plot shows individual studies included in the analysis according to random-effect beta estimates (x-axis) and the standard error of each study-specific beta (y-axis). The red vertical line indicates the pooled estimate for all studies combined and the gray lines indicate pseudo 95% confidence limits around the pooled estimate. Number of observed studies: 4 (TC) and 6 (HDLC).

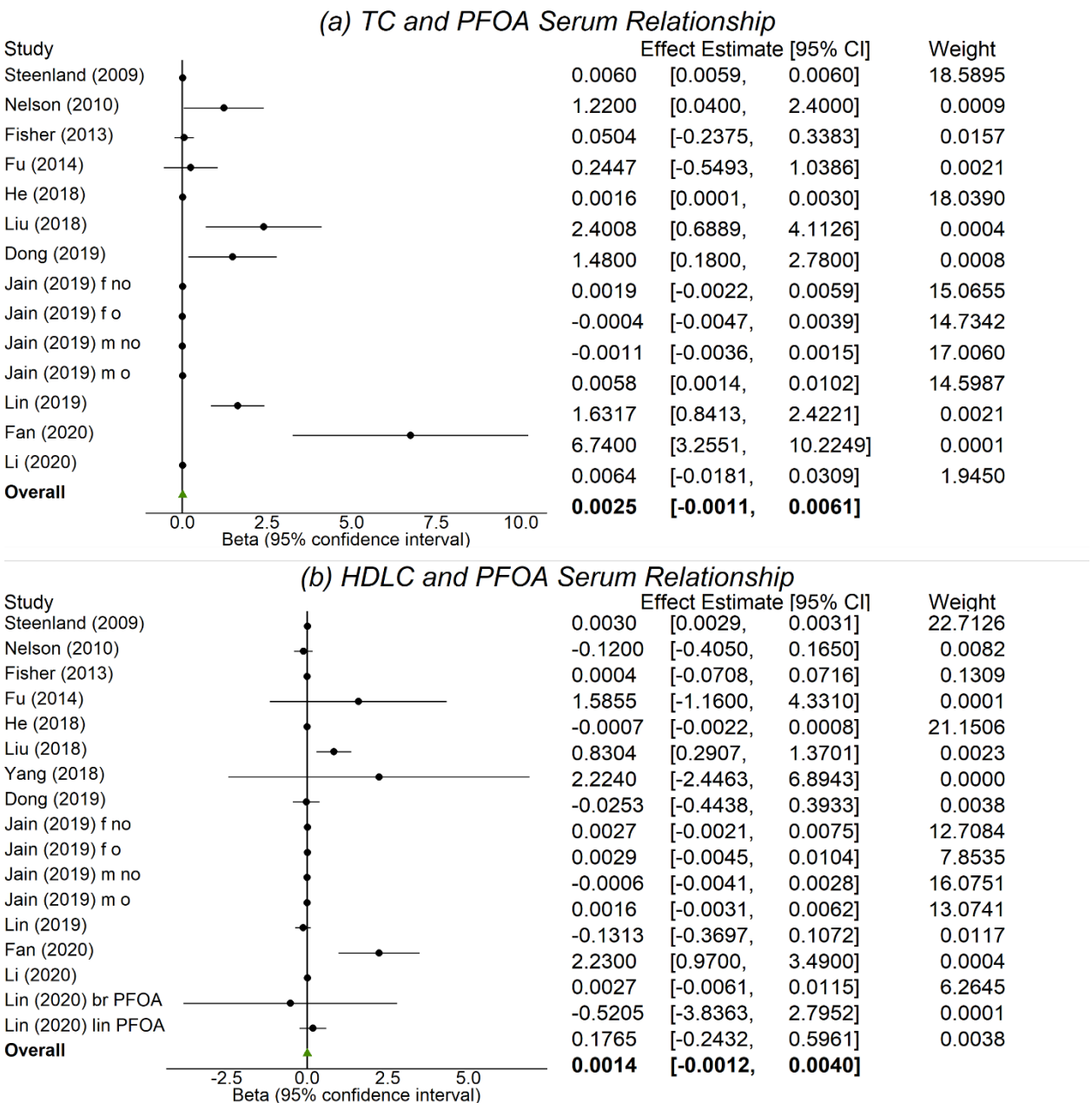



**Figure F-4: Forest Plots Showing the Beta Coefficients Relating TC and HDLC to PFOA Concentrations in Each Study, and Pooled Estimates After Random-Effects Meta-Analysis.**

Abbreviations: f – females; m – males; o – obese; no – non-obese

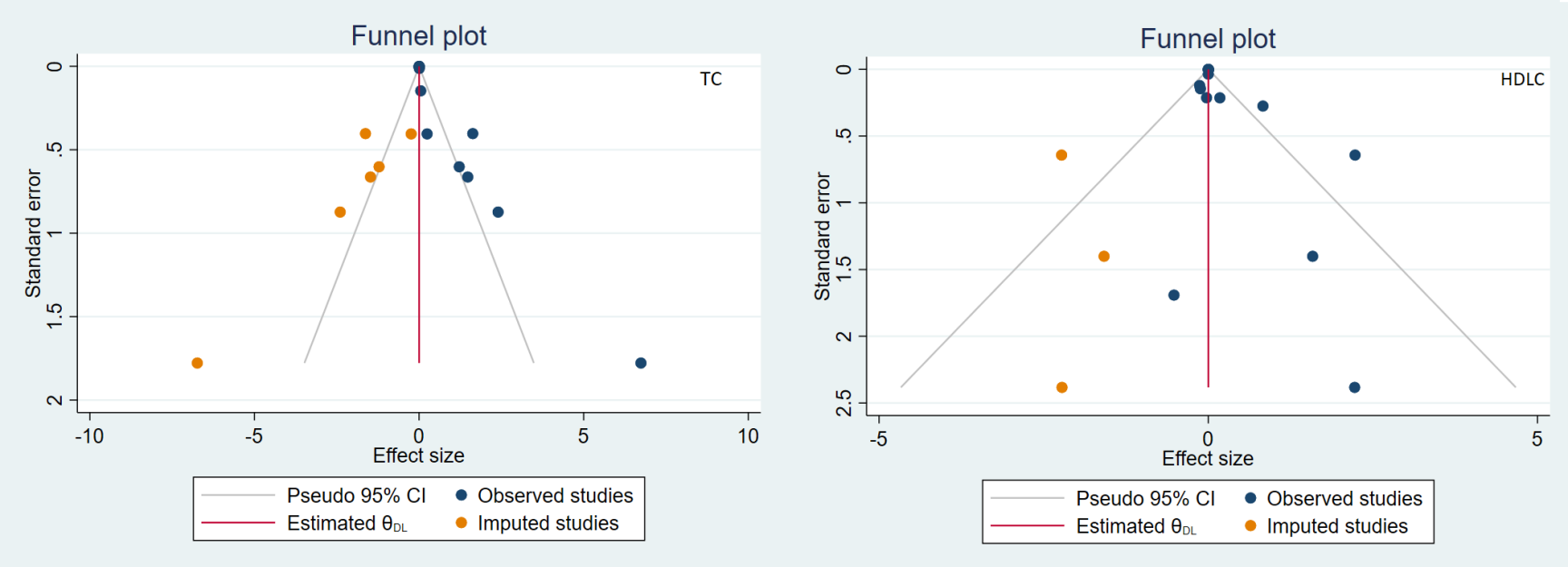



**Figure F-5: Filled-in Funnel Plots to Evaluate Publication Bias of the PF OA and TC (Left) or HDLC (Right) Association.**

Note: The funnel plot shows individual studies included in the analysis according to random-effect beta estimates (x-axis) and the standard error of each study-specific beta (y-axis). The red vertical line indicates the pooled estimate for all studies combined and the gray lines indicate pseudo 95% confidence limits around the pooled estimate. Number of observed studies: 11 (TC) and 13 (HDLC).

## F.4.2 Slope Estimation for PFOS

When including the five studies reporting linear associations, there was a positive increase in TC of 0.08 (95% CI: -0.01, 0.16) mg/dL per ng/mL serum PFOS (p-value=0.064, I2=84%) that was significant at the 0.10 level. The association for PFOS and HDLC was positive but not statistically significant (Table F-3, Figure F-6). Adjusting for possible publication bias through funnel plots and trim-and-fill analysis suggested the imputation of additional studies; however, the magnitude or significance of the pooled associations did not change significantly (Figure F-7).

When all studies were combined (12 studies, 15 results), EPA observed a borderline statistically significant positive increase in TC of 0.066 (95% CI: -0.001, 0.132) mg/dL per ng/mL serum PFOS (p-value=0.055, $I^2$=100%) (Table F-3, Figure F-8). Adjusting for possible publication bias through funnel plots and trim-and-fill analysis suggested the imputation of three additional studies for TC and five for HDLC; however, the pooled effect estimates did not change significantly (Figure F-9). EPA observed similar results in leave-one-out analyses, sensitivity analyses restricted to U.S or Canadian general population studies, and analyses excluding Jain et al. (2019), estimates. Similar results were observed when the analysis excluded the overlapping NHANES studies. When the analysis excluded the higher ROB studies, the association was significantly positive with an increase in in TC of 0.09 (95% CI: 0.01, 0.17) mg/dL per ng/mL serum PFOS (p-value=0.047).

The pooled estimate based on the studies reporting linear associations was 0.08 (95% CI: -0.01, 0.16) and significant at the 0.10 level (p-value=0.064) and there is evidence supporting a positive and significant relationship between PFOS and TC: EPA/OST's review of 41 recent epidemiological studies showed positive associations between PFOS and TC in the general population and the meta-analysis performed with all studies combined showed a positive increase in TC per ng/mL serum PFOS that was significant at the 0.10 level. Given this weight of evidence, the large degree of heterogeneity in the pooled associations when all data were included, and the likelihood of bias that back-transformation of effect estimates with log-transformed outcomes or exposures could introduce (and difficulty with estimating the directionality of this bias towards or away from the null), EPA relied on the results from analyses restricted to studies reporting similar models, favoring the pooled slope (from the six studies reporting linear associations) of 0.08 mg/dL TC and 0.05 mg/dL HDLC per ng/mL serum PFOS for interpretability and use in the CVD risk reduction analysis.[34]

[34] EPA characterizes uncertainty surrounding this estimate as described in Appendix M.

## Table F-3: Results for PFOS Meta-Analyses

| Group | Outcome | N Studies/ Number of Estimates | Beta (mg/dL per ng/mL) | 95% CIs | | p-value | Q[a] | p-value for Q | $I^2$ | $Tau^2$ |
|---|---|---|---|---|---|---|---|---|---|---|
| All Studies | TC | 12/15 | 0.066 | -0.001 | 0.132 | 0.055 | 630000 | < 0.001 | 100 | 0.012 |
| | HDLC | 14/19 | 0.0003 | -0.001 | 0.001 | 0.631 | 158.85 | < 0.001 | 88.67 | 0 |
| **Linear Models Only** | **TC** | **5** | **0.079** | **-0.005** | **0.162** | **0.064** | **25.84** | **< 0.001** | **84.52** | **0.004** |
| | **HDLC** | **6/7** | **0.050** | **-0.005** | **0.105** | **0.074** | **31.69** | **< 0.001** | **81.06** | **0.003** |
| **Sensitivity Analyses** | | | | | | | | | | |
| All lower risk of bias studies | TC | 9/12 | 0.086 | 0.001 | 0.170 | 0.047 | 450000 | < 0.001 | 100 | 0.016 |
| | HDLC | 10/15 | 0.001 | -0.001 | 0.002 | 0.606 | 84.54 | < 0.001 | 83.44 | 0 |
| Exclude Jain et al. (2019) | TC | 11 | 0.114 | 0.012 | 0.217 | 0.028 | 510000 | < 0.001 | 100 | 0.019 |
| | HDLC | 13/15 | -0.002 | -0.002 | 0.001 | 0.778 | 126.90 | < 0.001 | 88.97 | 0 |
| Exclude non-US/Canada and high exposure studies | TC | 8/11 | 0.001 | -0.0004 | 0.001 | 0.301 | 34.71 | < 0.001 | 71.20 | 0 |
| | HDLC | 8/11 | 0.001 | -0.0002 | 0.001 | 0.165 | 13.12 | < 0.001 | 23.76 | 0 |
| All studies, pooled Jain et al. (2019) | TC | 12 | 0.094 | 0.010 | 0.179 | 0.029 | 590000 | <0.001 | 100 | 0.015 |
| | HDLC | 14/16 | -0.0001 | -0.0014 | 0.0013 | 0.943 | 157.53 | <0.001 | 90.48 | 0 |
| All studies, no NHANES overlap | TC | 7 | 0.109 | -0.016 | 0.234 | 0.088 | 120000 | < 0.001 | 100 | 0.022 |
| | HDLC | 9/11 | -0.001 | -0.002 | 0.002 | 0.642 | 94.82 | < 0.001 | 89.45 | 0 |
| Linear models only, no NHANES overlap | TC | 2[b] | 0.192 | -0.162 | 0.546 | 0.288 | 6.88 | 0.009 | 85.46 | 0.057 |
| | HDLC | 3/4 | 0.078 | 0.001 | 0.155 | 0.048 | 7.32 | 0.062 | 59.03 | 0.003 |
| Linear-log models only | TC | 3/6 | 0.0003 | -0.0003 | 0.001 | 0.342 | 8.33 | 0.139 | 39.99 | 0 |
| | HDLC | 5/9 | 0.001 | -0.001 | 0.002 | 0.270 | 15.74 | 0.046 | 49.18 | 0 |
| P.-I. D. Lin et al. (2019) | TC | 1 | 0.132 | -0.005 | 0.269 | >0.05 | 0.00 | NA | NA | NA |
| | HDLC | 1 | -0.021 | -0.062 | 0.020 | >0.05 | 0.00 | NA | NA | NA |
| Dong et al. (2019) | TC | 1 | 0.40 | 0.13 | 0.67 | <0.01 | 0.00 | NA | NA | NA |
| | HDLC | 1 | 0.014 | -0.084 | 0.110 | >0.05 | 0.00 | NA | NA | NA |

Abbreviations: HDLC– High-Density Lipoprotein Cholesterol; TC– Total Cholesterol; PFOS– Perfluorooctanesulfonic Acid.
Notes:
[a]Q statistics for heterogeneity. $Tau^2$ is the between-studies variance. $I^2$ represents the proportion of total variance in the estimated model due to inter-study variation.
Abbreviations: CI – confidence interval; HDLC – High-Density Lipoprotein Cholesterol; NHANES – National Health and Nutrition Examination; TC – Total Cholesterol.
Notes:
[a]Q statistics for heterogeneity. $Tau^2$ is the between-studies variance.
[b]Data from Dong et al. (2019) and Château-Degat et al. (2010).

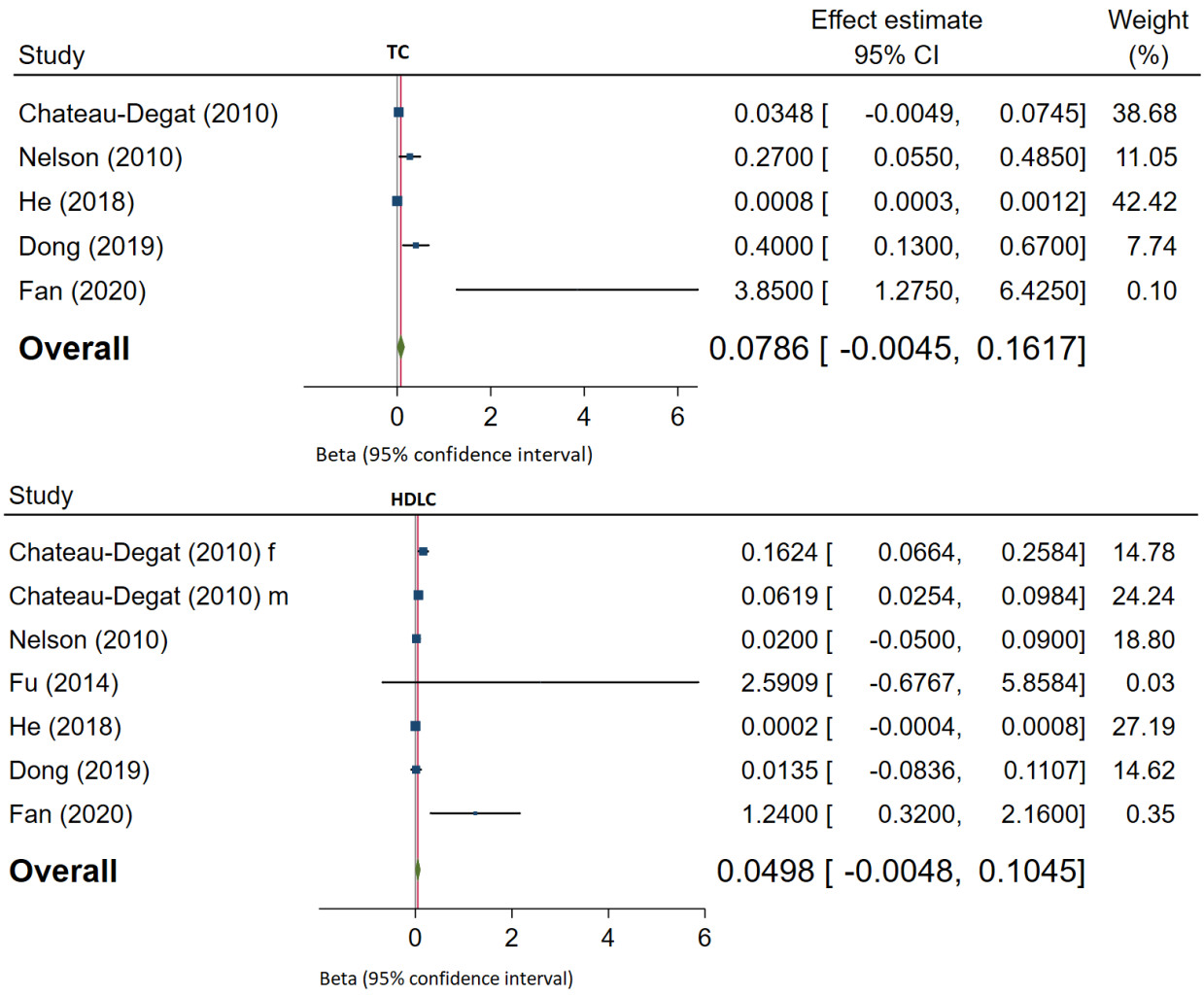



**Figure F-6: Forest Plots Showing the Beta Coefficients Relating TC and HDLC to PFOS Concentrations in Each Study Reporting Linear Associations, and Pooled Estimates After Random-Effects Meta-Analysis.**

Abbreviations: f – females; m – males; o – obese; no – non-obese

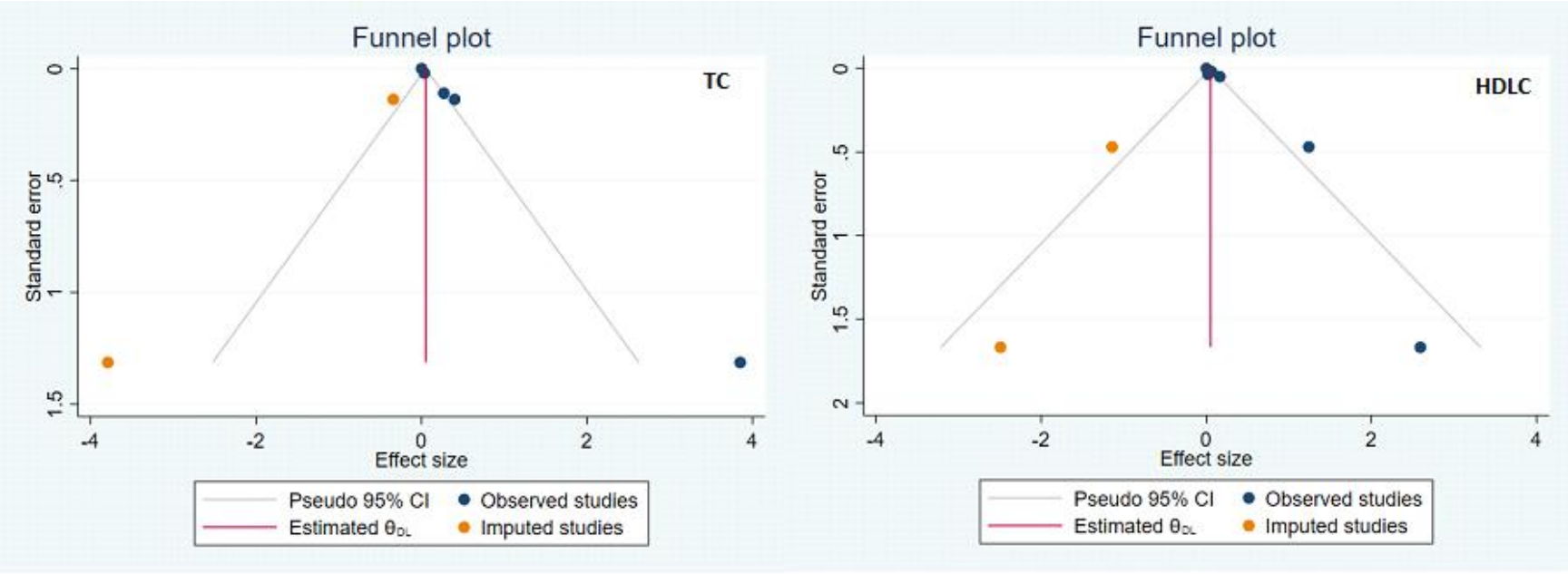



**Figure F-7: Filled-in Funnel Plots to Evaluate Publication Bias of the PFOS and TC (Left) or HDLC (Right) Association in Studies Reporting Linear Associations.**

Note: The funnel plot shows individual studies included in the analysis according to random-effect beta estimates (x-axis) and the standard error of each study-specific beta (y-axis). The red vertical line indicates the pooled estimate for all studies combined and the gray lines indicate pseudo 95% confidence limits around the pooled estimate. Number of observed studies: 5 (TC) and 6 (HDLC).

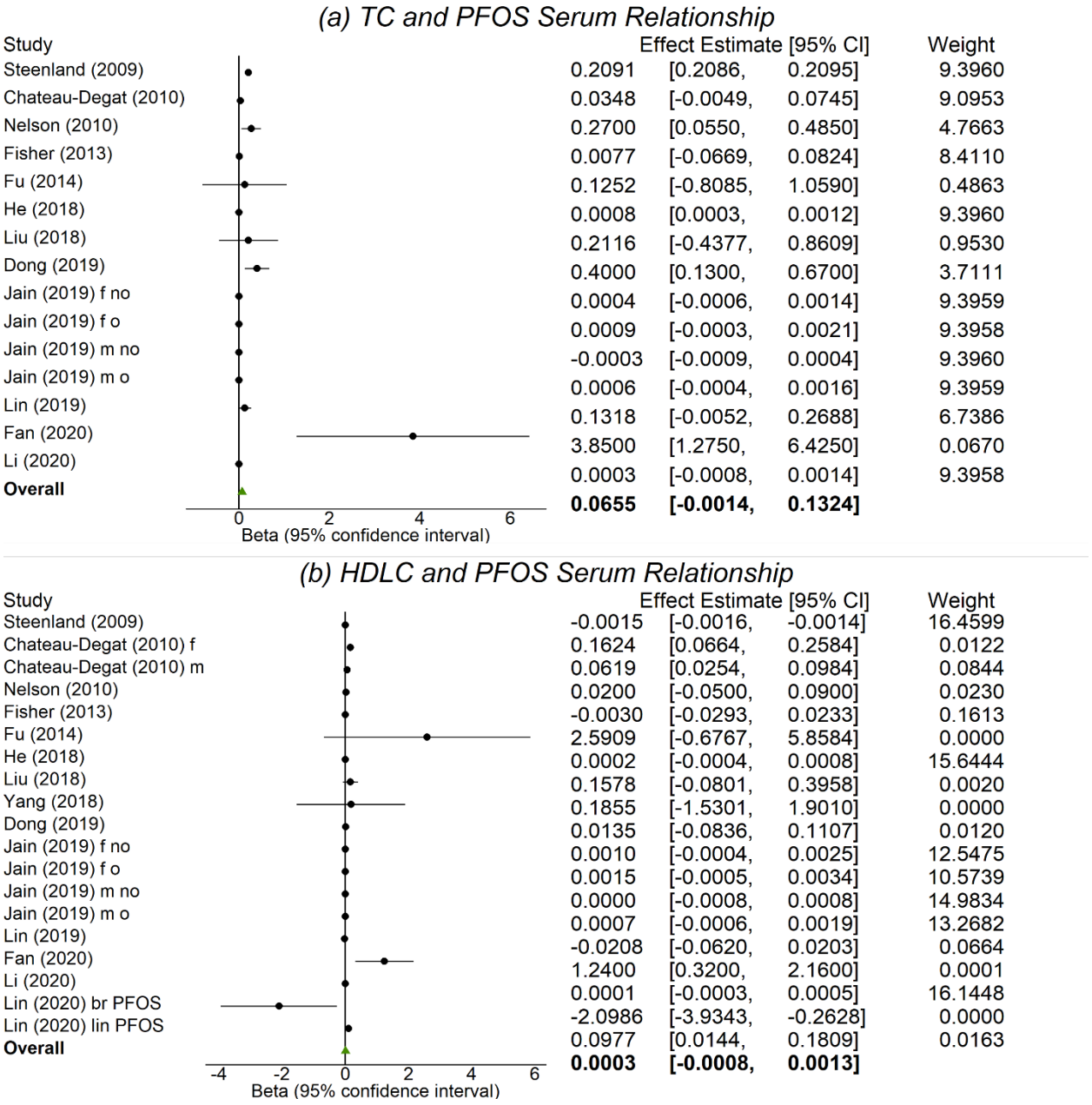



**Figure F-8: Forest Plots Showing the Beta Coefficients Relating PFOS Concentrations to TC and HDLC in Each Study, and Pooled Estimates After Random-Effects Meta-Analysis.**

Abbreviations: f – females; m – males; o – obese; no – non-obese.

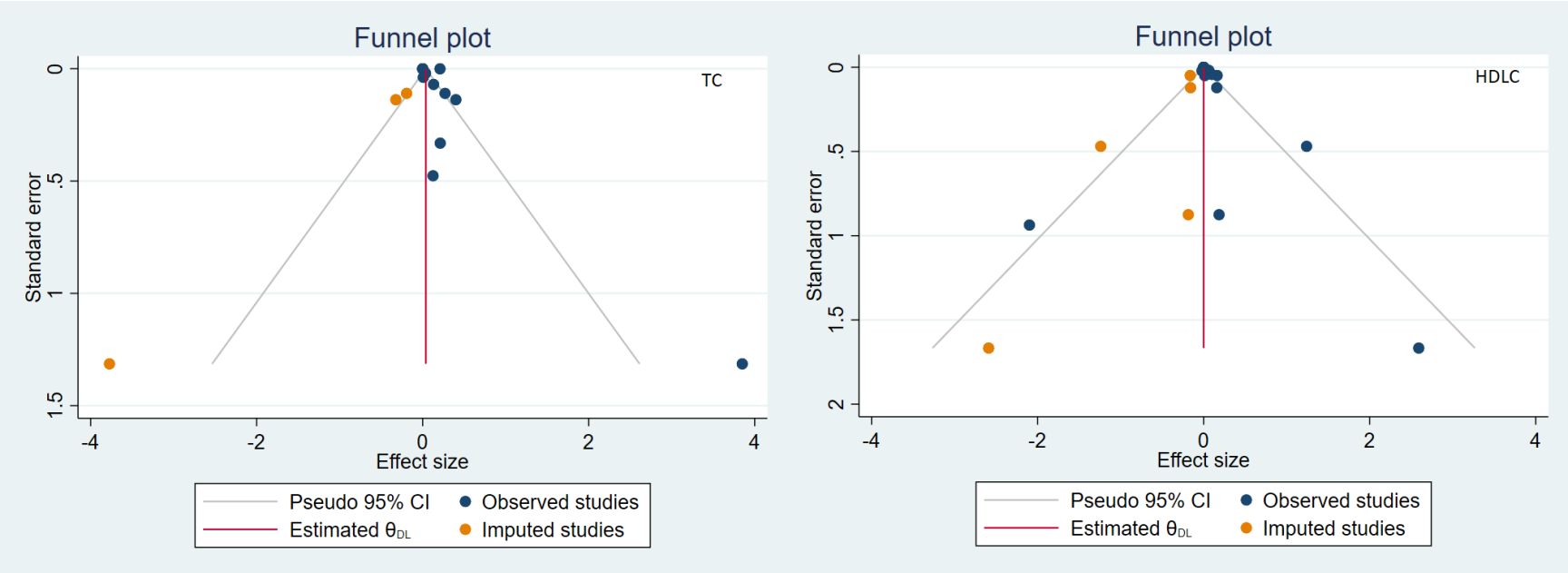



**Figure F-9: Filled-in Funnel Plots to Evaluate Publication Bias of the PFOS and TC (Left) or HDLC (Right) Association.**

Note: The funnel plot shows individual studies included in the analysis according to random-effect beta estimates (x-axis) and the standard error of each study-specific beta (y-axis). The red vertical line indicates the pooled estimate for all studies combined and the gray lines indicate pseudo 95% confidence limits around the pooled estimate. Number of observed studies: 12 (TC) and 14 (HDLC).

## F.4.3 Sensitivity Analyses

EPA considered two studies for use in single-study sensitivity analyses to understand the impact of using the estimates from the meta-analyses in the CVD risk reduction modeling output. These analyses are described in greater detail in Appendix K.

Using data from NHANES (2003–2014) on 8,948 adults, Dong et al. (2019) reported significant increases in TC: 1.48 (95% CI: 0.18, 2.78) mg/dL per ng/mL serum PFOA and 0.40 (95% CI: 0.13, 0.67) mg/dL per ng/mL PFOS (Table F-2). For HDLC the associations were of -0.03 (95% CI: -0.44, 0.39) mg/dL per ng/mL PFOA and 0.01 (95% CI: -0.08, 0.11) mg/dL per ng/mL PFOS. The results were adjusted for age, gender, race, family income index, body mass index, waist circumference, physical activities, diabetes status, smoking status, and number of alcoholic drinks per day. Participants using lipid-lowering medications were excluded. As part of developing EPA's *Toxicity Assessments and Proposed Maximum Contaminant Level Goals for PFOA and PFOS in Drinking Water*, EPA considered this *medium* quality study for estimating point of departure for potential use in toxicity value derivation (U.S. EPA, 2023a; U.S. EPA, 2023b).

The P.-I. D. Lin et al. (2019) study included participants in a clinical trial of the effect of lifestyle modifications on pre-diabetes. This study included 888 pre-diabetic adults who were recruited from 27 medical centers in the US during 1996-1999. The study considered both cross-sectional (baseline) and prospective assessments, with the results showing evidence of an association between PFOA and increased TC and hypertriglyceridemia. Each doubling of plasma PFOA concentration at baseline was associated with 6.1 mg/dL (95% CI: 3.1, 9.0) increase in TC. The results were adjusted for age, sex, race and ethnicity, marital status, educational attainment, drinking, smoking, percent of daily calorie from fat intake, daily fiber intake, physical activity level, and waist circumference at baseline. Participants using lipid-lowering medications were excluded. The results from the longitudinal analysis were not considered because they were not presented in a format amenable for dose-response analyses. The study provides another line of evidence to support associations with TC among adults with pre-diabetes and comparable plasma PFAS concentrations to the U.S. general population.

## F.4.4 Limitations and Uncertainties

Table F-4 summarizes limitations and sources of uncertainty associated with the estimated serum cholesterol dose-response functions. The effects of these limitations and sources of uncertainty on estimates of risk reduction and benefits evaluated in the PFAS National Primary Drinking Water Regulation (NPDWR) are uncertain.

**Table F-4: Limitations and Uncertainties in the Analysis of the Serum Cholesterol Dose Response Functions**

| Uncertainty/Assumption | Notes |
|---|---|
| All of the studies included in the meta-analysis, except one (P.-I. D. Lin et al., 2019), are cross-sectional designs with various design or methodologic limitations. The cross-sectional nature of designs could raise concerns about reverse causality. | Measuring PFOA or PFOS and serum lipids concurrently, as was the case in cross-sectional designs, was considered adequate in terms of exposure assessment timing. Given the long half-lives of PFOA and PFOS (with median half-lives of 2.7 and 3.5 years, respectively; Ying Li et al., 2018), current blood serum concentrations are expected to correlate well with past exposures. Furthermore, although reverse causality due to reverse causation due to hypothyroidism (Dzierlenga, Allen, et al., 2020) or enterohepatic cycling of bile acids (Fragki et al., 2021) has been suggested, there is not yet clear evidence to support these reverse causal pathways. Regarding methodology, several NHANES-based studies (Dong et al., 2019; He et al., 2018) did not clearly report whether sampling weights were used in the analyses to account for the complex sampling design (as is the norm in such survey-based studies). |
| Some NHANES-based studies used data from overlapping NHANES cycles. | Using study results with overlapping years of data could result in double counting certain data and may introduce uncertainty in the meta-analysis estimates. Dong et al. (2019) used data from 2003–2014, while He et al. (2018) used data from 2003–2012; Jain et al. (2019) used data from 2005–2014; Fan et al. (2020) used data from 2011–2014; Liu et al. (2018) used data from 2013–2014; and Nelson et al. (2010) used data from 2003–2004. A sensitivity analysis excluding the overlapping NHANES studies supported the main findings. |
| Studies used a variety of statistical models for estimating the associations of interest (including NHANES-based studies). | Most studies provided measurements of PFOA and PFOS in serum, except in three studies that used measurements in plasma (Château-Degat et al., 2010; Fisher et al., 2013; P.-I. D. Lin et al., 2019). Distribution of PFAS to plasma is chain-length dependent, and within human blood fractions, PFOS and PFOA accumulate to the highest levels in plasma, followed by whole blood and serum. Typically, the study-specific estimated associations are rescaled when the study-specific measurements are in whole blood, but in common practice serum and plasma-based associations are not rescaled. Including these studies in meta-analyses introduces uncertainty in the estimates. |

**Table F-4: Limitations and Uncertainties in the Analysis of the Serum Cholesterol Dose Response Functions**

| Uncertainty/Assumption | Notes |
|---|---|
| Existing approaches are limited in their ability to evaluate statistical heterogeneity and the potential for publication bias | EPA performed statistical evaluations to assess sources of heterogeneity in effect estimates, and to evaluate potential for publication bias. However, the approaches for evaluating heterogeneity and publication bias are sometimes limited in their ability to do so. Evaluating statistical heterogeneity in meta-analyses with a small number of studies is limited by the potential that the $I^2$ statistic can be imprecise and biased, and thus results should be interpreted cautiously (von Hippel, 2015).[a] In evaluating publication bias, the funnel plot asymmetry is a subjective assessment and is recommended only when at least 10 studies are included in the meta-analysis (Higgins et al., 2021). Furthermore, the Egger regression test and Begg's rank tests for publication bias (Begg et al., 1994; Egger et al., 1997; Egger et al., 2008) may suffer from inflated type I error and limited power in certain situations, especially when there is a high degree of heterogeneity (L. Lin et al., 2018). Finally, the small number of studies reporting slopes from similar models limits the power of the meta-analysis. |

Abbreviations: NHANES-The National Health and Nutrition Examination Survey; PFOA- Perfluorooctanoic acid; PFOS- Perfluorooctanesulfonic acid.
Note:
[a]$I^2$ represents the percentage of variation across studies that is due to heterogeneity rather than chance.

# Appendix G. CVD Benefits Model Details and Input Data

This appendix provides details of the CVD model linking changes in TC, HDLC, and systolic blood pressure to changes in incidence of first hard CVD events in populations exposed to PFOA/ PFOS through drinking water. These approaches have been peer reviewed by EPA's Science Advisory Board; input provided by that organization has been considered in finalizing this analysis (U.S. EPA, 2022). As discussed in the SAB in-person meetings and the final report (U.S. EPA, 2022), SAB members and the formal report considered the approaches taken in this document, including using the life table approach and ASCVD model, to be reasonable and valid approaches for estimating reduced CVD cases associated with reduced PFOA and PFOS.

TC and HDLC were linked to serum PFOA and serum PFOS, as described in Appendix F. However, evidence of an association between PFOA and PFOS and HDLC effects was inconclusive (U.S. EPA, 2023a; U.S. EPA, 2023b); therefore, EPA modeled HDLC effects only as part of a sensitivity analysis (see Appendix K). The relationship between BP and serum PFOS among those not using hypertensive medications is discussed in Section 6.5 of the Economic Analysis. First hard CVD events included in the model are non-fatal myocardial infarction (MI), non-fatal ischemic stroke (IS), and coronary heart disease (CHD) deaths. The model also captures post-acute CVD mortality experienced by the first non-fatal MI or IS survivors within 6 years of the initial event.

## G.1 Model Overview and Notation

The CVD model is designed to estimate a time series of hard CVD event incidence for a population cohort characterized by sex, race/ethnicity, birth year, and age at the beginning of the evaluation period (i.e., 2023), and birth year-, age- and sex-specific TC, HDLC, and BP level time series estimated upstream. The first hard CVD event incidence estimates are generated using the Pooled Cohort ASCVD model (Goff et al., 2014), whose predictors include age, cholesterol levels, blood pressure, smoking status, and diabetes status. For those ages 40–80, the ASCVD model predicts the 10-year probability of a hard CVD event—non-fatal MI, fatal and non-fatal IS, or CHD death—to be experienced by a person without a prior history of MI, IS, congestive heart failure, percutaneous coronary intervention, coronary bypass surgery, or atrial fibrillation. EPA models post-acute CVD mortality for survivors of the first MI or IS at ages 45–65 using race/ethnicity- and sex-specific estimates at 1-year and 5-year follow-up from Thom et al. (2001). For survivors of the first MI or IS at age 66 or older, EPA models post-acute CVD mortality using estimates at 1- to 6-year follow-ups from S. Li et al. (2019).

The CVD model integrates the ASCVD model predictions and post-acute CVD mortality estimates in the series of recurrent calculations that produce a life table estimate for the population cohort of interest (e.g., non-Hispanic White females aged 70 years at the beginning of the evaluation period). For each PWS, EPA evaluates population cohorts defined by a combination of birth year and age in or after 2023 (i.e., pairs of (2023,0), (2022,1), (2021,2), … , (1938,85+) and pairs of (2024,0), (2025,0), … , (2065,0)), sex (males and females), and race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, Other). In addition to the standard life table components, such as the annual number of all-cause survivors and deaths for

all ages, for ages 40+, the CVD model estimates the number of surviving persons with and without a history of hard CVD events, the number of persons experiencing hard CVD events at a given age, and deaths from CVD and non-CVD causes at a given age.

Figure G-1 summarizes the main types of CVD model calculations for a population cohort age 0 at the start of the evaluation period.[35] The CVD model calculations are identical across the race/ethnicity and sex demographic subgroups but use subgroup-specific coefficients.[36] For cohorts born prior to or in 2023, the CVD model is initialized using the PWS-, age-, race/ethnicity-, and sex-specific number of persons estimated to be alive in 2021. For cohorts born after 2023, the CVD model is initialized using the PWS-, race/ethnicity-, and sex-specific number of persons aged 0 estimated to be alive in 2021. PWS- and sex, race/ethnicity-, and age-specific population details are included in Appendix B. Once the model is initialized, the following types of calculations occur for each year within the simulation period:

- Recurrent standard life table calculations that rely on the all-cause age-specific annual mortality rates to evaluate the number of deaths among persons of a specific integer age and the number of survivors to the beginning of the next integer age. These calculations are executed whenever the current cohort age is in the 0–39 range. They are represented by the green segments of the timeline shown in Figure G-1.

- Recurrent life table calculations that separately track subpopulations with and without a history of hard CVD events, including estimation of the number of annual CVD and non-CVD deaths (in either subpopulation), as well as the number of annual post-acute CVD deaths experienced by survivors of the first hard CVD events that occurred, at most, 5 years ago. These calculations are executed whenever the current cohort age is over age 40.[37] These calculations are represented by the red segment of the timeline in Figure G-1. Figure G-2 further illustrates the year-specific calculations required for explicit tracking of subpopulations with and without a hard CVD event history.

[35] This initial population cohort age is chosen because it allows for the illustration of the full set of calculation types used in the CVD model.

[36] There are different ASCVD model coefficients for non-Hispanic White and non-Hispanic Black males and females. The figure shows the generalized approach of the CVD model.

[37] People 85 years or older are treated as a single cohort in the model. The mortality rates for this cohort are assumed to be the average mortality rate for those aged 85-100 years. EPA also relied on serum PFOA/PFOS values at age 85 for the 85+ cohort.

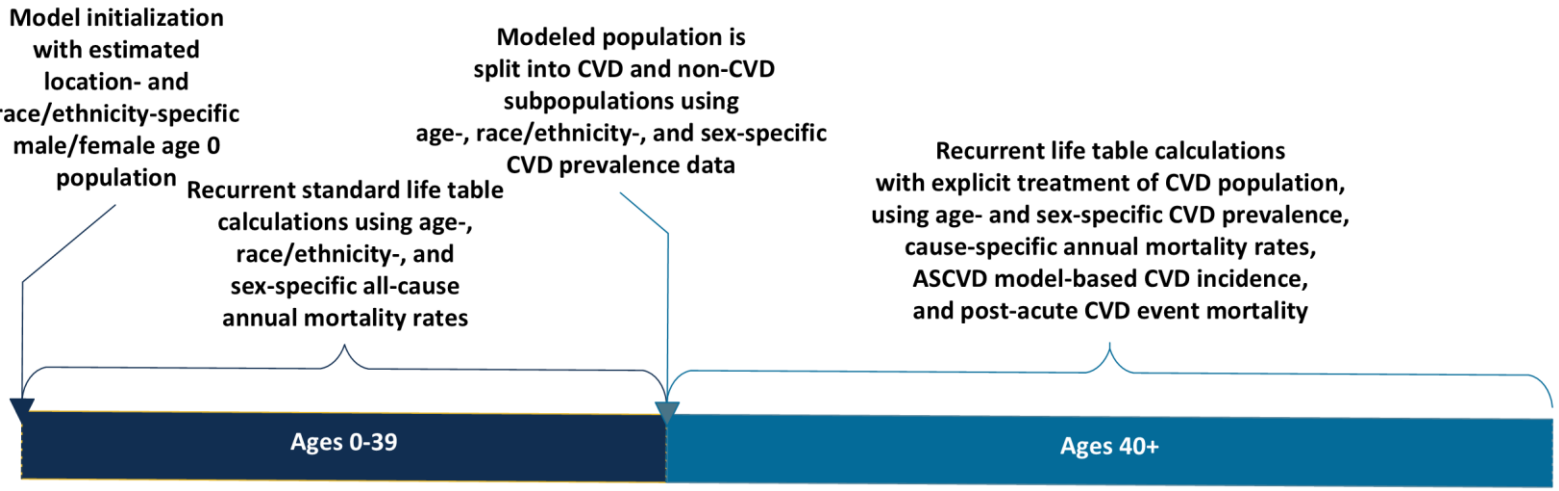



**Figure G-1: Overview of Life Table Calculations in the CVD Model.**

Note: The figure illustrates the model for population cohort age 0 at the beginning of the evaluation period (i.e., calendar year 2023). The model is initialized using an age 0 PWS-specific population (see Appendix B for PWS population details).

Figure G-2 provides additional information on the post-acute CVD mortality estimation. Each person included in the surviving current age-specific incident CVD subpopulation[38] (corresponding to the group F result in Figure G-2) is tracked for 5 additional years to estimate the number of CVD deaths occurring in that timeframe. The recurrent estimates rely on age-specific non-CVD mortality, estimated based on CDC life table data and age- and sex-specific annual CVD mortality rates, and age- and post-acute CVD mortality, estimated based on Thom et al. (2001) and S. Li et al. (2019).

[38] For example, persons who experienced their first non-fatal MI or IS at age 70 and survived through the first post-event year.

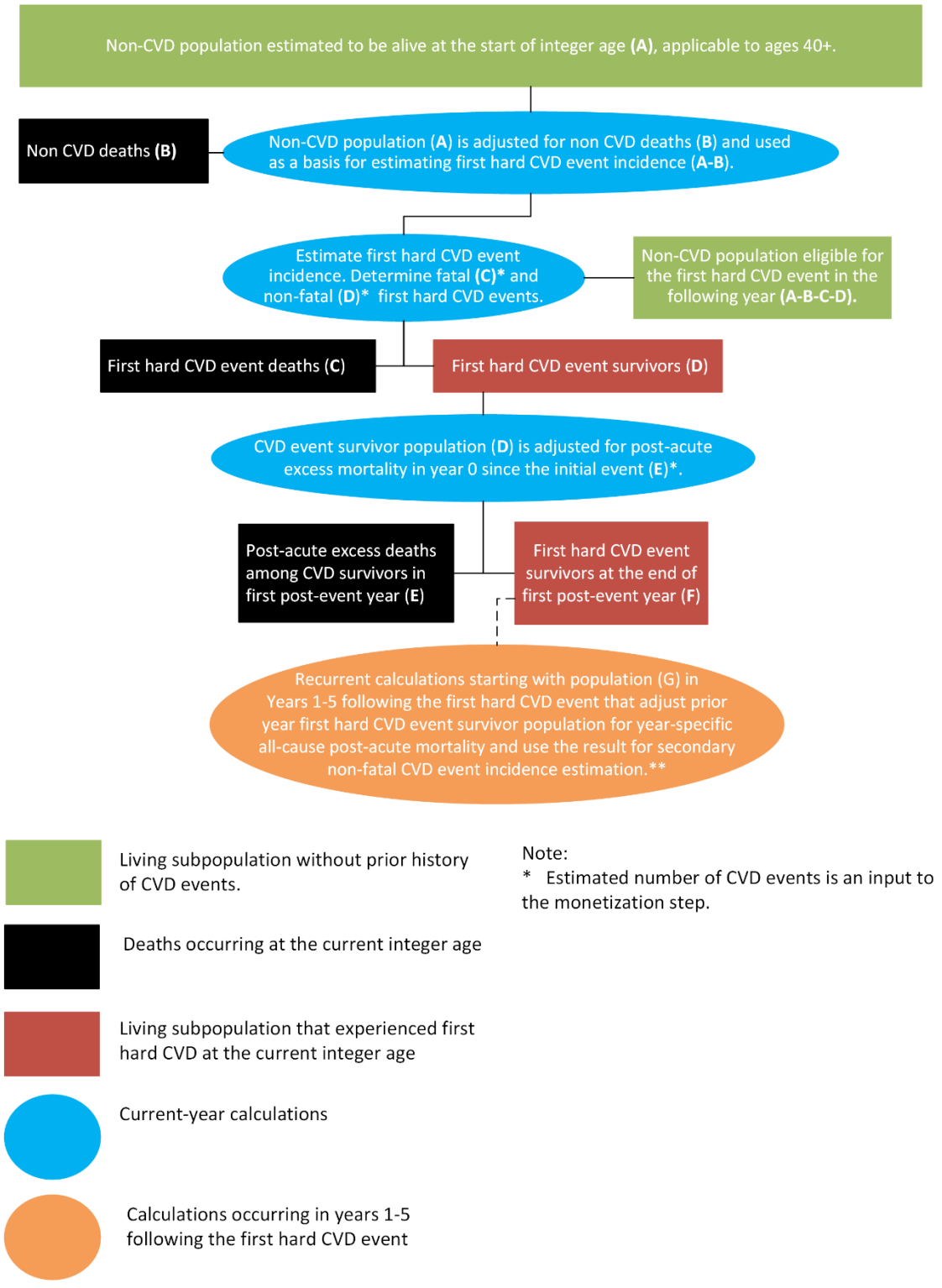



**Figure G-2: CVD Model Calculations Tracking CVD and Non-CVD Subpopulations for a Specific Current Age of Cohort.**

Table G-1 summarizes the data elements and notation of the CVD model.[39] The CVD model elements fall into four categories: indices, data, quantities computed upstream, and internally computed quantities. Information sources and computational notes for the model elements identified as "data" are fully described in Section G.5. Changes in the modeled biomarker levels ($\Delta\tau_{b,a,s,t}$) are a birth year, age, sex, and calendar year-specific quantities computed upstream for the regulatory alternatives as described in Section 6.5 of the Economic Analysis.[40] Section G.2 describes the estimation of first hard CVD event incidence and post-acute CVD mortality, which are internally computed quantities. Derivation of the remaining internally computed quantities for the baseline life table is given in Section G.3.1 and Section G.3.2, while derivation of those quantities for the regulatory alternative life table is given in Section G.3.3.

**Table G-1: CVD Life Table Model Elements and Notation Summary**

| Model Element | Element Type | Definition |
|---|---|---|
| $a$ | Index | Current integer age, $A = \{0,1,2,\ldots,99\}$. The life table model assumes that all persons are born on January 1. |
| $t$ | Index | Current calendar year, $t = 0$ marks the beginning evaluation period, $t = T$ marks the end of evaluation period |
| $b$ | Index | Calendar birth year, $B = \{-T,\ldots,0,1,\ldots,T-40\}$ |
| $s$ | Index | Sex, $S = \{\text{male}, \text{female}\}$ |
| $r$ | Index | Race/Ethnicity, $R = \{\text{non}-\text{Hispanic White}, \text{non}-\text{Hispanic Black}, \text{other}\}$ |
| $f$ | Index | First hard non-fatal CVD event type, $F = \{\text{non}-\text{fatal MI}, \text{non}-\text{fatal IS}\}$ |
| $p$ | Index | Population type: CVD – population with a history of hard CVD events; OTH – non-CVD population |
| $c$ | Index | Cause of death: CVD – cardiovascular disease death; OTH – death from causes other than CVD |
| $k$ | Index | Number of years elapsed since first hard CVD event, $K = \{0,1,2,3,4,5\}$ |
| $l_{b,a,s,r,\max(0,b)}$ | Data | Living population of age $a$, sex $s$, and race/ethnicity $r$, born in year $b$, at the beginning of the evaluation period for the cohort: $t = \max(0, b)$ |
| $l_{b,a,s,r,t}$ | Internally computed quantity | Living population born in year $b$, of sex $s$ and race/ethnicity $r$, at the beginning of integer age $a$ and calendar year $t$ |
| $d_{b,a,s,r,t}$ | Internally computed quantity | Number of all-cause deaths in population born in year $b$, of sex $s$ and race/ethnicity $r$, at integer age $a$ and calendar year $t$ |
| $\pi_{a,s,r}$ | Data | Prevalence rate of persons with past experience of hard CVD events at age $a$, sex $s$, and race/ethnicity $r$ |
| $l_{b,a,s,r,t,p}$ | Internally computed quantity | Living population born in year $b$, of type $p$, sex $s$, and race/ethnicity $r$, at the beginning of integer age $a$ and calendar year $t$. Note that $l_{b,0,s,r,t,\text{CVD}} \equiv 0$, i.e., EPA assumes that people who have just been born do not have CVD history by definition. |

[39] SafeWater was programmed for maximal computational efficiency and SafeWater performs a series of pre-calculations to reduce model runtime. Therefore, the specific equations in the SafeWater code differ from the equations in this Appendix, but the end result is mathematically consistent.

[40] Total cholesterol change for the baseline life table calculations is 0 by definition.

**Table G-1: CVD Life Table Model Elements and Notation Summary**

| Model Element | Element Type | Definition |
|---|---|---|
| $d_{b,a,s,r,t,p,c}$ | Internally computed quantity | Number of deaths from cause $c$ in population born in year $b$, of type $p$, sex $s$, and race/ethnicity $r$, throughout integer age $a$ and calendar year $t$; deaths from cardiovascular causes occur only in the CVD population (i.e., $d_{b,a,s,r,t,\mathrm{OTH,CVD}} \equiv 0$) |
| $q_{a,s,r}$ | Data | General population probability of all-cause death at integer age $a$, sex $s$, race/ethnicity $r$ |
| $q_{a,s,r,c}$ | Data | General population probability of death from cause $c$ at integer age $a$, sex $s$, race/ethnicity $r$ |
| $\Delta\tau_{b,a,s,t}$ | Quantity computed upstream | A 3-tuple of modeled changes in TC/HDLC/BP for population born in year $b$, of sex $s$, age $a$ , in calendar year $t$. Each element of the 3-tuple is set to 0 for baseline calculations for all three biomarkers. Additionally, the change in BP is set to 0 for persons using antihypertensive medications regardless of whether the baseline or the regulatory alternative is evaluated. |
| $i_{b,a,s,r,t}(\Delta\tau_{b,a,s,t})$ | Internally computed quantity | Incidence rate of first hard CVD events for persons born in year $b$, of sex $s$ and race/ethnicity $r$ at age $a$ and calendar year $t$; this rate is computed using the ASCVD model. |
| $\gamma_{a,s,r,f}$ | Data | Share of first non-fatal hard CVD event type $f$ among all first hard CVD events at age $a$ , sex $s$, race/ethnicity $r$ |
| $\rho_{b,a,s,r}$ | Internally computed quantity | Rate of CVD deaths in CVD population born in year $b$, alive at the beginning of age $a$, for sex $s$ and race/ethnicity $r$ |
| $\mu_{a,s,r,f,k}$ | Data | Probability of post-acute CVD death in age $a$, sex $s$, and race/ethnicity $r$ CVD population who experienced first type $f$ non-fatal hard CVD event $k$ integer years ago |
| $x_{b,a,s,r,t}$ | Internally computed quantity | Incident CVD population born in year $b$, of sex $s$ and race/ethnicity $r$, at the beginning of integer age $a$ and calendar year $t$ |
| $\chi_{b,a,s,r,t}$ | Internally computed quantity | Calibration factor for the incident CVD population born in year $b$, of sex $s$ and race/ethnicity $r$, at the beginning of integer age $a$ and calendar year $t$ |
| $\tilde{n}_{b,a,s,r,f,t,0}$ | Internally computed quantity | Uncalibrated number of living age $a$, sex $s$, and race/ethnicity $r$ persons born in year $b$, whose first type $f$ non-fatal hard CVD event occurred 0 years ago, corresponding to calendar year $t$ |
| $n_{b,a,s,r,f,t,k}$ | Internally computed quantity | Number of living age $a$, sex $s$, and race/ethnicity $r$ persons born in year $b$, whose first type $f$ non-fatal hard CVD event occurred $k$ years ago, corresponding to calendar year $t$ |
| $\tilde{m}_{b,a,s,r,t,0}$ | Internally computed quantity | Uncalibrated number of CVD deaths among those born in year $b$, age $a$, sex $s$, and race/ethnicity $r$ persons whose first hard CVD event occurred 0 years ago, corresponding to calendar year $t$ |
| $m_{b,a,s,r,t,k}$ | Internally computed quantity | Number of CVD deaths among those born in year $b$, age $a$, sex $s$, and race/ethnicity $r$ persons whose first hard CVD event occurred $k$ years ago, corresponding to calendar year $t$ |
| $\Delta n_{b,a,s,r,f,t}$ | Internally computed quantity | Difference between regulatory alternative and baseline number of persons born in year $b$, of sex $s$ and race/ethnicity $r$, whose first type $f$ non-fatal hard CVD event occurred at age $a$, corresponding to calendar year $t$ |

**Table G-1: CVD Life Table Model Elements and Notation Summary**

| Model Element | Element Type | Definition |
|---|---|---|
| $\Delta m_{b,a,s,r,t}$ | Internally computed quantity | Difference between calendar year $t$ regulatory alternative and baseline number of CVD deaths among age $a$, sex $s$, and race/ethnicity $r$ persons born in year $b$, who experienced their first hard CVD event during calendar years $t-5$, $t-4$, ... $t$ |
| $\Delta N_{f,t}$ | Internally computed quantity | Difference between regulatory alternative and baseline number of persons whose first type $f$ non-fatal hard CVD event occurred during calendar year $t$ |
| $\Delta M_t$ | Internally computed quantity | Difference between regulatory alternative and baseline number of year $t$ CVD deaths among persons whose first hard CVD event occurred during calendar years $t-5$, $t-4$, ... $t$ |

Abbreviations: ASCVD – atherosclerotic cardiovascular disease; BP – blood pressure; CVD – cardiovascular disease; HDLC – high-density lipoprotein cholesterol; TC – total cholesterol.

## G.2 Hard CVD Event Incidence Estimation

In this section, EPA describes the process for estimating the probability of the first hard CVD event $i_{b,a,s,r,t}(\Delta\tau_{b,a,s,t})$ using the ASCVD model (Section G.2.1); the prevalence of persons with a history of hard CVD events $\pi_{a,s,r}$ (Section G.2.2); the distribution of first hard CVD events by type, including the share of non-fatal first hard CVD events $\gamma_{a,s,r,f}$ (Section G.2.3); and post-acute CVD mortality rates $\mu_{a,s,r,f,k}$ within 6 years of the initial event (Section G.2.4).

### *G.2.1 Probability of the First Hard CVD Event*

The first hard CVD event incidence estimates are generated by the Pooled Cohort ASCVD model (Goff et al., 2014). The ASCVD model is commonly used in clinical practice to estimate CVD risk for those aged 40–80 years. The ASCVD model predicts the 10-year probability of a hard CVD event—fatal and non-fatal MI, fatal and non-fatal IS, or CHD death—to be experienced by a person without a prior history of MI, IS, congestive heart failure, percutaneous coronary intervention, coronary bypass surgery, or atrial fibrillation.

Four large longitudinal community-based epidemiologic cohort studies have been combined to develop a geographically and racially diverse dataset used for the ASCVD model estimation: (1) the Atherosclerosis Risk in Communities Study (Williams, 1989), (2) the Cardiovascular Health Study (Fried et al., 1991), (3) the Coronary Artery Risk Development in Young Adults Study (Friedman et al., 1988), and (4) the Framingham Original and Offspring Cohort Study (Mahmood et al., 2014). Note that there are several other studies whose design is similar to the one used in Goff et al. (2014), including D'Agostino et al. (2001), D'Agostino et al. (2000), D'Agostino et al. (2008), D'Agostino et al. (1994), Pencina et al. (2009), Pencina et al. (2011), Wilson et al. (1998), and Uno et al. (2011). Except for Uno et al. (2011), who also used the Breast Cancer Survival Study (Chang et al., 2005), including D'Agostino et al. (2001), D'Agostino et al. (2000), D'Agostino et al. (2008), D'Agostino et al. (1994), Pencina et al. (2009), Pencina et al. (2011), Wilson et al. (1998), and Uno et al. (2011). Except for Uno et al. (2011), who also used the Breast Cancer Survival Study (Chang et al., 2005), all of these studies used the Framingham cohort study data that are not as diverse as the data used to estimate the ASCVD model.

Table G-2 shows the ASCVD model coefficient estimates used in the analysis. The predictors of the ASCVD model include age, TC and HDLC concentrations, BP, current smoking, diagnosed diabetes, and whether the subject is undergoing treatment for high BP. The model has been fit separately to four population subgroups: non-Hispanic White females, non-Hispanic Black females, non-Hispanic White males, and non-Hispanic Black males. EPA applied sex-specific model coefficients for non-Hispanic Blacks to estimate CVD risk in Hispanic and non-Hispanic other race population subgroups based on validation of the ASCVD model against published statistics as described in Section G.4.

**Table G-2: ASCVD Model Coefficients**

| Variable Name | Model Coefficient | | | |
|---|---|---|---|---|
| | Non-Hispanic White Females | Non-Hispanic Black Females* | Non-Hispanic White Males | Non-Hispanic Black Males* |
| Ln Age (y) | -29.799 | 17.114 | 12.344 | 2.469 |
| Ln Age, squared | 4.884 | – | – | – |
| Ln Total Cholesterol (mg/dL) | 13.54 | 0.94 | 11.853 | 0.302 |
| Ln Age × Ln Total Cholesterol | -3.114 | – | -2.664 | – |
| Ln HDL-C (mg/dL) | -13.578 | -18.92 | -7.99 | -0.307 |
| Ln Age × Ln HDL-C | 3.149 | 4.475 | 1.769 | – |
| Ln Treated Systolic BP (mm Hg) | 2.019 | 29.291 | 1.797 | 1.916 |
| Ln Age x Ln Treated Systolic BP | – | -6.432 | – | – |
| Ln Untreated Systolic BP (mm Hg) | 1.957 | 27.82 | 1.764 | 1.809 |
| Ln Age x Ln Untreated Systolic BP | – | -6.087 | – | – |
| Current Smoker (1=Yes, 0=No) | 7.574 | 0.691 | 7.837 | 0.549 |
| Ln Age × Current Smoker | -1.665 | – | -1.795 | – |
| Diabetes (1=Yes, 0=No) | 0.661 | 0.874 | 0.658 | 0.645 |
| Mean (Coefficient × Value), $\bar{x}_{s,r}{}' \beta_{s,r}$ | -29.18 | 86.61 | 61.18 | 19.54 |
| ASCVD Baseline Survival, $S_{s,r}$ | 0.9665 | 0.9533 | 0.9144 | 0.8954 |

Abbreviations: ASCVD – atherosclerotic cardiovascular disease; BP – blood pressure; HDLC – high-density lipoprotein cholesterol.
Note:
* Based on the results of ASCVD model validation exercises (Section G.4), the models for non-Hispanic Black males and females are applied to other ethnic groups.

*Source: Goff et al. (2014), Table A*

In order to be used for risk estimation, the ASCVD model needs to be parameterized using values of the predictors shown in Table G-2 that are appropriate for the current age, sex, and race/ethnicity of the cohort being evaluated. As shown in Table G-1, current age, sex, and race/ethnicity are easily accessible indices of the CVD model. In turn, baseline values for the other ASCVD model predictors come from several public health surveys implemented by the Centers for Disease Control and Prevention, as detailed in Section G.5.

To compute the 10-year probability of the first hard CVD event for a birth year $b$, sex $s$ and race/ethnicity $r$ cohort at age $a$, EPA uses the ASCVD risk equation (Goff et al., 2014, Table G-5) adjusted to express the type of scenario being evaluated (i.e., baseline or regulatory alternative):

Equation G-1:

$$R_{b,a,s,r,t:t+9}\left(\Delta\tau_{b,a,s,t}\right) = 1 - S_{s,r}^{\exp\left(\ln\left(\tau_{a,s,r}+\Delta\tau_{b,a,s,t}\right)'\left[\beta_{\tau,s,r}+\beta_{a\tau,s,r}\cdot\ln(a)\right]+x_{-\tau,a,s,r}'\beta_{-\tau,s,r}-\bar{x}_{s,r}'\beta_{s,r}\right)}$$

where

$R_{b,a,s,r,t:t+9}\left(\Delta\tau_{b,a,s,t}\right)$ probability of the first hard CVD event to occur between years $t$ and $t+9$ for a birth year $b$, sex $s$ / race/ethnicity $r$ person whose age at time $t$ is $a$. $R_{b,a,s,r,t:t+9}(0)$ represents baseline 10-year first hard CVD event risk, whereas $R_{b,a,s,r,t:t+9}\left(\Delta\tau_{b,a,s,t}\right)$ expresses regulatory alternative risk consistent with a birth year $b$-, age $a$-, sex $s$-, calendar year $t$-specific change in the baseline TC/HDLC/BP levels $\Delta\tau_{b,a,s,t}$;

$S_{s,r}$ ASCVD baseline CVD event-free survival rate at 10 years, consistent with the sex $s$ and race/ethnicity $r$ of the cohort being evaluated (see parameter estimates in Table G-2);

$\tau_{a,s,r}$ a vector of baseline inputs for TC, HDLC, and BP consistent with the current age $a$, sex $s$, and race/ethnicity $r$ of the cohort being evaluated (see Section G.5);

$\beta_{\tau,s,r}$ a vector of ASCVD model coefficients for the log-TC, log-HDLC, log-BP predictors, consistent with the sex $s$ and race/ethnicity $r$ of the cohort being evaluated (see parameter estimates in Table G-2);

$\beta_{a\tau,s,r}$ a vector of ASCVD model coefficient for the interaction between log-current age and log-TC, log-HDLC, log-BP predictor, consistent with the sex $s$ and race/ethnicity $r$ of the cohort being evaluated (see parameter estimates in Table G-2);

$x_{-\tau,a,s,r}'\beta_{-\tau,s,r}$ inner product of the ASCVD model coefficient vector (excluding TC, HDLC, and BP-related coefficients) and a vector of baseline input values (excluding TC, HDLC, and BP-related inputs), consistent with the current age $a$, sex $s$, and race/ethnicity $r$ of the cohort being evaluated (see parameter estimates in Table G-2 and Section G.5); and

$\bar{x}_{s,r}'\beta_{s,r}$ inner product of the ASCVD model coefficient vector and a vector of average input values in the ASCVD estimation dataset (see parameter estimates in Table G-2).

To obtain the annual probability of the first hard CVD event, EPA adjusts $R_{b,a,s,r,t:t+9}(\Delta\tau_{b,a,s,t})$ as follows:

Equation G-2:

$$i_{b,a,s,r,t}(\Delta\tau_{b,a,s,t}) = 1 - \left(1 - R_{b,a,s,r,t:t+9}(\Delta\tau_{b,a,s,t})\right)^{\frac{1}{10}}$$

where

$i_{b,a,s,r,t}(\Delta\tau_{b,a,s,t})$ probability of the first hard CVD event to occur in year $t$ for a birth year $b$, sex $s$ / race/ethnicity $r$ person whose age at time $t$ is $a$; and

$R_{b,a,s,r,t:t+9}(\Delta\tau_{b,a,s,t})$ probability of the first hard CVD event to occur between years $t$ and $t + 9$ for a birth year $b$, sex $s$ / race/ethnicity $r$ person whose age at time $t$ is $a$.

## G.2.2 Prevalence of Past Hard CVD Events

Because the population evaluated for the first hard CVD event estimation excludes those with a history of hard CVD events, model inputs require information on the baseline prevalence of the past hard CVD event history in the U.S. population. EPA used the Medical Expenditure Panel Survey (MEPS) 2010–2017 data to estimate the prevalence of persons with a prior experience of hard CVD events, including MI, stroke, and other acute CHD events. MEPS is a nationally representative survey of the U.S. civilian non-institutionalized population implemented by the Agency for Healthcare Research and Quality (AHRQ). The survey has an overlapping panel design, tracking individuals for, at most, two years and interviewing participants, at most, six times. MEPS collects demographic, socioeconomic, and health status information on the first interview and in each subsequent interview asks about medical events experienced between the current and the previous interview (generally 4–5 months), as well as changes in employment status, health insurance coverage, and so forth. Section G.5 provides additional information on MEPS public use files that have been used in this analysis.

The prevalence of persons with a prior experience of hard CVD events has been estimated by dividing the number person-years in MEPS interview rounds with a reported history of MI, stroke, or other CHD by the total number of person-years in subpopulations defined by sex and round-specific age. The estimated ratios have been adjusted for MEPS complex survey design.

Table G-3 shows the resulting estimates of sex-, race/ethnicity-, and age category-specific prevalence of persons with prior experience of hard CVD events, along with 95% confidence intervals that reflect sampling uncertainty. Compared with the prevalence estimates for females, the estimated prevalence is higher for males in all age categories and for all CVD event categories. Among adults aged 65 or older, estimated MI, other CHD, and overall prevalence is highest for non-Hispanic White males, while stroke prevalence is highest among non-Hispanic Black males. Regardless of the age category, the estimated prevalence of an MI history is higher for males, while the prevalence of a stoke history is higher for females. The prevalence of other CHD event history is approximately three to 10 times higher compared with the prevalence of an MI or stroke history.

**Table G-3: Estimated Past Hard CVD Event Prevalence per 100,000**

| Sex | Age (years) | Race/ Ethnicity | MI | Stroke | Other CHD | Overall |
|---|---|---|---|---|---|---|
| Males | 18–44 | NH White | 632 (410–855) | 495 (317–673) | 5,709 (5,072–6,346) | 6,292 (5,620–6,965) |
| | 45–64 | NH White | 5,099 (4,569–5,629) | 3,314 (2,804–3,823) | 15,439 (14,523–16,355) | 17,963 (16,930–18,995) |
| | 65 or older | NH White | 16,477 (15,088–17,865) | 11,002 (9,956–12,047) | 41,600 (40,040–43,161) | 47,465 (45,831–49,099) |
| Males | 18–44 | NH Black | 436 (146–726) | 614 (304–924) | 3,886 (2,998–4,773) | 4,667 (3,651–5,684) |
| | 45–64 | NH Black | 4,786 (3,928–5,644) | 5,316 (4,222–6,409) | 12,261 (10,801–13,720) | 16,590 (14,898–18,282) |
| | 65 or older | NH Black | 13,768 (11,218–16,319) | 18,908 (16,185–21,631) | 30,307 (26,724–33,891) | 42,090 (38,368–45,812) |
| Males | 18–44 | Hispanic | 480 (293–667) | 180 (75–285) | 3,065 (2,479–3,651) | 3,417 (2,816–4,019) |
| | 45–64 | Hispanic | 4,299 (3,383–5,214) | 3,010 (2,225–3,796) | 9,979 (8,640–11,318) | 12,584 (11,045–14,124) |
| | 65 or older | Hispanic | 14,071 (11,569–16,573) | 8,254 (6,031–10,477) | 25,866 (22,420–29,313) | 30,548 (26,960–34,136) |
| Males | 18–44 | NH Other | 347 (122–572) | 342 (75–610) | 3,262 (2,330–4,194) | 3,669 (2,695–4,643) |
| | 45–64 | NH Other | 4,338 (3,012–5,665) | 2,693 (1,791–3,595) | 11,339 (9,033–13,645) | 13,638 (11,118–16,158) |
| | 65 or older | Other | 12,256 (9,167–15,344) | 12,354 (8,911–15,798) | 30,516 (25,051–35,982) | 36,932 (31,240–42,624) |
| Females | 18–44 | NH White | 439 (278–600) | 830 (608–1,052) | 6,262 (5,528–6,997) | 6,954 (6,223–7,685) |
| | 45–64 | NH White | 2,199 (1,841–2,557) | 3,127 (2,595–3,659) | 15,496 (14,522–16,469) | 17,925 (16,791–19,059) |
| | 65 or older | NH White | 7,510 (6,686–8,335) | 10,055 (9,098–11,011) | 31,861 (30,278–33,445) | 37,538 (35,913–39,162) |
| Females | 18–44 | NH Black | 393 (204–582) | 1,092 (783–1,402) | 4,628 (3,917–5,338) | 5,612 (4,847–6,378) |
| | 45–64 | NH Black | 3,484 (2,808–4,160) | 6,491 (5,640–7,343) | 15,292 (13,915–16,670) | 19,596 (17,981–21,210) |
| | 65 or older | NH Black | 8,803 (7,130–10,476) | 14,188 (12,304–16,071) | 29,296 (26,441–32,151) | 38,073 (35,102–41,045) |
| Females | 18–44 | Hispanic | 313 (171–454) | 717 (469–965) | 3,690 (3,182–4,199) | 4,363 (3,808–4,918) |
| | 45–64 | Hispanic | 2,597 (1,947–3,248) | 3,627 (2,864–4,391) | 10,335 (9,066–11,604) | 12,777 (11,361–14,193) |
| | 65 or older | Hispanic | 7,513 (5,953–9,073) | 9,469 (7,385–11,554) | 23,149 (20,350–25,948) | 29,186 (26,206–32,167) |
| Females | 18–44 | NH Other | 722 (123–1,320) | 383 (90–675) | 4,569 (3,181–5,957) | 4,884 (3,502–6,266) |
| | 45–64 | NH Other | 1,292 (710–1,874) | 2,770 (1,679–3,860) | 11,098 (8,978–13,218) | 13,148 (10,758–15,538) |
| | 65 or older | NH Other | 4,150 (2,557–5,742) | 7,321 (5,054–9,589) | 19,001 (15,308–22,694) | 23,463 (19,638–27,288) |

**Table G-3: Estimated Past Hard CVD Event Prevalence per 100,000**

| Sex | Age (years) | Race/ Ethnicity | MI | Stroke | Other CHD | Overall |
|---|---|---|---|---|---|---|

Abbreviations: MI – myocardial infarction (ICD9=410 or MIDX=1); NH – non-Hispanic; Other CHD – other coronary heart disease (ICD9=413,414,427,428 or CHDDX=1, ANGIDX=1, OHRTDX=1); Stroke (ICD9=433,434,435,436 or STRKDX=1); 95% confidence interval shown in parentheses below the point estimate.
*Source: EPA analysis based on MEPS, 2010–2017*

## *G.2.3 Distribution of Fatal and Non-Fatal First Hard CVD Events*

The ASCVD model predicts the risk of a composite hard CVD event (i.e., MI, IS, or CHD death). However, modeling requires separate tracking of morbidity and mortality for life table calculation purposes. In addition, acute-phase mortality and morbidity valuation depends on the endpoint (i.e., MI or IS). Therefore, EPA used MEPS 2010–2017 data to estimate the distribution of first hard CVD events by type of condition (i.e., MI, stroke, and other CHD). EPA estimated the incidence of first hard CVD events by dividing the number of person-years in MEPS interview rounds with reported new occurrences of MI, stroke, or other CHD by the number of person-years in MEPS interview rounds without resorted prior experience of CVD events, in subpopulations defined by race/ethnicity, sex and round-specific age. EPA adjusted the estimated ratios for MEPS complex survey design. Distribution of CVD events by condition type was calculated based on the estimated condition-specific incidence rates.

Table G-4 shows the resulting estimates of sex-, race/ethnicity-, and age category-specific first hard CVD event incidence, along with 95% confidence intervals that reflect sampling uncertainty. The table also shows the distribution of first hard CVD events by event type. In males, 15% to 17% of first hard CVD events are MIs, whereas 13% to 20% of first hard CVD events are strokes. In females, 8% to 12% of first hard CVD events are MIs, whereas 17% to 28% of first hard CVD events are strokes. The shares of MIs and strokes increase with age for both sexes. Among adults aged 65 or older, estimated MI, stroke, other CHD, and overall incidence are highest for non-Hispanic White males and females.

**Table G-4: Estimated First Hard CVD Event Incidence and Distribution by CVD Event Type**

| Sex | Age (years) | Race/ Ethnicity | MI | Stroke | Other CHD | Overall |
|---|---|---|---|---|---|---|
| | | | 82 | 57 | 454 | 540 |
| Males | 18–44 | NH White | (29–135) | (3–110) | (299–609) | (375–705) |
| | | | 356 | 333 | 1,536 | 2,048 |
| | 45–64 | NH White | (225–486) | (194–471) | (1,213–1,859) | (1,678–2,417) |
| | | | 1,326 | 2,001 | 6,233 | 8,125 |
| | 65 or older | NH White | (679–1,973) | (1,248–2,754) | (5,035–7,431) | (6,651–9,598) |
| | | | 23 | 81 | 363 | 447 |
| Males | 18–44 | NH Black | (-3–49) | (4–159) | (156–570) | (227–668) |
| | | | 235 | 805 | 1,039 | 1,862 |
| | 45–64 | NH Black | (64–407) | (399–1,211) | (676–1,401) | (1,339–2,385) |
| | | | 319 | 765 | 2,332 | 3,273 |
| | 65 or older | NH Black | (-1–639) | (76–1,454) | (1,217–3,447) | (1,926–4,621) |
| Males | 18–44 | Hispanic | 52 | 40 | 135 | 212 |

**Table G-4: Estimated First Hard CVD Event Incidence and Distribution by CVD Event Type**

| Sex | Age (years) | Race/ Ethnicity | MI | Stroke | Other CHD | Overall |
|---|---|---|---|---|---|---|
| | | | (6–99) | (-4–83) | (55–214) | (111–313) |
| | | | 276 | 421 | 735 | 1,142 |
| | 45–64 | Hispanic | (72–479) | (2–839) | (419–1,052) | (625–1,659) |
| | | | 951 | 816 | 2,747 | 3,915 |
| | 65 or older | Hispanic | (285–1,618) | (349–1,283) | (1,432–4,061) | (2,440–5,390) |
| | | | 72 | 85 | 121 | 278 |
| Males | 18–44 | NH Other | (-70–215) | (-54–223) | (35–207) | (63–493) |
| | | | 830 | 548 | 1,513 | 2,537 |
| | 45–64 | NH Other | (171–1,489) | (39–1,057) | (643–2,383) | (1,356–3,718) |
| | | | 665 | 1,232 | 2,940 | 4,251 |
| | 65 or older | NH Other | (-14–1,343) | (431–2,033) | (1,496–4,383) | (2,506–5,997) |
| | | | 56 | 135 | 492 | 646 |
| Females | 18–44 | NH White | (-21–134) | (54–216) | (317–668) | (437–856) |
| | | | 140 | 407 | 1,423 | 1,865 |
| | 45–64 | NH White | (56–225) | (193–620) | (1,109–1,737) | (1,490–2,240) |
| | | | 831 | 2,102 | 4,271 | 6,294 |
| | 65 or older | NH White | (533–1,130) | (1,498–2,705) | (3,461–5,081) | (5,358–7,231) |
| | | | 96 | 57 | 487 | 597 |
| Females | 18–44 | NH Black | (1–191) | (5–108) | (279–695) | (360–834) |
| | | | 196 | 530 | 1,168 | 1,754 |
| | 45–64 | NH Black | (74–318) | (247–812) | (793–1,543) | (1,285–2,223) |
| | | | 382 | 1,607 | 3,383 | 4,546 |
| | 65 or older | NH Black | (8–756) | (762–2,453) | (2,221–4,545) | (3,179–5,913) |
| | | | 38 | 78 | 308 | 392 |
| Females | 18–44 | Hispanic | (-24–100) | (25–131) | (130–487) | (190–595) |
| | | | 145 | 308 | 664 | 1,065 |
| | 45–64 | Hispanic | (33–257) | (76–541) | (393–936) | (699–1,432) |
| | | | 992 | 1,321 | 2,610 | 4,456 |
| | 65 or older | Hispanic | (215–1,768) | (611–2,031) | (1,670–3,550) | (3,348–5,564) |
| | | | 47 | | 315 | 315 |
| Females | 18–44 | NH Other | (-46–141) | Omitted | (42–589) | (42–589) |
| | | | 201 | 399 | 759 | 1,297 |
| | 45–64 | NH Other | (-6–409) | (74–724) | (259–1,259) | (627–1,967) |
| | | | 576 | 1,328 | 2,689 | 4,349 |
| | 65 or older | NH Other | (-43–1,195) | (381–2,276) | (1,234–4,144) | (2,463–6,234) |

Abbreviations: MI – myocardial infarction (ICD9=410 or MIDX=1); NH – non-Hispanic, Stroke (ICD9=433,434,435,436 or STRKDX=1); Other CHD – other coronary heart disease (ICD9=413,414,427,428 or CHDDX=1, ANGIDX=1, OHRTDX=1); 95% confidence interval shown in parentheses below the point estimate.

The ASCVD model predicts the risk of first MI (fatal and non-fatal), IS (fatal and non-fatal), or other fatal CHD within the next 10 years. Notably, other non-fatal CHD events are not included among the CVD event types predicted by the ASCVD model (Goff et al., 2014). Because MEPS data do not have sufficient information to estimate acute-phase CVD event mortality, EPA used AHRQ's Healthcare Cost and Utilization Project (HCUP) data on hospital mortality to allocate CVD events into fatal and non-fatal categories. Section G.5 provides additional information on the in-hospital mortality data.

Table G-5 shows sex- and age category-specific probability of in-hospital CVD event death based on HCUP 2017 inpatient data (Agency for Healthcare Research and Quality, 2017a). Probability of an in-hospital death is highest for MI events (4.64%), followed by IS events (4.01%), and then other CHD events (1.07%). This probability grows with age across all CVD event types and is higher for females when compared with males.

**Table G-5: Probability of Hospital Death for a Hard CVD Event**

| Category | MI (%) | IS (%) | Other CHD (%) |
|---|---|---|---|
| Overall | 4.65 | 4.01 | 1.07 |
| **Age (years)** | | | |
| 18–44 | 1.43 | 1.91 | 0 |
| 45–64 | 2.60 | 2.46 | 0.67 |
| 65–84 | 5.42 | 3.88 | 1.23 |
| 85 or older | 9.80 | 7.29 | 3.14 |
| **Sex** | | | |
| Males | 4.41 | 3.71 | 1.01 |
| Females | 5.04 | 4.30 | 1.20 |

Abbreviations: IS – ischemic stroke (ICD10=I63); MI – myocardial infarction (ICD10=I21); Other CHD – other coronary heart disease (ICD10=I20, I22-I25).
*Source: HCUP 2017 (Agency for Healthcare Research and Quality, 2017a)*

EPA combined estimates in Table G-4 and Table G-5 to derive the ASCVD event distribution over the following event types: non-fatal MI, non-fatal IS, and fatal CVD events (i.e., fatal MI, fatal IS, and other fatal CHD events). Table G-6 shows the final sex-, race/ethnicity-, and age category-specific estimates of the ASCVD event distribution needed as the CVD model input. For males, the share of non-fatal MI events is 22% to 58%, the share of non-fatal IS events is 39% to 77%, and the share of fatal CVD events is 2% to 13%. For females, the share of non-fatal MI events is 16% to 62%, the share of non-fatal IS events is 36% to 76%, and the share of fatal CVD events is 2% to 14%. The shares of non-fatal MI decrease with age, whereas the share of fatal CVD events increase with age. Shares of non-fatal MI are generally highest among non-Hispanic White males, while shares of non-fatal IS are highest among non-Hispanic Black males. Among non-Hispanic White females, shares of non-fatal IS are highest for those aged 45–64 years. Among non-Hispanic Black females, shares of non-fatal IS are highest for those aged 65–84 years. Among females aged 65 or older, shares of non-fatal MI are highest in the Hispanic population.

**Table G-6: Estimated Distribution of Fatal and Non-Fatal First Hard CVD Events**

| Sex | Age (years) | Race/Ethnicity | Non-Fatal MI (%) | Non-Fatal IS (%) | Fatal CVD Event (%) |
|---|---|---|---|---|---|
| Males | 18–44 | NH White | 58 | 40 | 1.5 |
| | 45–64 | NH White | 50 | 47 | 3.7 |
| | 65–84 | NH White | 37 | 57 | 6.2 |
| | 85 or older | NH White | 34 | 53 | 13 |
| Males | 18–44 | NH Black | 22 | 77 | 1.7 |
| | 45–64 | NH Black | 22 | 75 | 2.9 |
| | 65–84 | NH Black | 27 | 66 | 6.4 |
| | 85 or older | NH Black | 25 | 62 | 13 |
| Males | 18–44 | Hispanic | 56 | 42 | 1.5 |
| | 45–64 | Hispanic | 38 | 59 | 3 |
| | 65–84 | Hispanic | 50 | 44 | 6.1 |
| | 85 or older | Hispanic | 47 | 41 | 12 |
| Males | 18–44 | NH Other | 46 | 53 | 1.6 |
| | 45–64 | NH Other | 58 | 39 | 3.1 |
| | 65–84 | NH Other | 33 | 62 | 5.8 |
| | 85 or older | NH Other | 30 | 58 | 12 |
| Females | 18–44 | NH White | 29 | 69 | 1.9 |
| | 45–64 | NH White | 24 | 71 | 4.6 |
| | 65–84 | NH White | 26 | 67 | 6.5 |
| | 85 or older | NH White | 24 | 63 | 13 |
| Females | 18–44 | NH Black | 62 | 36 | 1.7 |
| | 45–64 | NH Black | 26 | 70 | 3.9 |
| | 65–84 | NH Black | 18 | 76 | 6.7 |
| | 85 or older | NH Black | 16 | 70 | 14 |
| Females | 18–44 | Hispanic | 32 | 66 | 1.9 |
| | 45–64 | Hispanic | 31 | 65 | 3.8 |
| | 65–84 | Hispanic | 40 | 54 | 6.4 |
| | 85 or older | Hispanic | 37 | 51 | 12 |
| Females | 18–44 | NH Other | 45 | 53 | 1.8 |
| | 45–64 | NH Other | 32 | 64 | 3.6 |
| | 65–84 | NH Other | 28 | 66 | 6.5 |
| | 85 or older | NH Other | 26 | 61 | 13 |

Abbreviations: Fatal CVD – includes fatal MI, fatal IS, and fatal other coronary heart disease events; IS – ischemic stroke; MI – myocardial infarction; NH – non-Hispanic.

## *G.2.4 Post-Acute CVD Mortality*

Persons who have experienced non-fatal MI and non-fatal IS events have elevated post-acute CVD mortality and morbidity (Roger et al., 2012). EPA identified four studies that examined risk factors for secondary hard CVD events. These studies differ in terms of outcomes tracked (e.g., recurrent MI, recurrent IS, angina, heart failure, CVD, and all-cause death), conditioning event definition (e.g., MI, IS, CHD), and the length of follow-up for which statistics are reported (e.g., 1-year follow-up, 5-year follow-up). The data used to estimate the risks of secondary CVD events differ with respect to average age, sex, and share of individuals who are White among the participants:

- Data used in Kannel et al. (1999) and D'Agostino et al. (2000) come from the Framingham Heart Survey (Mahmood et al., 2014) and represent White males and females approximately age 60.
- Data used in Thom et al. (2001) are from the pooled Atherosclerosis Risk in Communities Study (Williams, 1989), Cardiovascular Health Study (Fried et al., 1991), and Framingham Original and Offspring Cohort Study (Mahmood et al., 2014). This pooled dataset offers representation for Black males and females, in addition to White males and females, and captures persons aged 45 or older.
- Beatty et al. (2015) used two predominantly White male datasets developed based on the Heart and Soul Study (Whooley et al., 2008) and the PEACE trial (PEACE Trial Investigators, 2004), capturing persons aged 67 years and 64 years, on average, respectively.
- S. Li et al. (2019) used data for 2008 and 2012 and two types of conditioning events (i.e., MI and IS) to assess the risk of secondary events in four large Medicare cohorts: survivors of the first MI in 2008, survivors of the first IS in 2008, survivors of the first MI in 2012, and survivors of the first IS in 2012.[41] These data represent older populations (age 80, on average) and are not limited to a particular race/ethnicity or sex.

Of the studies that assessed risk factors for secondary hard CVD events, only three focused on developing a risk prediction model (Beatty et al., 2015; D'Agostino et al., 2000; Kannel et al., 1999) and only two have changes in cholesterol levels and systolic blood pressure as a primary predictors (Beatty et al., 2015; D'Agostino et al., 2000). In these two studies, TC, HDLC, and BP levels do not appear to significantly increase the risk of recurrent CVD events, although D'Agostino et al. (2000) identified statistically significant relationships between the ratio of TC to HDLC and probability of recurrent CVD events. Beatty et al. (2015) concluded that precautionary measures and medication taken by patients who had suffered from a primary CVD event may decrease the initial risk factors (i.e., TC, HDLC, BP) and may be a reason for the lack of correlation between secondary CVD events and the modeled biomarkers.

In sum, studies focusing on secondary CVD events point to an elevated risk of these events among survivors of the first hard CVD event. However, the link between these risks and TC, HDLC, and BP levels is less clear, with limited supporting evidence coming from decades-old data evaluated by D'Agostino et al. (2000). Therefore, the CVD model relies on the same secondary hard CVD event rates to estimate secondary hard CVD event incidence under baseline and regulatory alternatives. Specifically, EPA focuses on post-acute CVD mortality as the secondary event of interest, because other non-fatal secondary CVD events are captured in the available unit values for first non-fatal MI and IS (see, e.g., O'Sullivan et al., 2011). EPA selected estimates in Thom et al. (2001) to model post-acute CVD mortality for survivors of MI or IS at ages 40–65, because Thom et al. (2001) is the only study that analyzed this age group. EPA selected estimates in S. Li et al. (2019) to model post-acute CVD mortality for survivors of MI or IS at ages 66–89, because cohorts analyzed in S. Li et al. (2019) are the largest and most representative of the U.S. population compared with the cohorts analyzed by other studies.

[41] Note that relative to other studies with sample sizes of, at most, 10,000, the sizes of these cohorts are 20,000, on average.

## G.2.5 Survivors of the first hard CVD event at ages 40–65

EPA used estimates of all-cause post-acute mortality for MI survivors at the 1- and 5-year follow-ups from Thom et al. (2001) to model post-acute CVD mortality for survivors of non-fatal MI and non-fatal IS events at ages 45–65. While EPA was unable to identify comparable post-acute mortality statistics for non-fatal IS, an analysis of the Medicare population by S. Li et al. (2019) suggests that post-acute MI mortality is a reasonable approximation for post-acute IS mortality.[42]

Table G-7 shows estimated all-cause probability of death following first non-fatal MI by age category, race/ethnicity, and sex from Thom et al. (2001), as reported in Roger et al. (2012). These estimates are based on the analysis of pooled data from the Atherosclerosis Risk in Communities Study (Williams, 1989), the Cardiovascular Health Study (Fried et al., 1991), and the Framingham Original and Offspring Cohort Study (Mahmood et al., 2014). The estimates are available only for non-Hispanic Whites and non-Hispanic Blacks.

**Table G-7: Post-Acute All-Cause Mortality After the First Myocardial Infarction**

| Age Group (years) | Race/Ethnicity | Follow-Up Period (years) | Probability of All-Cause Death (%) | |
|---|---|---|---|---|
| | | | Males | Females |
| 45–64 | Non-Hispanic White | 1 | 5 | 9 |
| 45–64 | Non-Hispanic Black | 1 | 14 | 8 |
| 65 or older | Non-Hispanic White | 1 | 25 | 30 |
| 65 or older | Non-Hispanic Black | 1 | 25 | 30 |
| 45–64 | Non-Hispanic White | 5 | 11 | 18 |
| 45–64 | Non-Hispanic Black | 5 | 22 | 28 |
| 65 or older | Non-Hispanic White | 5 | 46 | 53 |
| 65 or older | Non-Hispanic Black | 5 | 54 | 58 |

Abbreviations: MI – myocardial infarction (ICD9=410; ICD10=I21).
*Source: Thom et al. (2001)*

Table G-8 shows estimated probabilities of post-acute CVD mortality after the first MI. EPA derived these probabilities by adjusting all-cause post-acute mortality probabilities reported in Table G-7 for the ages 45–64 group[43] to exclude the probability of death from non-CVD causes. Section G.5 provides details on an estimation of integer age-, race/ethnicity- and sex-specific probability of death from non-CVD causes based on the U.S. Life Tables, 2017 (Arias et al., 2019) and CVD death rates, 1999–2019 (Centers for Disease Control and Prevention, 2020c). The last two columns of Table G-8 show annual race/ethnicity- and sex-specific post-acute CVD death probabilities used by the CVD model in estimation of secondary mortality in years 1–5 following the first non-fatal MI or IS that occurred at ages 45–65. EPA used post-acute mortality data for non-Hispanic Whites to estimate mortality effects for the other race/ethnicity groups.

[42] For those aged 65 or older, S. Li et al. (2019) have estimated the probability of death within 1 year after a non-fatal IS to be 32.07% and the probability of death within 1 year after a non-fatal MI to be 32.09%.

[43] EPA applies post-acute mortality probabilities estimated for ages 45–64 to the survivors of first MI or IS, ages 45–65, because the magnitude of the annual death probability at age 65 is closer to the average annual death probability for ages 45–64 than to the average annual death probability for ages 66–99.

## Table G-8: Post-Acute Mortality After the First Myocardial Infarction

| Integer Year Since First MI[a] | All-Cause Death Probability (%) | | Non-CVD Death Probability (%)[b] | | CVD Death Probability (%)[c] | |
|---|---|---|---|---|---|---|
| | Males | Females | Males | Females | Males | Females |
| **All Races/Ethnicities[d]** | | | | | | |
| 0 | 5.6 | 8.8 | 0.56 | 0.38 | 5.0 | 8.4 |
| 1 | 1.5 | 2.7 | 0.60 | 0.41 | 0.93 | 2.3 |
| 2 | 1.5 | 2.7 | 0.65 | 0.44 | 0.88 | 2.3 |
| 3 | 1.5 | 2.7 | 0.70 | 0.48 | 0.83 | 2.3 |
| 4 | 1.5 | 2.7 | 0.75 | 0.51 | 0.78 | 2.2 |
| **Non-Hispanic White[e]** | | | | | | |
| 0 | 5.0 | 9.0 | – | – | 4.5 | 8.6 |
| 1 | 1.5 | 2.3 | – | – | 0.91 | 1.9 |
| 2 | 1.5 | 2.3 | – | – | 0.86 | 1.9 |
| 3 | 1.5 | 2.3 | – | – | 0.82 | 1.9 |
| 4 | 1.5 | 2.3 | – | – | 0.76 | 1.8 |
| **Non-Hispanic Black** | | | | | | |
| 0 | 14 | 8.0 | – | – | 12 | 7.7 |
| 1 | 2.0 | 5.0 | – | – | 1.2 | 4.3 |
| 2 | 2.0 | 5.0 | – | – | 1.1 | 4.2 |
| 3 | 2.0 | 5.0 | – | – | 1.1 | 4.1 |
| 4 | 2.0 | 5.0 | – | – | 1.0 | 4.1 |

Abbreviations: CVD – cardiovascular disease; MEPS – Medical Expenditure Panel Survey; MI – myocardial infarction (ICD9=410; ICD10=I21).

Notes:

[a]Post-acute death probabilities at 1- and 5-year follow-ups in Table G-9 are converted to the integer year-specific post-acute death probabilities by assuming that the annual death probabilities in years 1–4 are identical. This assumption is supported by data in S. Li et al. (2019), who report post-acute death probabilities at 1-, 2-, 3-, 4-, 5-, and 6-year follow-ups.

[b]Reported annual probability of non-CVD death is a weighted average of life table age-specific probabilities for ages 45–64. The weights are the sex-specific age distribution of the first MI survivor population, estimated using MEPS 2010–2017 data.

[c]For all race/ethnicity categories, CVD death probability is the difference between all-cause death probability and non-CVD death probability. For the non-Hispanic White and non-Hispanic Black race/ethnicity categories, EPA obtained the estimates by multiplying the corresponding all-cause post-acute death probability with the all-race/ethnicity ratio of post-acute CVD death probability to all-cause post-acute death probability.

[d]Race/Ethnicity-specific data for the ages 45–64 group in Table G-9 are pooled using a sex-specific race/ethnicity distribution of the first MI survivor population, estimated using MEPS 2010–2017 data.

[e]Post-acute CVD death probability for non-Hispanic Whites is used to estimate mortality effects for the other race/ethnicity groups.

*Sources: Thom et al. (2001); U.S. Life Tables, 2017 (Arias et al., 2019); CVD death rates, 1999–2019 (Centers for Disease Control and Prevention, 2020c)*

## G.2.6 Survivors of the first hard CVD event at ages 66+

EPA used the results in S. Li et al. (2019) to estimate the number of post-acute CVD deaths for survivors of the first MI and IS events, aged 66 years or older at the time of the initial event. Table G-9 summarizes the key results in S. Li et al. (2019) that are used to parameterize the CVD model and the results of adjustments that EPA made to incorporate CVD mortality information in the model. First, EPA estimated CVD death probabilities by subtracting non-CVD death probabilities from all-cause post-acute mortality probabilities reported in S. Li et al. (2019). EPA derived the sex- and age-specific non-CVD mortality rates from U.S. Life Tables, 2017 (Arias et al., 2019); CVD death rates, 1999–2019 (Centers for Disease Control and Prevention, 2020c); and U.S. Life Tables Eliminating Certain Causes of Death, 1999–2000 (Arias et al., 2013). EPA has averaged age- and sex-specific non-CVD death probabilities for those age 66 or older using the demographic characteristics of the MI and IS cohorts analyzed by S. Li et al. (2019). Second, EPA calculated CVD mortality probability as the difference between the all-cause death probability and the non-CVD death probability. Third, EPA calculated CVD mortality rate multipliers as a ratio of CVD mortality probability to the non-CVD death probability. EPA combined these multipliers (reported in Table G-9 for MI and IS survivors) with age-, sex-, and race/ethnicity-specific non-CVD death rates to obtain post-acute CVD mortality rates for each cohort included in the analysis.

**Table G-9: Post-Acute CVD Mortality Following the First Myocardial Infarction and First Ischemic Stroke in the Population Aged 66 Years or Older**

| | MI Survivors | | | | IS Survivors | | | |
|---|---|---|---|---|---|---|---|---|
| Follow-up Period (years) | All-Cause Death Probability (%)[a] | Non-CVD Death Probability (%)[b] | CVD Death Probability (%)[c] | CVD Mortality Rate Multiplier[d] | All-Cause Death Probability (%)[a] | Non-CVD Death Probability (%)[b] | CVD Death Probability (%)[c] | CVD Mortality Rate Multiplier[d] |
| 0 | 32 | 4.3 | 27 | 6.4 | 32 | 4.5 | 28 | 6.1 |
| 1 | 16 | 4.6 | 11 | 2.5 | 15 | 4.8 | 9.9 | 2.07 |
| 2 | 15 | 4.9 | 9.6 | 1.9 | 16 | 5.2 | 10 | 2.1 |
| 3 | 14 | 5.2 | 9.04 | 1.7 | 15 | 5.5 | 9.8 | 1.8 |
| 4 | 14 | 5.6 | 8.6 | 1.5 | 15 | 5.9 | 8.9 | 1.5 |
| 5 | 14 | 5.9 | 8.04 | 1.4 | 14 | 6.2 | 8.03 | 1.3 |

Abbreviations: CVD – cardiovascular disease; IS – ischemic stroke (ICD9=433, 434; ICD10=I63); MI – myocardial infarction (ICD9=410; ICD10=I21).

Notes:

[a]For MI, the follow-up year specific all-cause death probability is from S. Li et al. (2019) reported data for the 2008 MI survivor cohort (N=26,46). For IS, the follow-up year specific all-cause death probability is from S. Li et al. (2019) reported data for the 2008 IS survivor cohort (N=17,566).

[b]Non-CVD annual mortality rate is based on U.S. Life Tables 2017 (Arias et al., 2019); CVD death rates, 1999–2019 (Centers for Disease Control and Prevention, 2020c); and U.S. Life Tables Eliminating Certain Causes of Death, 1999–2000 (Arias et al., 2013) for those age 66 or older. The annual age- and sex-specific death probabilities were averaged using S. Li et al. (2019) MI/IS survivor cohort demographic characteristics.

[c]Post-acute CVD death probability rate is estimated by subtracting the non-CVD annual death probability from the all-cause post-acute death probability.

[d]The CVD mortality rate multiplier is defined as the difference between all-cause death probability and non-CVD death probability divided by the non-CVD death probability. The CVD model combines the baseline rate multiplier with race/ethnicity-, age-, and sex-specific non-CVD baseline death rates to obtain mortality rates that are appropriate for the race/ethnicity, age, and sex of each cohort included in the analysis.

*Sources: Li et al. (2019); U.S. Life Tables, 2017 (Arias et al., 2019); CVD death rates, 1999–2019 (Centers for Disease Control and Prevention, 2020c); U.S. Life Tables Eliminating Certain Causes of Death, 1999–2000 (Arias et al., 2013).*

## G.3 Detailed CVD Model Calculations

Table G-10 provides a guide to sections containing the recurrent CVD model calculations applicable under conditions defined by initial cohort age, current cohort age, and estimation type. Estimation types include baseline estimation, regulatory alternative estimation, and risk reduction estimation. Note that standard life table calculations for current cohort ages 0–39 in Section G.3.1 apply to both the baseline and regulatory alternative estimation types. The CVD risk reduction estimation equations in Section G.3.5 apply to ages 40+, for which the model explicitly estimates the number of first hard CVD events and the number of post-acute CVD deaths for survivors of the first hard CVD event.

**Table G-10: A Mapping of CVD Model Calculations by Initial Cohort Age, Current Cohort Age, and Estimation Type**

| Initial Cohort Age (years) | Current Cohort Age (years) | | |
|---|---|---|---|
| | 0–39 | 40–65 | 66+ |
| | | **Baseline Estimation** | |
| 0–39 | Section G.3.1 | Section G.3.2, Section G.3.4 | Section G.3.2, Section G.3.4 |
| 40–85+ | – | Section G.3.2, Section G.3.4 | Section G.3.2, Section G.3.4 |
| | | **Regulatory Alternative Estimation** | |
| 0–39 | Section G.3.1 | Section G.3.3, Section G.3.4 | Section G.3.3, Section G.3.4 |
| 40–85+ | – | Section G.3.3, Section G.3.4 | Section G.3.3, Section G.3.4 |
| | | **Risk Reduction Estimation** | |
| 0–39 | – | Section G.3.5 | Section G.3.5 |
| 40–85+ | – | Section G.3.5 | Section G.3.5 |

Abbreviations: CVD – cardiovascular disease.

## G.3.1 Baseline Recurrent Calculations Without Explicit Treatment of the CVD Population

The number of deaths occurring in year $t$ is estimated using the number of persons alive at the start of the year, $l_{b,a,s,r,t}$, and all-cause annual probability of death, $q_{a,s,r}$:

Equation G-3:

$$d_{b,a,s,r,t} = q_{a,s,r} \cdot l_{b,a,s,r,t}$$

The number of persons surviving to the start of the next year is calculated as the difference between the number of persons alive at the start of the year, $l_{b,a,s,r,t}$, and the number of deaths estimated to occur during the year, $d_{b,a,s,r,t}$:

Equation G-4:

$$l_{b,a+1,s,r,t+1} = l_{b,a,s,r,t} - d_{b,a,s,r,t}$$

## G.3.2 Baseline Recurrent Calculations with Explicit Treatment of the CVD Population

The population of persons alive at the start of year $t$, $l_{b,a,s,r,t}$, is split into CVD and non-CVD subpopulations using externally estimated age-, race/ethnicity-, and sex-specific CVD prevalence, $\pi_{a,s,r}$:

Equation G-5:

$$l_{b,a,s,r,t,\text{CVD}} = \pi_{a,s,r} \cdot l_{b,a,s,r,t}$$

Equation G-6:

$$l_{b,a,s,r,t,\text{OTH}} = \left(1 - \pi_{a,s,r}\right) \cdot l_{b,a,s,r,t}$$

The year $t$ number of non-CVD deaths in the CVD and non-CVD subpopulations is estimated by applying the annual age-, race/ethnicity-, and sex-specific probability of non-CVD death, $q_{a,s,r,\text{OTH}}$, to the number of persons alive at the start of the year in each subpopulation ($l_{b,a,s,r,t,\text{CVD}}$ and $l_{b,a,s,r,t,\text{OTH}}$), respectively:

Equation G-7:

$$d_{b,a,s,r,t,\text{CVD,OTH}} = q_{a,s,r,\text{OTH}} \cdot l_{b,a,s,r,t,\text{CVD}}$$

Equation G-8:

$$d_{b,a,s,r,t,\text{OTH,OTH}} = q_{a,s,r,\text{OTH}} \cdot l_{b,a,s,r,t,\text{OTH}}$$

The year $t$ number of CVD deaths in the CVD subpopulation is estimated by applying the annual CVD death probability, $q_{a,s,r,\text{CVD}}$, to the total population alive at the start of the year, $l_{b,a,s,r,t}$, net of deaths from other causes, $q_{a,s,r,\text{OTH}}$, estimated to occur during the year:

Equation G-9:

$$d_{b,a,s,r,t,\text{CVD,CVD}} = q_{a,s,r,\text{CVD}} \cdot \left(1 - q_{a,s,r,\text{OTH}}\right) \cdot l_{b,a,s,r,t}$$

The number of persons surviving to the start of the next year is estimated as:

Equation G-10:

$$l_{b,a+1,s,r,t+1} = l_{b,a,s,r,t} - d_{b,a,s,r,t,\text{CVD,CVD}} - d_{b,a,s,r,t,\text{OTH,OTH}} - d_{b,a,s,r,t,\text{CVD,OTH}}$$

The *uncalibrated* number of persons experiencing their first hard CVD event in year $t$ is estimated by applying the baseline annual probability of first hard CVD event, $i_{b,a,s,r,t}(0)$, to the start-of-the-year number of persons in the non-CVD subpopulation, $l_{b,a,s,r,t,\text{OTH}}$, net of non-CVD deaths, $d_{b,a,s,r,t,\text{OTH,OTH}}$. The ASCVD model applies to ages 40–80 and predicts a 10-year probability of the first hard CVD event. However, EPA uses the ASCVD model to estimate 10-year probability of the first hard CVD event for adults ages 81+ years. For those in 85+ age group, EPA uses age 85 as the input to ASCVD model at the start of the evaluation period. Finally, EPA uses the externally estimated share of non-fatal first hard CVD events, $\gamma_{a,s,r,f}$, and same-year post-acute CVD mortality probability, $\mu_{a,s,r,f,0}$, to compute the number of persons surviving their first hard type $f$ CVD event in year $t$:

Equation G-11:

$$\tilde{n}_{b,a,s,r,f,t,0} = \left(1 - \mu_{a,s,r,f,0}\right) \cdot \gamma_{a,s,r,f} \cdot i_{b,a,s,r,t}(0) \cdot \left(l_{b,a,s,r,t,\text{OTH}} - d_{b,a,s,r,t,\text{OTH,OTH}}\right)$$

EPA uses the externally estimated share of fatal first hard CVD events, $1 - \sum_{f \in F} \gamma_{a,s,r,f}$, and same-year post-acute CVD mortality probability, $\mu_{a,s,r,f,0}$, to compute the *uncalibrated* number of year $t$ deaths in the incident CVD population at baseline:

Equation G-12:

$$\tilde{m}_{b,a,s,r,t,0} = \left[1 + \sum_{f \in F}\left(\mu_{a,s,r,f,0} - 1\right) \cdot \gamma_{a,s,r,f}\right] \cdot i_{b,a,s,r,t}(0) \cdot \left(l_{b,a,s,r,t,\text{OTH}} - d_{b,a,s,r,t,\text{OTH,OTH}}\right)$$

For calibration purposes, EPA calculated the incident CVD population size, $x_{b,a,s,r,t}$, that is consistent with the reported CVD prevalence rates, $\pi_{a,sr,}$ and $\pi_{a+1,s,r}$, and cause-specific mortality rates, $q_{a,s,r,\text{CVD}}$ and $q_{a,s,r,\text{OTH}}$:

Equation G-13:

$$x_{b,a,s,r,t} = \pi_{a+1,s,r} l_{b,a+1,s,r,t+1} - l_{b,a,s,r,t,\text{CVD}} + d_{b,a,s,r,t,\text{CVD,CVD}} + d_{b,a,s,r,t,\text{CVD,OTH}}$$

EPA used the incident CVD population size to estimate a calibration factor for scaling raw ASCVD model-based results:

Equation G-14:

$$\chi_{b,a,s,r,t} = \frac{x_{b,a,s,r,t}}{\sum_{f \in F} \tilde{n}_{b,a,s,r,f,t,0} + \tilde{m}_{b,a,s,r,t,0}}$$

Using the estimated calibration factor, EPA adjusted the raw number of persons surviving their first hard type $f$ CVD event in year $t$, $\tilde{n}_{b,a,s,r,f,t,0}$, and the raw number of year $t$ deaths in the incident CVD population at baseline, $\tilde{m}_{b,a,s,r,t,0}$, to ensure that EPA does not project a larger number of incident events than is consistent with the CVD prevalence statistics and mortality rates:

Equation G-15:

$$n_{b,a,s,r,f,t,0} = min\,(1, \chi_{b,a,s,r,t}) \cdot \tilde{n}_{b,a,s,r,f,t,0}$$

Equation G-16:

$$m_{b,a,s,r,t,0} = min\,(1, \chi_{b,a,s,r,t}) \cdot \tilde{m}_{b,a,s,r,t,0}$$

Finally, EPA uses the overall number of year $t$ CVD deaths, $d_{b,a,s,r,t,\mathrm{CVD},\mathrm{CVD}}$, net of the number of deaths in the incident CVD population, $m_{b,a,s,r,t,0}$, and the size of CVD population alive at the start of the year, $l_{b,a,s,r,t,\mathrm{CVD}}$, to estimate the baseline CVD death rate in the prevalent CVD population. This quantity is needed to support regulatory alternative estimation:

Equation G-17:

$$\rho_{b,a,s,r} = \left(d_{b,a,s,r,t,CVD,CVD} - m_{b,a,s,r,t,0}\right) / l_{b,a,s,r,t,CVD}$$

## G.3.3 Regulatory Alternative Recurrent Calculations with Explicit Treatment of the CVD Population

If current cohort age $a$ is equal to the initial cohort age, the sizes of CVD and non-CVD subpopulations at the start of year 0 are calculated using externally estimated CVD prevalence, $\pi_{a,s,r}$, and the initial population size, $l_{b,a,s,r,t}$. If, however, the current cohort age $a$ is greater than the initial cohort age, then the sizes of CVD and non-CVD subpopulations at the start of year $t$ are the same as the end-of-year $t-1$ CVD and non-CVD subpopulation sizes. That is, the CVD and non-CVD populations are computed in a recurrent manner.

Equation G-18 :

$$l_{b,a,s,r,t,CVD} = \begin{cases} \pi_{a,s,r} \cdot l_{b,a,s,r,t} & if\ a = max(a-t, 40) \\ l_{b,a-1,s,r,t-1,CVD} & if\ a > max(a-t, 40) \end{cases}$$

Equation G-19:

$$l_{b,a,s,r,t,OTH} = \begin{cases} \left(1 - \pi_{a,s,r}\right) \cdot l_{b,a,s,r,t} & if\ a = max(a-t, 40) \\ l_{b,a-1,s,r,t-1,OTH} & if\ a > max(a-t, 40) \end{cases}$$

The year $t$ number of non-CVD deaths in CVD and non-CVD subpopulations is estimated by applying the annual age-, race/ethnicity-, and sex-specific probability of non-CVD death, $q_{a,s,r,\mathrm{OTH}}$, to the number of persons alive at the start of the year in each subpopulation, respectively:

Equation G-20:

$$d_{b,a,s,r,t,CVD,OTH} = q_{a,s,r,OTH} \cdot l_{b,a,s,r,t,CVD}$$

Equation G-21:

$$d_{b,a,s,r,t,OTH,OTH} = q_{a,s,r,OTH} \cdot l_{b,a,s,r,t,OTH}$$

The uncalibrated number of fatal and non-fatal first hard CVD events under the regulatory alternative is estimated using the same equations (i.e., Eq. G-11 and Eq. G-12) as the ones used for the baseline scenario, except for the non-zero difference between regulatory alternative and baseline total cholesterol $\Delta\tau_{b,a,s,t}$:

Equation G-22:

$$\tilde{n}_{b,a,s,r,f,t,0} = \left(1 - \mu_{a,s,r,f,0}\right) \cdot \gamma_{a,s,r,f} \cdot i_{b,a,s,r,t}\left(\Delta\tau_{b,a,s,t}\right) \cdot \left(l_{b,a,s,r,t,OTH} - d_{b,a,s,r,t,OTH,OTH}\right)$$

Equation G-23:

$$\tilde{m}_{b,a,s,r,t,0} = \left[1 + \sum_{f \in F}\left(\mu_{a,s,r,f,0} - 1\right) \cdot \gamma_{a,s,r,f}\right] \cdot i_{b,a,s,r,t}\left(\Delta\tau_{b,a,s,t}\right) \cdot \left(l_{b,a,s,r,t,\mathrm{OTH}} - d_{b,a,s,r,t,\mathrm{OTH},\mathrm{OTH}}\right)$$

These estimates are used in combination with the baseline calibration factor, $\chi_{b,a,s,r,t}$, and EPA-estimated regulatory alternative incident CVD population size, $x_{b,a,s,r,t}$:

Equation G-24:

$$x_{b,a,s,r,t} = \chi_{b,a,s,r,t}\left(\sum_{f \in F} \tilde{n}_{b,a,s,r,f,t,0} + \tilde{m}_{b,a,s,r,t,0}\right)$$

Using the estimated baseline calibration factor, $\chi_{b,a,s,r,t}$, EPA adjusted the raw number of persons surviving their first hard type $f$ CVD event in year $t$, $\tilde{n}_{b,a,s,r,f,t,0}$, and the raw number of year $t$ deaths in the incident CVD population, $\tilde{m}_{b,a,s,r,t,0}$:

Equation G-25:

$$n_{b,a,s,r,f,t,0} = min\,(1, \chi_{b,a,s,r,t}) \cdot \tilde{n}_{b,a,s,r,f,t,0}$$

Equation G-26:

$$m_{b,a,s,r,t,0} = min\,(1, \chi_{b,a,s,r,t}) \cdot \tilde{m}_{b,a,s,r,t,0}$$

The number of CVD deaths at age $a$ during year $t$ is estimated as the sum of the number of deaths among those whose CVD event history began before age $a$, $\rho_{b,a,s,r} \cdot l_{b,a,s,r,t}$, and the number of deaths among those who experienced their first CVD event at age $a$, $m_{b,a,s,r,t,0}$. The number of deaths among those whose CVD event history began before age $a$ is the product of the baseline CVD death rate in the CVD subpopulation, $\rho_{b,a,s,r}$, and the size of the CVD subpopulation at the start of year $t$, $l_{b,a,s,r,t}$:

Equation G-27:

$$d_{b,a,s,r,t,CVD,CVD} = \rho_{b,a,s,r} \cdot l_{b,a,s,r,t} + m_{b,a,s,r,t,0}$$

Finally, the following recurrent equations are used to compute the sizes of total, CVD, and non-CVD populations surviving through to the beginning of year $t + 1$:

Equation G-28:

$$l_{b,a+1,s,r,t+1} = l_{b,a,s,r,t} - d_{b,a,s,r,t,CVD,CVD} - d_{b,a,s,r,t,OTH,OTH} - d_{b,a,s,r,t,CVD,OTH}$$

Equation G-29:

$$l_{b,a+1,s,r,t+1,CVD} = l_{b,a,s,r,t,CVD} + x_{b,a,s,r,t} - d_{b,a,s,r,t,CVD,CVD} - d_{b,a,s,r,t,CVD,OTH}$$

Equation G-30:

$$l_{b,a+1,s,r,t+1,OTH} = l_{b,a,s,r,t,OTH} - x_{b,a,s,r,t} - d_{b,a,s,r,t,OTH,OTH}$$

## G.3.4 Recurrent Estimation of Post-Acute CVD Mortality

Survivors of the first type $f$ non-fatal hard CVD event at age $a$ in year $t$, $n_{b,a,s,r,f,t,0}$, are followed for five future years (i.e., $k = 1,2,3,4,5$) to evaluate post-acute CVD mortality.

EPA estimates the number of post-acute CVD deaths among survivors of a first hard CVD event in year $k$ since the initial event at age $a$, $m_{b,a+k,s,r,t+k,k}$, by (1) adjusting the number of those who survived $k - 1$ years after the initial event, $n_{b,a+k-1,s,r,f,t+k-1,k-1}$, for non-CVD mortality using externally estimated non-CVD mortality rate, $q_{a+k,s,r,\mathrm{OTH}}$,; (2) multiplying the result by

externally estimated post-acute CVD mortality rate, $\mu_{a+k,s,r,f,k}$; and (3) summing over the first hard CVD event type $f$:

Equation G-31:

$$m_{b,a+k,s,r,t+k,k} = \sum_{f \in F} \left[\mu_{a+k,s,r,f,k} \cdot \left(1 - q_{a+k,s,r,OTH}\right) \cdot n_{b,a+k-1,s,r,f,t+k-1,k-1}\right]$$

EPA estimates the number of survivors of type $f$ first hard CVD event in year $k$ since the initial event at age $a$, $n_{b,a+k,s,r,f,t+k,k}$, by adjusting the number of those who survived $k-1$ years after the initial event, $n_{b,a+k-1,s,r,f,t+k-1,k-1}$, for mortality using externally estimated non-CVD mortality rate, $q_{a+k,s,r,\mathrm{OTH}}$, and post-acute CVD mortality using rate, $\mu_{a+k,s,r,f,k}$:

Equation G-32:

$$n_{b,a+k,s,r,f,t+k,k} = \left(1 - \mu_{a+k,s,r,f,k}\right) \cdot \left(1 - q_{a+k,s,r,OTH}\right) \cdot n_{b,a+k-1,s,r,f,t+k-1,k-1}$$

## G.3.5 Risk Reduction Calculations

Assuming that the regulatory alternative is associated with a lower incidence of first hard CVD events (via lower total cholesterol levels due to lower serum PFAS), at the end of time period $t$, the number of avoided type $f$ non-fatal first hard CVD events in the sex $s$ and race/ethnicity $r$ cohort born in year $b$ and currently age $a$ is estimated as:

Equation G-33:

$$\Delta n_{b,a,s,r,f,t} = n_{b,a,s,r,f,t,0}^{Baseline\ Scenario} - n_{b,a,s,r,f,t,0}^{Regulatory\ Alternative}$$

The number of avoided year $t$ CVD deaths in the first hard CVD population in the sex $s$ and race/ethnicity $r$ cohort born in year $b$ and currently age $a$ years is:

Equation G-34:

$$\Delta m_{b,a,s,r,t} = \sum_{k=0}^{5} \left(m_{b,a,s,r,t,k}^{Baseline\ Scenario} - m_{b,a,s,r,t,k}^{Regulatory\ Alternative}\right)$$

Total number of avoided type $f$ non-fatal first hard CVD events in year $t$ is:

Equation G-35:

$$\Delta N_{f,t} = \sum_{a \in A, b \in B} \sum_{s \in S} \sum_{r \in R} \Delta n_{b,a,s,r,f,t}$$

Total number of avoided CVD deaths in the first hard CVD population in year $t$ is:

Equation G-36:

$$\Delta M_t = \sum_{a \in A, b \in B} \sum_{s \in S} \sum_{r \in R} \Delta m_{b,a,s,r,t}$$

## G.4 ASCVD Model Validation

The validation analysis described herein relied on methodology implemented in R software and differs slightly from SafeWater MCBC methods. Specifically, SafeWater performs a set of pre-calculations to maximize computational efficiency and, as such, the order of analytical steps across R and SafeWater models differs; however, results across models are mathematically consistent. Furthermore, the R-based model version treats each integer age cohort between 85 and 99 separately, implements the CVD calculations for those aged 40-89 years only, and applies the ASCVD model-based annual incidence at age 80 years to ages 81-89 because the ASCVD model has been fit to those aged 40-80 years and predicts the 10-year probability of the first CVD event.

EPA generated life table CVD model results for race/ethnicity subpopulations under different assumptions regarding the applicability of ASCVD coefficients for non-Hispanic Whites and non-Hispanic Blacks to Hispanic and non-Hispanic other subpopulations. CVD model inputs are summarized in Table G-12. The size of each subpopulation cohort was estimated using the 2020 U.S. population size and nationally representative age / sex / race/ethnicity distribution from the American Community Survey, 2017 (U.S. Census Bureau, 2017). EPA evaluated the alignment among age-, sex-, and race/ethnicity-specific CVD incidence prediction using the ASCVD model and age-, sex-, and race/ethnicity-specific CVD incidence prediction calculated by the CVD model on the basis of race-, sex-, and age-specific prevalence of persons with a history of CVD events based on MEPS 2010–2017 (see Section G.2.2); U.S. Life Tables, 2017 (Arias et al., 2019); and CVD death rates, 1999–2019 (Centers for Disease Control and Prevention, 2020c).

For each race/ethnicity, sex, and age combination, EPA first computed the ratio of CVD incidence based on reported data and incidence based on the ASCVD model. EPA then computed the absolute value of the deviation of this ratio from 1 and averaged the results over age using population weights for each sex and race/ethnicity subpopulation. Table G-11 reports the resulting alignment metrics for each combination of subpopulation and ASCVD model coefficient set. Results show that the ASCVD model coefficients for the non-Hispanic Black model are more consistent with data on CVD prevalence and mortality for Hispanic and non-Hispanic other race subpopulations than the ASCVD model coefficients for the non-Hispanic White model.

**Table G-11: Summary of ASCVD Model Validation**

| Sex | Race/Ethnicity | Alignment of ASCVD Model Predictions with Prevalence and Mortality Statistics[a] | |
|---|---|---|---|
| | | ASCVD Model Coefficients Estimated in Non-Hispanic White Sample | ASCVD Model Coefficients Estimated in Non-Hispanic Black Sample |
| Males | Non-Hispanic White | 0.64 | – |
| | Non-Hispanic Black | – | 0.22 |
| | Hispanic | 0.44 | 0.23 |
| | Non-Hispanic Other | 0.57 | 0.18 |
| Females | Non-Hispanic White | 2.00 | – |
| | Non-Hispanic Black | – | 1.37 |
| | Hispanic | 1.53 | 0.90 |
| | Non-Hispanic Other | 1.44 | 1.07 |

Note:
[a]Alignment is represented by the population-weighted absolute value of age-specific |R – 1| within each sex and race/ethnicity subpopulation, where R is the race/ethnicity-, age-, and sex-specific ratio of CVD incidence computed from reported data and incidence computed from the ASCVD model.

## G.5 CVD Model Inputs

Table G-12 summarizes the inputs and data sources used in the CVD model, including survey health data, model coefficients, Centers for Disease Control and Prevention life tables, hospitalization data, and mortality incidence data.

**Table G-12: Summary of Inputs and Data Sources Used in the CVD Model**

| Data Element | Modeled Variability | Data Source | Notes |
|---|---|---|---|
| Percentage of population with high blood pressure | Age: 10-year age groups (ages 40–79)<br>Sex: males, females<br>Race/Ethnicity: non-Hispanic White, non-Hispanic Black, non-Hispanic other, Hispanic | NHANES 2011–2016 (Centers for Disease Control and Prevention, 2013b, 2015a, 2015b, 2016b, 2017b, 2017c) | EPA used the percentage of population with high blood pressure in 10-year age groups to estimate the number of exposed individuals with high blood pressure who are exposed to PFOA/PFOS in drinking water. The blood pressure measurement NHANES datasets from 2011–2016 were combined with corresponding respondent-specific demographic profile, medical questionnaire, and blood pressure questionnaire datasets to summarize the percentage of the non-CVD population that has high blood pressure for each age-, sex-, and race-specific stratum. |

**Table G-12: Summary of Inputs and Data Sources Used in the CVD Model**

| Data Element | Modeled Variability | Data Source | Notes |
|---|---|---|---|
| Percentage of population receiving blood pressure treatment | Age: 10-year age groups (ages 40–79)<br>Sex: males, females<br>Race/Ethnicity: non-Hispanic White, non-Hispanic Black, non-Hispanic other, Hispanic | NHANES 2011–2016 (Centers for Disease Control and Prevention, 2013b, 2015a, 2015b, 2016b, 2017b, 2017c) | To determine the percentage of the population with controlled high blood pressure, the percentage of the populations per age group and sex who have high blood pressure was multiplied by the percentage of the populations per age group and sex who received treatment for high blood pressure. The blood pressure measurement NHANES datasets from 2011–2016 were combined with corresponding respondent-specific demographic profile, medical questionnaire, and blood pressure questionnaire datasets to summarize the percentage of the non-CVD population that is being treated for having high blood pressure for each age-, sex-, and race-specific stratum. |
| Treated, untreated, and normal systolic blood pressure measurements | Age: age groups 40–59, 60+<br>Sex: males, females<br>Race/Ethnicity: non-Hispanic White, non-Hispanic Black, non-Hispanic other, Hispanic<br>Treatment status: controlled, uncontrolled-high, uncontrolled-normal | NHANES 2011–2016 (Centers for Disease Control and Prevention, 2013b, 2015a, 2015b, 2016b, 2017b, 2017c) | The blood pressure measurement NHANES datasets from 2011–2016 were combined with corresponding respondent-specific demographic profile, medical questionnaire, and blood pressure questionnaire datasets to summarize the percentage of the non-CVD population that is being treated for having high blood pressure for each treatment status-, age-, sex-, and race-specific stratum. |
| Baseline total cholesterol level | Age: 10-year age groups (ages 40–79)<br>Sex: males, females<br>Race/Ethnicity: non-Hispanic White, non-Hispanic Black, non-Hispanic other, Hispanic | NHANES 2011–2016 (Centers for Disease Control and Prevention, 2013b, 2015a, 2015b, 2016b, 2017b, 2017c) | The total cholesterol NHANES datasets from 2011–2016 were combined with corresponding respondent-specific demographic profile and medical questionnaire datasets to summarize weighted average total cholesterol levels in mg/dL for each age-, sex-, and race-specific stratum in the non-CVD population. |
| Baseline high density lipoprotein cholesterol level (HDLC) | Age: 10-year age groups (ages 40–79)<br>Sex: males, females<br>Race/Ethnicity: non-Hispanic White, non-Hispanic Black, non-Hispanic other, Hispanic | NHANES 2011–2016 (Centers for Disease Control and Prevention, 2013a, 2015a, 2015b, 2016a, 2017a, 2017c) | The HDLC NHANES datasets from 2011–2016 were combined with corresponding respondent-specific demographic profile and medical questionnaire datasets to summarize weighted average HDLC levels in mg/dL for each age-, sex-, and race-specific stratum in the non-CVD population. |

**Table G-12: Summary of Inputs and Data Sources Used in the CVD Model**

| Data Element | Modeled Variability | Data Source | Notes |
|---|---|---|---|
| Smoking prevalence | Age: 10-year age groups (ages 40–79)<br>Sex: males, females<br>Smoking status: fraction of smokers | NHANES 2011–2016 (Centers for Disease Control and Prevention, 2013d, 2015a, 2015b, 2015d, 2017c, 2017e) | The percentage of smokers and non-smokers in each stratum were used as inputs in the ASCVD model, providing results similar to using binary variables representing that an individual is either a smoker or a non-smoker and further stratifying the sample. The smoking NHANES datasets from 2011–2016 were combined with corresponding respondent-specific demographic profile and medical questionnaire datasets to summarize the percentage of the non-CVD population that smokes for each age-, sex-, and race-specific stratum. |
| Diabetes prevalence | Age: 10-year age groups (ages 40–79)<br>Sex: males, females<br>Diabetes status: fraction of diabetics | NHANES 2011–2016 (Centers for Disease Control and Prevention, 2013c, 2015a, 2015b, 2015c, 2017c, 2017d) | The percentage of the population with and without diabetes in each stratum were used as inputs in the ASCVD model, providing results similar to using binary variables representing that an individual has or does not have diabetes and further stratifying the sample. The diabetes NHANES datasets from 2011–2016 were combined with corresponding respondent-specific demographic profile and medical questionnaire datasets to summarize the percentage of the non-CVD population that has diabetes for each age-, sex-, and race-specific stratum. |
| ASCVD model coefficients | Sex: males, females<br>Race: non-Hispanic White, non-Hispanic Black | Goff et al. (2014), Table A | For modeling purposes, the Hispanic subpopulation was assigned coefficients estimated for the non-Hispanic White subpopulation. The model applies to ages 40–89. ASCVD regressors include age, TC, HDLC, treated systolic BP, untreated systolic BP, smoking status, and diabetes status. |
| Annual all-cause death probability | Sex: males, females<br>Age: integer ages 0 … 100<br>Race/Ethnicity: all, non-Hispanic White, non-Hispanic Black, Hispanic | U.S. Life Tables, 2017 (Arias et al., 2019) | The quantity used in modeling is $q_x$ (i.e., the probability of dying between ages x and x + 1). Life table data for the non-Hispanic other race category are not available; for subsequent modeling, all-race life tables are used for this category. |

**Table G-12: Summary of Inputs and Data Sources Used in the CVD Model**

| Data Element | Modeled Variability | Data Source | Notes |
|---|---|---|---|
| Annual non-CVD death probability for age 90+ | Sex: males, females<br>Age: integer ages 90 … 100<br>Race/Ethnicity: all, non-Hispanic White, non-Hispanic Black, Hispanic | U.S. Life Tables, 2017 (Arias et al., 2019); U.S. Life Tables Eliminating Certain Causes of Death, 1999–2000 (Arias et al., 2013) | Annual non-CVD death probability is estimated by multiplying $q_x$ from the 2017 U.S. life tables by the sex-specific ratio of non-CVD $q_x$ to all-cause $q_x$ from 1999–2000 U.S. life tables eliminating certain causes. Life table data for the non-Hispanic other race category are not available; for subsequent modeling, all-race life tables are used for this category. The 1999–2000 U.S. life tables eliminating certain causes are not race/ethnicity-specific; the U.S. general population ratios of non-CVD $q_x$ to all-cause $q_x$ were applied to all race/ethnicity categories. The 1999–2000 U.S. life tables eliminating certain causes are abridged and report 5-year rates. The corresponding 5-year ratios are applied to all individual years within the 5-year range. |
| Annual non-CVD death probability for ages 40+ | Sex: males, females<br>Age: integer ages 40 … 89<br>Race/Ethnicity: non-Hispanic White, non-Hispanic Black, non-Hispanic other, Hispanic | U.S. Life Tables 2017 (Arias et al., 2019); CVD death rates, 1999–2019 (Centers for Disease Control and Prevention, 2020c) | Annual non-CVD death probability is estimated by multiplying $q_x$ from 2017 U.S. life tables by the ratio of non-CVD $q_x$ to all-cause $q_x$. The non-CVD $q_x$ estimate was obtained for each integer age by sex combination as the difference between all-cause $q_x$ from U.S. 2017 life tables and CVD $q_x$ from CDC 1999–2019 cause-specific mortality rates. U.S. 2017 life table data for the non-Hispanic other race category are not available; life tables for the U.S. general population are used for this category. |
| CVD prevalence | Sex: males, females<br>Age: age groups 18–44, 45–64, 65+<br>Race/Ethnicity: non-Hispanic White, non-Hispanic Black, non-Hispanic other, Hispanic<br>Condition: MI, IS, other CHD, MI + IS + other CHD conditions combined | MEPS 2010–2017 (Agency for Healthcare Research and Quality, 2011, 2012a, 2012b, 2013a, 2013b, 2014a, 2014b, 2015a, 2015b, 2016a, 2016b, 2017b, 2017c, 2018, 2019a, 2019b, 2019c) | MEPS longitudinal files were used to obtain survey weights, design variables, and information on cardiovascular conditions (including age at diagnosis) that began prior to the start date for the survey panel. MEPS medical conditions files were used to obtain information on the newly diagnosed conditions of interest. Specifically, MI events were identified using ICD9=410 or MIDX=1, stroke events were identified using ICD9=433,434,435,436 or STRKDX=1, other CHD were identified using ICD9=413,414,427,428 or CHDDX=1, ANGIDX=1, OHRTDX=1. CVD prevalence was estimated based on persons whose condition started at an age prior to the age at which the MEPS round interview was conducted. |

**Table G-12: Summary of Inputs and Data Sources Used in the CVD Model**

| Data Element | Modeled Variability | Data Source | Notes |
|---|---|---|---|
| CVD incidence in the non-CVD population | Sex: males, females<br>Age: age groups 18–44, 45–64, 65+<br>Race/Ethnicity: non-Hispanic White, non-Hispanic Black, non-Hispanic other, Hispanic<br>Condition: MI, IS, other CHD | MEPS 2010–2017 (Agency for Healthcare Research and Quality, 2011, 2012a, 2012b, 2013a, 2013b, 2014a, 2014b, 2015a, 2015b, 2016a, 2016b, 2017b, 2017c, 2018, 2019a, 2019b, 2019c) | MEPS longitudinal files were used to obtain survey weights, design variables, and information on cardiovascular conditions (including age at diagnosis) that began prior to the start date for the survey panel. MEPS medical conditions files were used to obtain information on the newly diagnosed conditions of interest. Specifically, MI events were identified using ICD9=410 or MIDX=1, stroke events were identified using ICD9=433,434,435,436 or STRKDX=1, other CHD were identified using ICD9=413,414,427,428 or CHDDX=1, ANGIDX=1, OHRTDX=1. CVD incidence was estimated based on persons whose condition started at an age that was the same as the age at which the MEPS round interview was conducted. |
| In-hospital death probability for CVD events | Sex: males, females<br>Age: age groups 18–44, 45–64, 65–84, 85+<br>Condition: MI, IS, other CHD | HCUP 2017 (Agency for Healthcare Research and Quality, 2017a) | Hospital death probabilities were estimated from condition-specific hospitalizations identified using the following ICD10 codes: ICD10=I21 for MI, ICD10=I63 for IS, and ICD10=I20, I22–I25 for other CHD. HCUP reports death probabilities separately by sex or within age groups. EPA estimated age group- and sex-specific hospital death probabilities by assuming that male/female relative risk does not vary across age groups. |
| 1-year, 2-year, 3-year, 4-year, and 5-year all-cause mortality incidence in MI survivors ages 40–64 | Sex: males, females<br>Race: all<br>Age: age groups 40–65<br>Condition: MI | Thom et al. (2001); MI incidence based on the MEPS 2010–2017 analysis, U.S. Life Tables, 2017 (Arias et al., 2019) | Thom et al. (2001) sex- and race-specific estimates for 1-year follow-up and 5-year follow-up all-cause mortality for ages 45–64 MI survivors are as reported in Roger et al. (2012) (the text of the original report is not accessible). Thom et al. (2001) generated separate estimates for non-Hispanic White and non-Hispanic Black persons. To derive sex-specific all-race/ethnicity estimates, EPA used MEPS-based race/ethnicity- and sex-specific MI incidence for ages 45–64 and assumed that non-Hispanic White mortality estimates apply to other race/ethnicity categories. To derive 2-year, 3-year, and 4-year all-cause post-MI mortality incidence, EPA further assumed that the annual probability of death between 1-year follow-up and 5-year follow-up was constant. Finally, EPA assumed that the resulting estimates apply to ages 40–44 MI survivors and age 65 MI survivors. |

**Table G-12: Summary of Inputs and Data Sources Used in the CVD Model**

| Data Element | Modeled Variability | Data Source | Notes |
|---|---|---|---|
| 1-year, 2-year, 3-year, 4-year, 5-year, and 6-year all-cause mortality incidence in MI survivors and IS survivors age 65+ | Sex: all<br>Race: all<br>Age: age group 65+<br>Condition: MI, IS | S. Li et al. (2019) | S. Li et al. (2019) estimates based on 2008 MI and 2008 IS Medicare cohorts (see Figure 1 of the paper) were used. Note that these estimates are neither race- nor sex-specific. |
| 1-year, 2-year, 3-year, 4-year, and 5-year CVD mortality incidence in MI survivors ages 40–65 | Sex: males, females<br>Race: non-Hispanic White, non-Hispanic Black,<br>Age: age groups 40–65<br>Condition: MI | Thom et al. (2001); MI incidence based on the MEPS 2010–2017 analysis, U.S. Life Tables, 2017 (Arias et al., 2019); CVD death rates 1999–2019 (Centers for Disease Control and Prevention, 2020c) | EPA used estimated annual age- and sex-specific non-CVD death probability (estimated as described above) to calculate the probability of non-CVD death within the next 1, 2, 3, 4, and 5 years. These probabilities were averaged over ages 45–64 using MI incidence-based weights estimated from MEPS 2010–2017 (estimated as described above). EPA then subtracted these estimates from 1-, 2-, 3-, 4-, and 5-year sex-specific all-cause mortality incidence in MI survivors ages 45–64 (estimated as described above) to obtain 1-, 2-, 3-, 4-, and 5-year CVD mortality incidence. Based on this result, EPA estimated the sex-specific ratios of CVD mortality to all-cause mortality in MI survivors 1, 2, 3, 4, and 5 years after the initial event. These ratios were applied to non-Hispanic White and non-Hispanic Black all-cause post-MI mortality reported in Thom et al. (2001) to obtain post-acute CVD mortality estimates for these races. The other race/ethnicity categories used in modeling were assigned post-acute CVD mortality rates for non-Hispanic Whites. Finally, EPA assumed that the resulting estimates applied to ages 40-44 MI survivors and to age 65 MI survivors. |
| 1-year, 2-year, 3-year, 4-year, 5-year, and 6-year CVD mortality incidence in MI survivors and IS survivors ages 65+ | Sex: male, female<br>Race: all<br>Age: ages 66 … 89<br>Condition: MI, IS | S. Li et al. (2019); U.S. Life Tables, 2017 (Arias et al., 2019); CVD death rates, 1999–2019 (Centers for Disease Control and Prevention, 2020c); U.S. Life Tables Eliminating Certain Causes of Death, 1999–2000 (Arias et al., 2013) | EPA used estimated annual age- and sex-specific non-CVD death probability (estimated as described above) to calculate the probability of non-CVD death within the next 1, 2, 3, 4, 5, and 6 years. These results were averaged using S. Li et al. (2019) 2008 MI/IS cohort age and sex characteristics. In conjunction with all-cause post-MI/IS mortality estimates from S. Li et al. (2019), these estimates were used to estimate the ratio of CVD mortality to the general population non-CVD mortality 1, 2, 3, 4, 5, and 6 years after the initial MI/IS event. The sex- and age-specific probabilities of CVD death 1, 2, 3, 4, 5, and 6 years after the initial MI/IS event were estimated by applying these ratios to sex- and age-specific non-CVD mortality probabilities. |

**Table G-12: Summary of Inputs and Data Sources Used in the CVD Model**

| Data Element | Modeled Variability | Data Source | Notes |
|---|---|---|---|

Abbreviations: ASCVD – atherosclerotic cardiovascular disease; CHD – coronary heart disease; CVD – cardiovascular disease; HCUP – Healthcare Cost and Utilization Project; IS – ischemic stroke; MEPS – Medical Expenditure Panel Survey; MI – myocardial infarction; NCHS – National Center for Health Statistics; NHANES – National Health and Nutrition Examination Survey; PFOA – perfluorooctanoic acid; PFOS – perfluorooctanesulfonic acid.

# Appendix H. Cancer Benefits Model Details and Input Data

This appendix details the cancer life table approach, the data used to estimate reduced RCC cases resulting from changes in exposure to PFOA via drinking water, and the data used to estimate reduced bladder cancer cases resulting from changes in exposures to disinfection byproducts (DBPs) via drinking water. This appendix also provides baseline kidney and bladder cancer statistics.

## H.1 Details on the Cancer Life Table Approach

This appendix details the life table calculations used to estimate reduced cancer cases among population cohorts affected by reductions in PFAS and co-occurring contaminant levels at PWS following implementation of drinking water treatment technologies.

The life table is a metric designed to represent the longevity of people from a certain population. The inputs to the life table are the age-specific probability of death and the initial population size (e.g., the retail population served at a given PWS). Based on this information, the life table computes the number of persons surviving to a specific age, the number of deaths occurring at a given age, the number of person-years lived at a given age, the number of person-years lived beyond a given age, and age-specific life expectancy. The details of standard life table calculations can be found in Anderson (1999). EPA has previously used life table approaches in regulatory analyses, including the analysis of lead-associated health effects in the 2015 Benefit and Cost Analysis for the Effluent Limitations Guidelines, Standards for the Steam Electric Power Generating Point Source Category (U.S. EPA, 2015), and $PM_{2.5}$-related health effects in revisions to the National Ambient Air Quality Standards for ground-level ozone (U.S. EPA, 2008). Other examples of use of a life table approach among federal agencies include EPA's analysis of Benefits and Costs of the Clean Air Act from 1990 to 2020 (U.S. EPA, 2011a) and the Occupational Safety and Health Administration (OSHA) assessment of lifetime excess lung cancer, nonmalignant respiratory disease mortality, and silicosis risks from exposure to respirable crystalline silica (81 FR 16285, March 25, 2016; OSHA, 2010).

To estimate the health effects of changes in exposures to cancer-causing pollutants, the health risk model tracks evolution of two populations over time – the cancer-free population and the population living with cancer.[44] These two populations are modeled for both the baseline annual exposure scenario and for the regulatory alternative annual exposure scenario. Populations in the baseline and regulatory alternative exposure scenarios are demographically identical, but they differ in the pollutant levels to which they are exposed. EPA assumes that the population is exposed to baseline pollutant levels prior to technology implementation year (i.e., change in a given pollutant equals 0) and to alternative pollutant levels that reflect the impact of treatment implementation under the regulatory alternative. All PWSs with baseline PFAS exceedances are assumed to upgrade their treatment by 2026 to comply with the proposed regulation. To capture these effects while being consistent with the remainder of the benefit framework, EPA modeled

[44] When referring to the "cancer-free" population, EPA is referring to the population that is free of the specific type of cancer modeled in this analysis, rather than the population that is free of all cancers.

changes in health outcomes resulting from changes in exposure over an evaluation period that starts in 2023 and ends in 2104.[45]

The model tracks all-cause mortality and cancer experience for a set of model populations defined by sex, location (if modeled), birth year $B = 1938, \ldots, 2023, 2024, \ldots, 2104$, and age attained by 2023 (for those alive in 2023), which is denoted by $A = 0,1,2,3, \ldots 85+$.[46] Each model population is followed from age 0 in year $B$ to age $\min(100, 2104 - B)$ in year $\min(B + 100, 2104)$, using a one-year time step. For cohorts born prior to or in 2023, the model is initialized using the location- (if modeled), age-, race/ethnicity- (if modeled), and sex-specific number of persons estimated to be alive in 2021. For cohorts born after 2023, the model is initialized using the location- (if modeled), race/ethnicity-, and sex-specific number of persons age 0 estimated to be alive in 2021. Location- and sex, race/ethnicity-, and age-specific population details are included in Appendix B.

Below, EPA provides a list of variables included in the health risk model (Table H-1) and describes the process for quantifying the evolution of model population defined by $B$ and $A$ under baseline exposure assumptions.[47] EPA omits sex and location-specific indices because calculation steps do not differ across sexes and locations. EPA then describes the process for quantifying the evolution of the population under regulatory alternative exposures. Finally, EPA describes the process for estimating the total calendar year $y$-specific health benefits. EPA aggregates benefits estimates over all model populations ($(B, A) = \{(1938,85+), \ldots, (2023,0), (2024,0), \ldots, (2104,0)\}$).

**Table H-1: Health Risk Model Variable Definitions**

| Variable | Definition |
|---|---|
| $a$ | Current age or age at cancer diagnosis |
| $x_a$ | A person's lifetime pollutant exposure under the regulatory alternative by age $a$ |
| $z_a$ | A person's lifetime baseline pollutant exposure by age $a$ |
| $LR_a$ | Lifetime risk of cancer per person within age interval $[0, a)$ under the baseline conditions |
| $IR_a$ | Age-specific baseline annual cancer incidence rate per person |
| $B$ | Birth year |
| $A$ | Age in 2023 (years) for those alive in 2023, 0 for those born after 2023 |
| $P$ | Number of affected persons of age $A$ in 2023 or persons aged 0 born after 2023 |
| $y$ | Calendar year |
| $x_{a,y}$ | A person's lifetime pollutant exposure under the regulatory alternative by age $a$ given that this age occurs in year $y$ |
| $z_{a,y}$ | A person's lifetime baseline pollutant exposure by age $a$ given that this age occurs in year $y$ |
| $l_{C=0,a,y}(z_{a,y})$ | The baseline number of cancer-free living individuals at the beginning of age $a$ given that this age occurs in year $y$ |

[45] Although benefits of lagged changes in lifetime cancer risk after 2104 may be attributed to changes in contaminant exposure during the analysis period, EPA did not model effects beyond this period.

[46] Note that those born after the start of the evaluation period in 2023 (i.e., during 2023-2104) are always tracked starting from age 0. As with the CVD model, those aged 85 years or older at the start of the analysis are treated as a single cohort, with mortality statistics averaged over ages 85-100 years and serum PFOA/PFOS set at values corresponding to age 85 years at the beginning of evaluation.

[47] SafeWater was programmed for maximal computational efficiency and SafeWater performs a series of pre-calculations to reduce model runtime. Therefore, the specific equations in the SafeWater code differ from the equations in this Appendix, but the end result is mathematically consistent.

**Table H-1: Health Risk Model Variable Definitions**

| Variable | Definition |
|---|---|
| $d_{C=0,a,y}(z_{a,y})$ | The baseline number of deaths among cancer-free individuals at age $a$ given that this age occurs in year $y$ |
| $l_{C=1,a,y}(z_{a,y})$ | The baseline number of new cancer cases at age $a$ given that this age occurs in year $y$ |
| $q_a$ | Probability of a general population all-cause death at age $a$ |
| $\tau_a$ | Share of cancer deaths among all-cause deaths at age $a$ |
| $\gamma_a$ | Baseline probability of a new cancer diagnosis at age $a$ |
| $k$ | Cancer duration in years |
| $s$ | Cancer stage (localized, regional, distant, unstaged) |
| $\delta_{S=s,a}$ | Age-specific share of new stage $s$ cancers |
| $\tilde{l}_{S=s,a,y,0}(z_{a,y})$ | The baseline number of new stage $s$ cancers occurring at age $a$ given that this age occurs in year $y$ |
| $r_{S=s,a,k}$ | Relative survival rate $k$ years after stage $s$ cancer occurrence at age $a$ |
| $\tilde{q}_{S=s,a,k}$ | Stage-specific probability of death in the cancer population whose cancer was diagnosed at age $a$ and they lived $k$ years after the diagnosis. Current age of these individuals is $a+k$. |
| $\tilde{d}_{S=s,a,y,0}(z_{a,y})$ | The baseline number of deaths in the stage $s$ cancer population in the year of diagnosis (i.e., when $k = 0$), given the current age $a$ and the corresponding year $y$. |
| $\tilde{l}_{S=s,a,y,k}(z_{a,y-k})$ | The baseline number of individuals living with the stage $s$ cancer in the $k$-th year after diagnosis in year $y$, given the cancer diagnosis at age $a$ and the cumulative exposure through to that age and year $y-k$. |
| $\tilde{d}_{S=s,a,y,k}(z_{a,y-k})$ | The baseline number of deaths among those with the stage $s$ cancer in the $k$-th year after diagnosis in year $y$, given the cancer diagnosis at age $a$ and the cumulative exposure through to that age and year $y-k$. |
| $\tilde{e}_{S=s,a,y,k}(z_{a,y-k})$ | The baseline number of excess cancer deaths (i.e., the number of deaths in the cancer population over and above the number of deaths expected in the general population of the same age) among those with the stage $s$ cancer in the $k$-th year after diagnosis in year $y$, given the cancer diagnosis at age $a$ and the cumulative exposure through to that age and year $y-k$. |
| $LR_{a,y}(z_{a,y})$ | Recursive estimate of the lifetime risk of cancer within age interval [0, $a$) under the baseline conditions, given that age $a$ occurs in year $y$ |
| $RR(x_{a,y}, z_{a,y})$ | Relative risk of cancer by age $a$ given that this age occurs in year $y$, baseline exposure $z_{a,y}$ and regulatory alternative exposure $x_{a,y}$ |
| $LR_{a,y}(x_{a,y})$ | Recursive estimate of the lifetime risk of cancer within age interval [0, $a$) under the regulatory alternative, given that age $a$ occurs in year $y$ |
| $NC_{B,A,y,s}$ | The incremental number of new stage $s$ cancer cases in year $y$ for the model population $(B,A)$. |
| $LC_{B,A,y,s}$ | The incremental number of individuals living with stage $s$ cancer in year $y$ for the model population $(B,A)$. |
| $ED_{B,A,y}$ | The incremental number of excess in stage $s$ cancer population in year $y$ for the model population $(B,A)$. |

## *H.1.1 Evolution of Model Population (B,A) under Baseline Pollutant Exposure*

Given a model population $(B,A)$, for each current age $a$ and calendar year $y$, the following baseline exposure $z_{a,y} = \frac{1}{a}\sum_{i=0}^{a-1} \text{Baseline Pollutant}_{i,y-a+i}$ dependent quantities are computed:

$l_{C=0,a,y}(z_{a,y})$: The number of cancer-free living individuals at the beginning of age $a$, in year $y$;
$d_{C=0,a,y}(z_{a,y})$: The number of deaths among cancer-free individuals aged $a$ during the year $y$;

$l_{C=1,a,y}(z_{a,y})$: The number of new cancer cases among individuals aged $a$ during the year $y$.

To compute each quantity above, EPA makes assumptions about the priority of events that terminate a person's existence in the pool of cancer-free living individuals. These events are general population non-cancer deaths that occur with probability[48] $q_{\,a}(1-\tau_a)$ and new cancer diagnoses that occur with probability $\gamma_a$, which is approximated by age-specific annual cancer incidence rate $IR_a$. In the model, EPA assumes that the new cancer diagnoses occur after general population non-cancer deaths and use the following recurrent equations for ages $a > 0$:[49]

Equation H-1:

$$l_{C=0,a,y}(z_{a,y}) = l_{C=0,a-1,y-1}(z_{a-1,y-1}) - d_{C=0,a-1,y-1}(z_{a-1,y-1}) - l_{C=1,a-1,y-1}(z_{a-1,y-1})$$

Equation H-2:

$$d_{C=0,a,y}(z_{a,y}) = q_{\,a}(1-\tau_a) \cdot l_{C=0,a,y}(z_{a,y})$$

Equation H-3:

$$l_{C=1,a,y}(z_{a,y}) = \gamma_a \cdot \left(l_{C=0,a,y}(z_{a,y}) - d_{C=0,a,y}(z_{a,y})\right)$$

To initiate each set of recurrent equations for those alive in 2023, EPA estimates the number of cancer-free individuals at age $a = 0$, denoted by $l_{C=0,0,y-A}(z_{0,y-A})$, that is consistent with the number of affected persons of age $A$ in 2023, denoted by $P$. To this end, Equation H-1, Equation H-2, and Equation H-3 are estimated as find $l_{C=0,0,y-A}(z_{0,y-A}) = P/\prod_{i=0}^{A-1}(1-q_i)$ where $P \equiv l_{C=0,A,2023}(z_{A,2023})$. To initiate each set of recurrent equations for those born after 2023, EPA uses the PWS-, race/ethnicity-, sex, and scenario-specific number of persons who died in the previous year of the analysis, thereby ensuring that the size of the modeled population remains constant throughout the analysis period.

[48] The model does not index the general population death rates using the calendar year, because the model relies on the most recent static life tables.

[49] EPA notes that this is a conservative assumption that results in a lower bound estimate of the regulatory alternative impact (with respect to this particular uncertainty factor). An upper bound estimate of the regulatory alternative impact can be obtained by assuming that new cancer diagnoses occur *before* general population deaths. In a limited sensitivity analysis performed as part of the Benefit and Cost Analysis for Proposed Revisions to the Effluent Limitations Guidelines and Standards for the Steam Electric Power Generating Source Category (U.S. EPA, 2019), EPA found that estimates generated using this alternative assumption were approximately 5 percent larger than the estimates assuming that new cancer diagnoses occur *after* general population deaths.

Consistent with available cancer survival statistics, EPA models mortality experience in the cancer populations $l_{C=1,a,y}(z_{a,y})$ as dependent on the age-at-onset $a$, disease duration $k$, and cancer stage $s$ (e.g., localized, regional, distant, unstaged). Given each age-specific share of new cancer cases $l_{C=1,a,y}(z_{a,y})$ and age-specific share of new stage $s$ cancers $\delta_{S=s,a}$, EPA calculates the number of new stage $s$ cancers occurring at age $a$ in year y:

Equation H-4:

$$\tilde{l}_{S=s,a,y,0}(z_{a,y}) = \delta_{S=s,a} \cdot l_{C=1,a,y}(z_{a,y})$$

For a model population $(B, A)$ and cancer stage $s$, EPA separately tracks $\min(85,2104 - B) - A + 1$ new stage-specific cancer populations from age-at-onset $a$ to age $\min(85,2104 - B)$.[50] Next, a set of cancer duration $k$-dependent annual death probabilities is derived for each population from available data on relative survival rates[51] $r_{S=s,a,k}$ and general population annual death probabilities $q_{a+k}$ as follows:

Equation H-5:

$$\tilde{q}_{S=s,a,k} = 1 - \frac{r_{S=s,a,k+1}}{r_{S=s,a,k}}(1 - q_{a+k})$$

EPA estimates deaths in the cancer population in the year of diagnosis (*i.e.*, when $k = 0$) as follows:

Equation H-6:

$$\tilde{d}_{S=s,a,y,0}(z_{a,y}) = \tilde{q}_{S=s,a,0} \cdot \tilde{l}_{S=s,a,y,0}(z_{a,y})$$

In years that follow the initial diagnosis year (*i.e.*, $k > 0$), EPA uses the following recurrent equations to estimate the number of people living with cancer and the annual number of deaths in the cancer population:

Equation H-7:

$$\tilde{l}_{S=s,a,y,k}(z_{a,y-k}) = \tilde{l}_{S=s,a,y,k-1}(z_{a,y-k}) - \tilde{d}_{S=s,a,y,k-1}(z_{a,y-k})$$

Equation H-8:

$$\tilde{d}_{S=s,a,y,k}(z_{a,y-k}) = \tilde{q}_{S=s,a,k} \cdot \tilde{l}_{S=s,a,y,k}(z_{a,y-k})$$

[50] In total, there are $4 \cdot (\min(85,2104 - B) - A + 1)$ new cancer populations being tracked for each model population.

[51] Note that $r_{S=s,a,k}$ is a multiplier that modifies the general probability of survival to age $a + k$ to reflect the fact that the population under consideration has developed cancer $k$ years ago.

Because the Agency is interested in cancer-related deaths rather than all deaths in the cancer population, EPA also tracks the number of excess cancer population deaths (*i.e.*, the number of deaths in the cancer population over and above the number of deaths expected in the general population of the same age). The excess deaths are computed as:

Equation H-9:

$$\tilde{e}_{S=s,a,y,k}(z_{a,y-k}) = \tilde{q}_{S=s,a,k} \cdot \tilde{l}_{S=s,a,y,k}(z_{a,y-k}) - q_{a+k} \cdot \tilde{l}_{S=s,a,y,k}(z_{a,y-k})$$

## H.1.2 Evolution of Model Population (B,A) under the Regulatory Alternative Pollutant Exposure

Under the baseline conditions when the change in contaminant levels is zero (i.e., before 2026), EPA approximates the annual cancer probability $\gamma_a$ by age-specific annual cancer incidence rate $IR_a$. EPA computes the pollutant-dependent annual new cancer cases under the regulatory alternative conditions, $l_{C=1,a,y}(x_{a,y})$, in three steps. First, EPA recursively estimates $LR_{a,y}(z_{a,y})$, the lifetime risk of cancer within age interval $[0, a)$ under the baseline conditions:

Equation H-10:

$$LR_{a,y}(z_{a,y}) = \frac{1}{l_{C=0,0,y-A}(z_{0,y-A})} \cdot \sum_{j=0}^{a-1} l_{C=1,j}(z_{j,y-A+j}),\ a > 0 \text{ and } LR_{0,y-A}(z_{0,y-A}) = 0$$

Second, the result of Equation H-10 is combined with the relative risk estimate $RR(x_{a,y}, z_{a,y})$, associated with each cancer type:

Equation H-11:

$$LR_{a,y}(x_{a,y}) = RR(x_{a,y}, z_{a,y}) LR_{a,y}(z_{a,y})$$

This results in a series of lifetime cancer risk estimates under the regulatory alternative. Third, EPA computes a series of new annual cancer case estimates under the regulatory alternative as follows:

Equation H-12:

$$l_{C=1,a,y}(x_{a,y}) = \left(LR_{a+1,y+1}(x_{a+1,y+1}) - LR_{a,y}(x_{a,y})\right) \cdot l_{C=0,0,y-A}(z_{0,y-A})$$

## H.1.3 Health Effects and Benefits Attributable to the Regulatory Alternatives

To characterize the overall impact of the regulatory alternatives in a given year $y$, for each model population defined by $(B, A)$, sex, and location, EPA calculates three quantities: the incremental number of new stage $s$ cancer cases ($NC_{A,y,s}$), the incremental number of individuals living with stage $s$ cancer ($LC_{A,y,s}$), and the incremental number of excess deaths in the cancer population ($ED_{A,y}$). The formal definitions of each of these quantities are given below:

Equation H-13:

$$NC_{B,A,y,s} = [0 \le y - \max(2023, B) + A \le \min(85, 2104 - B)\,] \cdot \left(\tilde{l}_{S=s,y-\max(2023,B)+A,y,0}\left(z_{y-\max(2023,B)+A,y}\right) - \tilde{l}_{S=s,y-\max(2023,B)+A,0}\left(x_{y-\max(2023,B)+A,y}\right)\right)$$

Equation H-14:

$$LC_{B,A,y,s} = \sum_{k=1}^{100} [0 \le y - \max(2023, B) + A + k \le \min(85, 2104 - B)\,] \cdot \left(\tilde{l}_{S=s,y-\max(2023,B)+A-k,y,k}\left(z_{y-\max(2023,B)+A-k,y-k}\right) - \tilde{l}_{S=s,y-\max(2023,B)+A-k,y,k}\left(x_{y-\max(2023,B)+A-k,y-k}\right)\right)$$

Equation H-15:

$$ED_{B,A,y} = \sum_{k=0}^{100} [0 \le y - \max(2023, B) + A + k \le \min(85, 2104 - B)\,] \sum_{s \in S} \left(\tilde{e}_{S=s,y-\max(2023,B)+A-k,y,k}\left(z_{y-\max(2023,B)+A-k,y-k}\right) - \tilde{e}_{S=s,y-\max(2023,B)+A-k,y,k}\left(x_{y-\max(2023,B)+A-k,y-k}\right)\right)$$

These calculations are carried out to 2104.

## H.2 Cancer Life Table Model Input Data

As noted in Section 6.6.2 of the Economic Analysis, EPA relied on data sources including EPA SDWIS, age-, race/ethnicity- and sex-specific population from U.S. Census Bureau (2020) (See Appendix B), the Surveillance, Epidemiology, and End Results (SEER) program database (National Cancer Institute), and the Centers for Disease Control and Prevention (CDC) National Center for Health Statistics (NCHS) to characterize sex-, race/ethnicity- and age group-specific general population mortality rates and cancer incidence rates used in model simulations. Table H-2 summarizes these data sources; Appendix B provides details on the population size estimates.

**Table H-2: Summary of Data Sources Used in Cancer Lifetime Risk Models**

| Data Element | Modeled Variability | Data Source | Notes |
|---|---|---|---|
| Cancer incidence rate (IR) per 100,000 persons | Age at diagnosis: 1-year groups (ages 0 to 100)<br>Sex: males, females<br>Cancer type: Kidney Cancer; Urinary Bladder (Invasive & In Situ) Cancer<br>Race/ethnicity: All, non-Hispanic White, non- | Surveillance, Epidemiology, and End Results (SEER) 21 cancer incidence rates by age, sex, and race at diagnosis for 2014-2018 (Surveillance Research Program - National Cancer Institute, 2020b) | Distinct SEER 21 IR data were available for ages 0, 1-4, 5-9, 10-14, 15-19, 20-24, 25-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80-84, 85+. EPA assumed that the same IR applies to all ages within each age group. EPA assumed that non-Hispanic Black iRs can be approximated |

**Table H-2: Summary of Data Sources Used in Cancer Lifetime Risk Models**

| Data Element | Modeled Variability | Data Source | Notes |
|---|---|---|---|
| | Hispanic Black, Hispanic, non-Hispanic Other | | by Black iRs. EPA assumed that non-Hispanic Other iRs can be approximated by all race iRs. |
| General population probability of death | Age: 1-year groups (ages 0 to 100)<br>Sex: males, females<br>Race/ethnicity: All, non-Hispanic White, non-Hispanic Black, Hispanic, non-Hispanic Other | Centers for Disease Control and Prevention (CDC)/National Center for Health Statistics (NCHS) United States Life Tables, 2017 (Arias et al., 2019) | EPA used race/ethnicity-, age- and sex-specific probabilities of dying within the integer age intervals. EPA assumed that non-Hispanic Other data can be approximated by all race data. |
| Share of cancer deaths among all-cause deaths | Age at diagnosis: 1-year groups (ages 0 to 100)<br>Sex: males, females<br>Cancer type: Kidney Cancer; Urinary Bladder (Invasive & In Situ) Cancer<br>Race/ethnicity: All, non-Hispanic White, non-Hispanic Black, Hispanic, non-Hispanic Other | Underlying Cause of Death, 1999-2019 on CDC WONDER Online Database (Centers for Disease Control and Prevention, 2020c) | EPA calculated share of cancer deaths among all-cause deaths by race/ethnicity, age and sex by dividing the number of cancer deaths during 1999-2019 with the number of all-cause deaths during 1999-2019. |
| Share of bladder cancer incidence at specific cancer stage | Age at diagnosis: 1-year groups (ages 0 to 100)<br>Sex: males, females<br>Cancer stage: localized, regional, distant, unstaged<br>Cancer type: Urinary Bladder (Invasive & In Situ) Cancer | SEER 21 distribution of bladder cancer incidence over stages by age and sex at diagnosis for 2008-2018 (Surveillance Research Program - National Cancer Institute, 2020b) | Distinct SEER 21 data were available for ages 0-15, 15-39, 40-64, 65-74, 75+. EPA assumed that the same cancer incidence shares by stage apply to all ages within each age group. |
| Share of kidney cancer incidence at specific cancer stage | Age at diagnosis: 1-year groups (ages 0 to 100)<br>Sex: males, females<br>Cancer stage: localized, regional, distant, unstaged<br>Cancer type: Kidney Cancer<br>Race/ethnicity: All, non-Hispanic White, non-Hispanic Black, Hispanic, non-Hispanic Other | SEER 21 distribution of kidney cancer incidence over stages by race/ethnicity, age and sex at diagnosis for 2008-2018 (Surveillance Research Program - National Cancer Institute, 2020b) | Distinct SEER 21 data were available for ages 0-15, 15-39, 40-64, 65-74, 75+. EPA assumed that the same cancer incidence shares by stage apply to all ages within each age group. EPA assumed that non-Hispanic Black data can be approximated by Black data. EPA assumed that non-Hispanic Other data can be approximated by all race data. |
| Relative bladder cancer survival by cancer stage | Age at diagnosis: 1-year groups (ages 0 to 100)<br>Sex: males, females<br>Duration: 1-year groups (durations 0 to 100 years)<br>Cancer stage: localized, regional, distant, unstaged<br>Cancer type: Urinary | SEER 18 relative bladder cancer survival by age at diagnosis, sex, cancer stage and duration with diagnosis for 2000-2017 (Surveillance Research Program - National Cancer Institute, 2020a) | Distinct SEER 18 data were available for ages at diagnosis 0-14, 15-39, 40-64, 65-74, 75+. EPA assumed that the same cancer relative survival patterns apply to all ages within each age group. SEER 18 contained data on relative survival among persons that had bladder cancer for 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and |

**Table H-2: Summary of Data Sources Used in Cancer Lifetime Risk Models**

| Data Element | Modeled Variability | Data Source | Notes |
|---|---|---|---|
| | Bladder (Invasive & In Situ) Cancer | | 10 years. For disease durations longer than 10 years EPA applied 10-year relative survival rates. |
| Relative kidney cancer survival by cancer stage | Age at diagnosis: 1-year groups (ages 0 to 100)<br>Sex: males, females<br>Duration: 1-year groups (durations 0 to 100 years)<br>Cancer stage: localized, regional, distant, unstaged<br>Cancer type: Kidney Cancer<br>Race/ethnicity: All, non-Hispanic White, non-Hispanic Black, Hispanic, non-Hispanic Other | SEER 18 relative kidney cancer survival by race/ethnicity, age at diagnosis, sex, cancer stage and duration with diagnosis for 2000-2017 (Surveillance Research Program - National Cancer Institute, 2020a) | Distinct SEER 18 data were available for ages at diagnosis 0-14, 15-39, 40-64, 65-74, 75+. EPA assumed that the same cancer relative survival patterns apply to all ages within each age group. EPA assumed that non-Hispanic Black data can be approximated by Black data. EPA assumed that non-Hispanic Other data can be approximated by all race data. SEER 18 contained data on relative survival among persons that had kidney cancer for 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10 years. For disease durations longer than 10 years EPA applied 10-year relative survival rates. |

Abbreviations: CDC – Centers for Disease Control and Prevention; EPA – U.S. Environmental Protection Agency; IR – Incidence Ratio; NCHS – National Center for Health Statistics; SEER – Surveillance, Epidemiology, and End Results.

## H.3 Baseline Kidney Cancer Statistics

Table H-3 provides baseline kidney cancer incidence data used in the life-table model. Kidney cancer incidence rates per 100,000 range from 0.25 to 44 for females and from 0.16 to 96 for males. Kidney cancer incidence rates are highest for men in their 60s, 70s, and 80s, ranging from 62 per 100,000 to 96 per 100,000. Localized kidney cancers comprise 37%-84% of all kidney cancer incidence, whereas regional kidney cancers comprise 8.0%-34%, distant kidney cancers comprise 6.0%-26%, and unstaged kidney cancers comprise 1.7%-11% of all kidney cancer incidence. Table H-4 provides baseline kidney cancer incidence data by race/ethnicity used in the life-table model.

**Table H-3: Summary of Baseline Kidney Cancer Incidence Data Used in the Model**

| Age | Females | | | | | Males | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Incidence per 100K | Percent of Incidence in Stage | | | | Incidence per 100K | Percent of Incidence in Stage | | | |
| | | Localized | Regional | Distant | Unstaged | | Localized | Regional | Distant | Unstaged |
| <1 | 1.6 | 37 | 34 | 26 | 3.1 | 1.9 | 43 | 33 | 21 | 3.3 |
| 1-4 | 2.0 | 37 | 34 | 26 | 3.1 | 1.8 | 43 | 33 | 21 | 3.3 |
| 5-9 | 0.82 | 37 | 34 | 26 | 3.1 | 0.53 | 43 | 33 | 21 | 3.3 |
| 10-14 | 0.25 | 37 | 34 | 26 | 3.1 | 0.18 | 43 | 33 | 21 | 3.3 |
| 15-19 | 0.27 | 84 | 8.0 | 6.0 | 1.9 | 0.16 | 81 | 10 | 7.7 | 1.7 |
| 20-24 | 0.60 | 84 | 8.0 | 6.0 | 1.9 | 0.51 | 81 | 10 | 7.7 | 1.7 |
| 25-29 | 1.1 | 84 | 8.0 | 6.0 | 1.9 | 1.3 | 81 | 10 | 7.7 | 1.7 |
| 30-34 | 2.7 | 84 | 8.0 | 6.0 | 1.9 | 3.5 | 81 | 10 | 7.7 | 1.7 |
| 35-39 | 4.7 | 84 | 8.0 | 6.0 | 1.9 | 7.2 | 81 | 10 | 7.7 | 1.7 |
| 40-44 | 7.8 | 77 | 11 | 10 | 1.8 | 14 | 70 | 14 | 13 | 2.1 |
| 45-49 | 11 | 77 | 11 | 10 | 1.8 | 22 | 70 | 14 | 13 | 2.1 |
| 50-54 | 16 | 77 | 11 | 10 | 1.8 | 33 | 70 | 14 | 13 | 2.1 |
| 55-59 | 22 | 77 | 11 | 10 | 1.8 | 47 | 70 | 14 | 13 | 2.1 |
| 60-64 | 29 | 77 | 11 | 10 | 1.8 | 62 | 70 | 14 | 13 | 2.1 |
| 65-69 | 37 | 71 | 14 | 13 | 2.9 | 81 | 67 | 16 | 14 | 3.2 |
| 70-74 | 41 | 71 | 14 | 13 | 2.9 | 91 | 67 | 16 | 14 | 3.2 |
| 75-79 | 44 | 59 | 12 | 17 | 11 | 96 | 57 | 16 | 17 | 9.3 |
| 80-84 | 40 | 59 | 12 | 17 | 11 | 84 | 57 | 16 | 17 | 9.3 |
| 85+ | 33 | 59 | 12 | 17 | 11 | 68 | 57 | 16 | 17 | 9.3 |

**Table H-4: Summary of Race/Ethnicity-Specific Baseline Kidney Cancer Incidence Data Used in the Model**

| Race/Ethnicity | Age | Females | | | | | Males | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Incidence per 100K | Percent of Incidence in Stage | | | | Incidence per 100K | Percent of Incidence in Stage | | | |
| | | | Localized | Regional | Distant | Unstaged | | Localized | Regional | Distant | Unstaged |
| Non-Hispanic White | <1 | 1.4 | 38 | 33 | 27 | 2.5 | 2.5 | 40 | 35 | 22 | 3.6 |
| | 1-4 | 2.2 | 38 | 33 | 27 | 2.5 | 2.1 | 40 | 35 | 22 | 3.6 |
| | 5-9 | 1 | 38 | 33 | 27 | 2.5 | 0.54 | 40 | 35 | 22 | 3.6 |
| | 10-14 | 0.2 | 38 | 33 | 27 | 2.5 | 0.19 | 40 | 35 | 22 | 3.6 |
| | 15-19 | 0.32 | 87 | 7.8 | 4 | 1.7 | - | 85 | 8.9 | 5 | 1.1 |
| | 20-24 | 0.52 | 87 | 7.8 | 4 | 1.7 | 0.46 | 85 | 8.9 | 5 | 1.1 |
| | 25-29 | 1.2 | 87 | 7.8 | 4 | 1.7 | 1.5 | 85 | 8.9 | 5 | 1.1 |
| | 30-34 | 2.9 | 87 | 7.8 | 4 | 1.7 | 4 | 85 | 8.9 | 5 | 1.1 |
| | 35-39 | 4.9 | 87 | 7.8 | 4 | 1.7 | 7.7 | 85 | 8.9 | 5 | 1.1 |
| | 40-44 | 8 | 76 | 12 | 10 | 1.6 | 14 | 70 | 15 | 13 | 1.9 |
| | 45-49 | 12 | 76 | 12 | 10 | 1.6 | 23 | 70 | 15 | 13 | 1.9 |
| | 50-54 | 16 | 76 | 12 | 10 | 1.6 | 35 | 70 | 15 | 13 | 1.9 |
| | 55-59 | 22 | 76 | 12 | 10 | 1.6 | 48 | 70 | 15 | 13 | 1.9 |
| | 60-64 | 28 | 76 | 12 | 10 | 1.6 | 62 | 70 | 15 | 13 | 1.9 |
| | 65-69 | 37 | 70 | 14 | 13 | 2.7 | 82 | 66 | 17 | 14 | 3 |
| | 70-74 | 40 | 70 | 14 | 13 | 2.7 | 94 | 66 | 17 | 14 | 3 |
| | 75-79 | 46 | 58 | 13 | 17 | 11 | 99 | 58 | 16 | 17 | 9.4 |
| | 80-84 | 41 | 58 | 13 | 17 | 11 | 89 | 58 | 16 | 17 | 9.4 |
| | 85+ | 33 | 58 | 13 | 17 | 11 | 72 | 58 | 16 | 17 | 9.4 |
| Non-Hispanic Black | <1 | - | 34 | 39 | 23 | 3.6 | - | 40 | 34 | 22 | 3.9 |
| | 1-4 | 2.4 | 34 | 39 | 23 | 3.6 | 1.7 | 40 | 34 | 22 | 3.9 |
| | 5-9 | 0.88 | 34 | 39 | 23 | 3.6 | 0.58 | 40 | 34 | 22 | 3.9 |
| | 10-14 | - | 34 | 39 | 23 | 3.6 | - | 40 | 34 | 22 | 3.9 |
| | 15-19 | - | 75 | 8.3 | 14 | 2.7 | - | 68 | 12 | 17 | 2.7 |
| | 20-24 | 0.84 | 75 | 8.3 | 14 | 2.7 | 0.78 | 68 | 12 | 17 | 2.7 |
| | 25-29 | 1.1 | 75 | 8.3 | 14 | 2.7 | 1.5 | 68 | 12 | 17 | 2.7 |
| | 30-34 | 2.4 | 75 | 8.3 | 14 | 2.7 | 3.4 | 68 | 12 | 17 | 2.7 |
| | 35-39 | 3.8 | 75 | 8.3 | 14 | 2.7 | 8.1 | 68 | 12 | 17 | 2.7 |
| | 40-44 | 7.4 | 81 | 9 | 7.9 | 2.4 | 15 | 76 | 9.5 | 11 | 2.8 |
| | 45-49 | 11 | 81 | 9 | 7.9 | 2.4 | 26 | 76 | 9.5 | 11 | 2.8 |
| | 50-54 | 16 | 81 | 9 | 7.9 | 2.4 | 38 | 76 | 9.5 | 11 | 2.8 |
| | 55-59 | 23 | 81 | 9 | 7.9 | 2.4 | 54 | 76 | 9.5 | 11 | 2.8 |
| | 60-64 | 38 | 81 | 9 | 7.9 | 2.4 | 79 | 76 | 9.5 | 11 | 2.8 |
| | 65-69 | 46 | 78 | 8.6 | 10 | 3.8 | 95 | 74 | 11 | 11 | 3.5 |
| | 70-74 | 49 | 78 | 8.6 | 10 | 3.8 | 94 | 74 | 11 | 11 | 3.5 |
| | 75-79 | 47 | 67 | 8.2 | 14 | 11 | 103 | 63 | 10 | 17 | 8.9 |
| | 80-84 | 46 | 67 | 8.2 | 14 | 11 | 82 | 63 | 10 | 17 | 8.9 |
| | 85+ | 37 | 67 | 8.2 | 14 | 11 | 61 | 63 | 10 | 17 | 8.9 |

**Table H-4: Summary of Race/Ethnicity-Specific Baseline Kidney Cancer Incidence Data Used in the Model**

| Race/Ethnicity | Age | Females | | | | | Males | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Incidence per 100K | Percent of Incidence in Stage | | | | Incidence per 100K | Percent of Incidence in Stage | | | |
| | | | Localized | Regional | Distant | Unstaged | | Localized | Regional | Distant | Unstaged |
| Hispanic | <1 | - | 35 | 35 | 27 | 3 | 1.6 | 50 | 28 | 20 | 1.7 |
| | 1-4 | 1.7 | 35 | 35 | 27 | 3 | 1.7 | 50 | 28 | 20 | 1.7 |
| | 5-9 | 0.57 | 35 | 35 | 27 | 3 | 0.51 | 50 | 28 | 20 | 1.7 |
| | 10-14 | - | 35 | 35 | 27 | 3 | - | 50 | 28 | 20 | 1.7 |
| | 15-19 | - | 84 | 8.6 | 5.4 | 1.7 | - | 79 | 11 | 8.2 | 2.1 |
| | 20-24 | 0.63 | 84 | 8.6 | 5.4 | 1.7 | 0.47 | 79 | 11 | 8.2 | 2.1 |
| | 25-29 | 1 | 84 | 8.6 | 5.4 | 1.7 | 0.92 | 79 | 11 | 8.2 | 2.1 |
| | 30-34 | 2.8 | 84 | 8.6 | 5.4 | 1.7 | 3 | 79 | 11 | 8.2 | 2.1 |
| | 35-39 | 5.9 | 84 | 8.6 | 5.4 | 1.7 | 6.4 | 79 | 11 | 8.2 | 2.1 |
| | 40-44 | 9.2 | 76 | 12 | 10 | 2.1 | 13 | 67 | 15 | 15 | 2.4 |
| | 45-49 | 13 | 76 | 12 | 10 | 2.1 | 20 | 67 | 15 | 15 | 2.4 |
| | 50-54 | 19 | 76 | 12 | 10 | 2.1 | 30 | 67 | 15 | 15 | 2.4 |
| | 55-59 | 24 | 76 | 12 | 10 | 2.1 | 45 | 67 | 15 | 15 | 2.4 |
| | 60-64 | 34 | 76 | 12 | 10 | 2.1 | 62 | 67 | 15 | 15 | 2.4 |
| | 65-69 | 42 | 69 | 14 | 14 | 2.9 | 83 | 66 | 16 | 15 | 3.6 |
| | 70-74 | 46 | 69 | 14 | 14 | 2.9 | 91 | 66 | 16 | 15 | 3.6 |
| | 75-79 | 45 | 59 | 12 | 17 | 12 | 96 | 54 | 18 | 19 | 9 |
| | 80-84 | 39 | 59 | 12 | 17 | 12 | 79 | 54 | 18 | 19 | 9 |
| | 85+ | 35 | 59 | 12 | 17 | 12 | 70 | 54 | 18 | 19 | 9 |
| Other | <1 | 1.6 | 37 | 34 | 26 | 3.1 | 1.9 | 43 | 33 | 21 | 3.3 |
| | 1-4 | 2 | 37 | 34 | 26 | 3.1 | 1.8 | 43 | 33 | 21 | 3.3 |
| | 5-9 | 0.82 | 37 | 34 | 26 | 3.1 | 0.53 | 43 | 33 | 21 | 3.3 |
| | 10-14 | 0.25 | 37 | 34 | 26 | 3.1 | 0.18 | 43 | 33 | 21 | 3.3 |
| | 15-19 | 0.27 | 84 | 8 | 6 | 1.9 | 0.16 | 81 | 10 | 7.7 | 1.7 |
| | 20-24 | 0.6 | 84 | 8 | 6 | 1.9 | 0.51 | 81 | 10 | 7.7 | 1.7 |
| | 25-29 | 1.1 | 84 | 8 | 6 | 1.9 | 1.3 | 81 | 10 | 7.7 | 1.7 |
| | 30-34 | 2.7 | 84 | 8 | 6 | 1.9 | 3.5 | 81 | 10 | 7.7 | 1.7 |
| | 35-39 | 4.7 | 84 | 8 | 6 | 1.9 | 7.2 | 81 | 10 | 7.7 | 1.7 |
| | 40-44 | 7.8 | 77 | 11 | 10 | 1.8 | 14 | 70 | 14 | 13 | 2.1 |
| | 45-49 | 11 | 77 | 11 | 10 | 1.8 | 22 | 70 | 14 | 13 | 2.1 |
| | 50-54 | 16 | 77 | 11 | 10 | 1.8 | 33 | 70 | 14 | 13 | 2.1 |
| | 55-59 | 22 | 77 | 11 | 10 | 1.8 | 47 | 70 | 14 | 13 | 2.1 |
| | 60-64 | 29 | 77 | 11 | 10 | 1.8 | 62 | 70 | 14 | 13 | 2.1 |
| | 65-69 | 37 | 71 | 14 | 13 | 2.9 | 81 | 67 | 16 | 14 | 3.2 |
| | 70-74 | 41 | 71 | 14 | 13 | 2.9 | 91 | 67 | 16 | 14 | 3.2 |
| | 75-79 | 44 | 59 | 12 | 17 | 11 | 96 | 57 | 16 | 17 | 9.3 |
| | 80-84 | 40 | 59 | 12 | 17 | 11 | 84 | 57 | 16 | 17 | 9.3 |
| | 85+ | 33 | 59 | 12 | 17 | 11 | 68 | 57 | 16 | 17 | 9.3 |

Table H-5 shows relative kidney cancer survival rates[52] by sex, age group at diagnosis, cancer stage, and the number of years post diagnosis. The relative kidney cancer survival ranges from 3.2% to 100%, and generally decreases as the number of years post-diagnosis increases. The table also shows the absolute survival probability, averaged over the age range for which the relative survival data were available; these probabilities are a product of general population survival probability and the relative kidney cancer survival probability by sex, age group at diagnosis, and the number of years post-diagnosis. The life-table model uses derived absolute survival probabilities to model all-cause mortality experience in kidney cancer populations for the baseline scenario and the regulatory alternatives. Table H-6 provides kidney cancer survival rates by race/ethnicity used in the life-table model. Finally, Table H-7 shows all-cause and kidney cancer mortality rates used in the life-table model. Kidney cancer deaths represent <1% of all-cause mortality among females and <2% of all-cause mortality among males. Table H-8 provides all-cause and kidney cancer mortality rates by race/ethnicity used in the life-table model.

[52] Relative kidney cancer survival rate is the probability of being alive K years after diagnosis at age A divided by the general probability to survive K years for a person alive at age A without such a diagnosis.

**Table H-5: Summary of Relative and Absolute Kidney Cancer Survival Used in the Model**

| Age at Diagnosis | Follow-Up Time | Females | | | | | | | | Males | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | |
| | | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged |
| Ages <15 | 1 year | 99 | 99 | 92 | 100 | 99 | 98 | 91 | 99 | 99 | 99 | 88 | - | 99 | 98 | 88 | - |
| Ages <15 | 2 years | 98 | 97 | 86 | 100 | 98 | 97 | 85 | 99 | 99 | 96 | 79 | - | 98 | 95 | 78 | - |
| Ages <15 | 3 years | 98 | 95 | 83 | 96 | 97 | 94 | 82 | 96 | 97 | 95 | 76 | - | 96 | 95 | 75 | - |
| Ages <15 | 4 years | 97 | 94 | 81 | 92 | 97 | 93 | 81 | 92 | 97 | 95 | 74 | - | 96 | 94 | 73 | - |
| Ages <15 | 5 years | 97 | 93 | 80 | 92 | 96 | 93 | 79 | 92 | 97 | 94 | 73 | - | 96 | 93 | 72 | - |
| Ages <15 | 6 years | 96 | 93 | 79 | 92 | 95 | 93 | 79 | 92 | 96 | 94 | 72 | - | 95 | 93 | 71 | - |
| Ages <15 | 7 years | 95 | 93 | 79 | 87 | 95 | 92 | 79 | 86 | 96 | 94 | 71 | - | 95 | 93 | 70 | - |
| Ages <15 | 8 years | 95 | 93 | 78 | 87 | 95 | 92 | 78 | 86 | 96 | 94 | 70 | - | 95 | 93 | 69 | - |
| Ages <15 | 9 years | 95 | 93 | 78 | 87 | 95 | 92 | 78 | 86 | 96 | 92 | 69 | - | 95 | 91 | 68 | - |
| Ages <15 | 10 years | 95 | 93 | 78 | 87 | 95 | 92 | 78 | 86 | 96 | 92 | 69 | - | 95 | 90 | 68 | - |
| Ages 15-39 | 1 year | 99 | 93 | 50 | 90 | 99 | 92 | 49 | 89 | 99 | 92 | 42 | 91 | 97 | 90 | 41 | 89 |
| Ages 15-39 | 2 years | 99 | 85 | 32 | 83 | 98 | 84 | 31 | 82 | 99 | 85 | 27 | 84 | 97 | 83 | 26 | 83 |
| Ages 15-39 | 3 years | 98 | 80 | 24 | 77 | 97 | 79 | 24 | 76 | 98 | 78 | 20 | 83 | 96 | 76 | 19 | 81 |
| Ages 15-39 | 4 years | 98 | 75 | 21 | 77 | 97 | 74 | 21 | 76 | 98 | 74 | 15 | 83 | 95 | 72 | 14 | 81 |

**Table H-5: Summary of Relative and Absolute Kidney Cancer Survival Used in the Model**

| Age at Diagnosis | Follow-Up Time | Females | | | | | | | | Males | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | |
| | | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged |
| Ages 15-39 | 5 years | 97 | 73 | 16 | 77 | 96 | 72 | 16 | 76 | 97 | 71 | 12 | 79 | 94 | 69 | 12 | 77 |
| Ages 15-39 | 6 years | 97 | 72 | 15 | 77 | 96 | 71 | 15 | 76 | 96 | 69 | 10 | 72 | 93 | 67 | 10 | 70 |
| Ages 15-39 | 7 years | 97 | 71 | 14 | 77 | 95 | 70 | 14 | 76 | 95 | 68 | 9 | 69 | 92 | 65 | 9 | 67 |
| Ages 15-39 | 8 years | 96 | 70 | 13 | 77 | 95 | 69 | 13 | 76 | 95 | 66 | 8 | 66 | 92 | 64 | 7 | 64 |
| Ages 15-39 | 9 years | 96 | 69 | 13 | 77 | 94 | 68 | 12 | 76 | 94 | 65 | 8 | 66 | 91 | 62 | 7 | 63 |
| Ages 15-39 | 10 years | 95 | 69 | 13 | 77 | 93 | 68 | 12 | 76 | 94 | 65 | 8 | 66 | 90 | 62 | 7 | 63 |
| Ages 40-64 | 1 year | 99 | 91 | 43 | 73 | 94 | 87 | 40 | 70 | 99 | 92 | 46 | 78 | 90 | 84 | 42 | 71 |
| Ages 40-64 | 2 years | 98 | 85 | 28 | 67 | 92 | 80 | 26 | 63 | 97 | 86 | 31 | 69 | 89 | 78 | 28 | 63 |
| Ages 40-64 | 3 years | 97 | 80 | 21 | 64 | 91 | 75 | 19 | 60 | 96 | 81 | 23 | 64 | 87 | 73 | 20 | 58 |
| Ages 40-64 | 4 years | 96 | 77 | 17 | 61 | 89 | 72 | 15 | 57 | 95 | 77 | 18 | 61 | 85 | 69 | 16 | 54 |
| Ages 40-64 | 5 years | 95 | 74 | 14 | 60 | 88 | 69 | 13 | 55 | 94 | 74 | 14 | 58 | 83 | 65 | 13 | 51 |
| Ages 40-64 | 6 years | 94 | 71 | 12 | 56 | 87 | 66 | 11 | 52 | 92 | 71 | 12 | 55 | 81 | 62 | 11 | 48 |
| Ages 40-64 | 7 years | 93 | 69 | 11 | 55 | 85 | 63 | 10 | 50 | 91 | 68 | 11 | 52 | 79 | 58 | 9 | 45 |
| Ages 40-64 | 8 years | 92 | 66 | 10 | 52 | 83 | 60 | 9 | 47 | 90 | 65 | 9 | 50 | 77 | 55 | 8 | 43 |

**Table H-5: Summary of Relative and Absolute Kidney Cancer Survival Used in the Model**

| Age at Diagnosis | Follow-Up Time | Females | | | | | | | | Males | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | |
| | | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged |
| Ages 40-64 | 9 years | 91 | 64 | 9 | 50 | 82 | 57 | 8 | 45 | 89 | 63 | 9 | 48 | 75 | 53 | 7 | 40 |
| Ages 40-64 | 10 years | 90 | 63 | 8 | 50 | 80 | 56 | 7 | 44 | 87 | 60 | 8 | 45 | 72 | 50 | 6 | 38 |
| Ages 65-74 | 1 year | 98 | 89 | 38 | 66 | 90 | 82 | 35 | 61 | 98 | 90 | 41 | 67 | 87 | 80 | 37 | 60 |
| Ages 65-74 | 2 years | 97 | 82 | 24 | 58 | 88 | 75 | 22 | 53 | 97 | 84 | 26 | 60 | 84 | 73 | 23 | 52 |
| Ages 65-74 | 3 years | 95 | 76 | 17 | 53 | 85 | 68 | 16 | 47 | 95 | 78 | 19 | 54 | 80 | 66 | 16 | 45 |
| Ages 65-74 | 4 years | 94 | 73 | 14 | 49 | 82 | 64 | 12 | 43 | 94 | 74 | 15 | 48 | 77 | 60 | 13 | 39 |
| Ages 65-74 | 5 years | 92 | 69 | 11 | 47 | 79 | 59 | 9 | 40 | 92 | 70 | 12 | 44 | 73 | 55 | 10 | 35 |
| Ages 65-74 | 6 years | 90 | 66 | 10 | 46 | 75 | 55 | 8 | 38 | 91 | 67 | 10 | 42 | 69 | 52 | 8 | 32 |
| Ages 65-74 | 7 years | 88 | 63 | 8 | 44 | 72 | 51 | 7 | 36 | 89 | 65 | 9 | 37 | 65 | 48 | 7 | 27 |
| Ages 65-74 | 8 years | 87 | 61 | 8 | 39 | 68 | 48 | 6 | 31 | 87 | 63 | 8 | 37 | 61 | 44 | 6 | 26 |
| Ages 65-74 | 9 years | 85 | 57 | 7 | 35 | 65 | 43 | 5 | 27 | 86 | 61 | 8 | 34 | 58 | 41 | 5 | 23 |
| Ages 65-74 | 10 years | 83 | 53 | 6 | 34 | 60 | 39 | 5 | 25 | 85 | 57 | 7 | 32 | 54 | 37 | 4 | 20 |
| Ages 75+ | 1 year | 92 | 78 | 22 | 49 | 47 | 40 | 11 | 25 | 94 | 83 | 28 | 52 | 46 | 41 | 14 | 26 |
| Ages 75+ | 2 years | 91 | 71 | 12 | 38 | 46 | 35 | 6 | 19 | 93 | 77 | 17 | 45 | 44 | 37 | 8 | 21 |

**Table H-5: Summary of Relative and Absolute Kidney Cancer Survival Used in the Model**

| Age at Diagnosis | Follow-Up Time | Females | | | | | | | | Males | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | |
| | | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged |
| Ages 75+ | 3 years | 89 | 66 | 9 | 32 | 43 | 32 | 5 | 16 | 92 | 74 | 12 | 38 | 42 | 34 | 5 | 17 |
| Ages 75+ | 4 years | 88 | 61 | 7 | 29 | 41 | 29 | 4 | 13 | 89 | 70 | 9 | 32 | 39 | 31 | 4 | 14 |
| Ages 75+ | 5 years | 86 | 57 | 6 | 25 | 39 | 26 | 3 | 11 | 88 | 67 | 7 | 27 | 36 | 28 | 3 | 11 |
| Ages 75+ | 6 years | 84 | 54 | 5 | 24 | 36 | 24 | 2 | 10 | 87 | 62 | 6 | 23 | 34 | 24 | 2 | 9 |
| Ages 75+ | 7 years | 81 | 51 | 5 | 22 | 34 | 21 | 2 | 9 | 85 | 60 | 6 | 20 | 31 | 22 | 2 | 7 |
| Ages 75+ | 8 years | 78 | 50 | 5 | 19 | 31 | 20 | 2 | 8 | 82 | 57 | 5 | 19 | 28 | 20 | 2 | 7 |
| Ages 75+ | 9 years | 74 | 47 | 4 | 18 | 28 | 18 | 1 | 7 | 81 | 55 | 4 | 17 | 26 | 17 | 1 | 5 |
| Ages 75+ | 10 years | 72 | 42 | 3 | 18 | 25 | 15 | 1 | 6 | 79 | 52 | 4 | 16 | 23 | 15 | 1 | 5 |

**Table H-6: Summary of Race/Ethnicity-Specific Relative and Absolute Kidney Cancer Survival Used in the Model**

| Race/Ethnicity | Age at Diagnosis | Follow-Up Time | Females | | | | | | | | Males | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | |
| | | | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged |
| Non-Hispanic White | Ages <15 | 1 year | 100 | 98 | 95 | - | 99 | 98 | 94 | - | 99 | 99 | 92 | - | 98 | 99 | 92 | - |
| | Ages <15 | 2 years | 99 | 98 | 90 | - | 98 | 98 | 90 | - | 99 | 95 | 88 | - | 98 | 95 | 88 | - |
| | Ages <15 | 3 years | 98 | 94 | 85 | - | 98 | 94 | 85 | - | 96 | 95 | 85 | - | 95 | 95 | 85 | - |
| | Ages <15 | 4 years | 98 | 94 | 85 | - | 97 | 93 | 85 | - | 96 | 95 | 84 | - | 95 | 95 | 84 | - |
| | Ages <15 | 5 years | 98 | 93 | 83 | - | 97 | 92 | 82 | - | 96 | 94 | 84 | - | 95 | 94 | 83 | - |
| | Ages <15 | 6 years | 98 | 93 | 83 | - | 97 | 92 | 82 | - | 96 | 94 | 83 | - | 95 | 94 | 82 | - |
| | Ages <15 | 7 years | 97 | 93 | 83 | - | 96 | 92 | 82 | - | 96 | 93 | 82 | - | 95 | 92 | 81 | - |
| | Ages <15 | 8 years | 97 | 93 | 83 | - | 96 | 92 | 82 | - | 96 | 93 | 82 | - | 95 | 92 | 81 | - |
| | Ages <15 | 9 years | 97 | 93 | 83 | - | 96 | 92 | 82 | - | 96 | 91 | 82 | - | 95 | 90 | 81 | - |
| | Ages <15 | 10 years | 97 | 93 | 83 | - | 96 | 92 | 82 | - | 96 | 91 | 82 | - | 95 | 90 | 81 | - |
| | Ages 15-39 | 1 year | 100 | 97 | 58 | - | 99 | 96 | 58 | - | 99 | 91 | 52 | 96 | 97 | 89 | 51 | 94 |
| | Ages 15-39 | 2 years | 99 | 91 | 38 | - | 98 | 90 | 38 | - | 99 | 87 | 33 | 84 | 97 | 85 | 33 | 82 |
| | Ages 15-39 | 3 years | 99 | 85 | 27 | - | 98 | 84 | 27 | - | 99 | 83 | 25 | 84 | 96 | 81 | 24 | 82 |
| | Ages 15-39 | 4 years | 99 | 82 | 21 | - | 97 | 81 | 21 | - | 98 | 78 | 18 | 84 | 96 | 76 | 18 | 82 |
| | Ages 15-39 | 5 years | 98 | 80 | 18 | - | 97 | 79 | 18 | - | 97 | 77 | 14 | 84 | 95 | 75 | 14 | 81 |
| | Ages 15-39 | 6 years | 98 | 77 | 18 | - | 96 | 76 | 18 | - | 97 | 75 | 13 | 79 | 94 | 73 | 13 | 77 |

**Table H-6: Summary of Race/Ethnicity-Specific Relative and Absolute Kidney Cancer Survival Used in the Model**

| Race/Ethnicity | Age at Diagnosis | Follow-Up Time | Females | | | | | | | | Males | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | |
| | | | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged |
| | Ages 15-39 | 7 years | 98 | 76 | 17 | - | 96 | 74 | 16 | - | 96 | 73 | 10 | 79 | 93 | 70 | 10 | 77 |
| | Ages 15-39 | 8 years | 97 | 74 | 17 | - | 96 | 73 | 16 | - | 96 | 72 | 7.2 | 79 | 92 | 69 | 7 | 77 |
| | Ages 15-39 | 9 years | 97 | 74 | 17 | - | 95 | 73 | 16 | - | 95 | 72 | 7.2 | 79 | 91 | 69 | 7 | 76 |
| | Ages 15-39 | 10 years | 96 | 74 | 17 | - | 94 | 73 | 16 | - | 94 | 72 | 7.2 | 79 | 91 | 69 | 6.9 | 76 |
| | Ages 40-64 | 1 year | 99 | 92 | 44 | 71 | 94 | 87 | 42 | 67 | 99 | 93 | 47 | 77 | 91 | 85 | 43 | 70 |
| | Ages 40-64 | 2 years | 98 | 85 | 28 | 65 | 93 | 80 | 26 | 61 | 98 | 87 | 32 | 69 | 89 | 79 | 29 | 63 |
| | Ages 40-64 | 3 years | 97 | 80 | 22 | 63 | 91 | 75 | 20 | 59 | 96 | 82 | 24 | 65 | 87 | 74 | 21 | 58 |
| | Ages 40-64 | 4 years | 96 | 77 | 17 | 61 | 90 | 72 | 16 | 57 | 95 | 78 | 18 | 61 | 85 | 70 | 16 | 54 |
| | Ages 40-64 | 5 years | 96 | 74 | 15 | 60 | 88 | 69 | 14 | 55 | 94 | 75 | 15 | 57 | 83 | 66 | 13 | 50 |
| | Ages 40-64 | 6 years | 95 | 71 | 13 | 57 | 87 | 65 | 12 | 52 | 93 | 72 | 13 | 54 | 81 | 63 | 11 | 48 |
| | Ages 40-64 | 7 years | 94 | 69 | 11 | 55 | 86 | 62 | 10 | 50 | 92 | 69 | 11 | 52 | 79 | 59 | 10 | 45 |
| | Ages 40-64 | 8 years | 93 | 66 | 10 | 51 | 84 | 59 | 8.6 | 46 | 91 | 67 | 10 | 49 | 78 | 57 | 8.2 | 42 |
| | Ages 40-64 | 9 years | 92 | 64 | 8.6 | 51 | 82 | 57 | 7.7 | 45 | 90 | 64 | 8.8 | 49 | 76 | 54 | 7.4 | 41 |
| | Ages 40-64 | 10 years | 91 | 63 | 8.1 | 50 | 80 | 56 | 7.2 | 44 | 88 | 61 | 7.9 | 46 | 73 | 51 | 6.5 | 38 |

**Table H-6: Summary of Race/Ethnicity-Specific Relative and Absolute Kidney Cancer Survival Used in the Model**

| Race/Ethnicity | Age at Diagnosis | Follow-Up Time | Females | | | | | | | | Males | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | |
| | | | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged |
| | Ages 65-74 | 1 year | 98 | 89 | 38 | 65 | 91 | 83 | 35 | 60 | 98 | 91 | 42 | 65 | 87 | 81 | 37 | 58 |
| | Ages 65-74 | 2 years | 97 | 82 | 24 | 58 | 88 | 75 | 22 | 52 | 97 | 85 | 26 | 59 | 84 | 73 | 23 | 51 |
| | Ages 65-74 | 3 years | 96 | 77 | 18 | 50 | 86 | 69 | 16 | 45 | 96 | 79 | 20 | 52 | 81 | 67 | 17 | 44 |
| | Ages 65-74 | 4 years | 95 | 75 | 14 | 46 | 83 | 65 | 13 | 40 | 94 | 75 | 15 | 47 | 78 | 61 | 13 | 38 |
| | Ages 65-74 | 5 years | 93 | 70 | 11 | 44 | 79 | 60 | 9.4 | 38 | 93 | 71 | 13 | 44 | 74 | 57 | 10 | 35 |
| | Ages 65-74 | 6 years | 91 | 67 | 9.3 | 42 | 76 | 56 | 7.7 | 35 | 91 | 69 | 11 | 43 | 70 | 53 | 8.2 | 33 |
| | Ages 65-74 | 7 years | 89 | 64 | 7.9 | 39 | 72 | 52 | 6.4 | 32 | 89 | 67 | 9.2 | 39 | 66 | 49 | 6.7 | 29 |
| | Ages 65-74 | 8 years | 87 | 61 | 7.2 | 36 | 68 | 48 | 5.6 | 28 | 87 | 65 | 8.5 | 38 | 62 | 46 | 6 | 27 |
| | Ages 65-74 | 9 years | 85 | 57 | 6.4 | 34 | 65 | 43 | 4.9 | 26 | 86 | 63 | 7.9 | 35 | 58 | 43 | 5.4 | 24 |
| | Ages 65-74 | 10 years | 82 | 54 | 6 | 33 | 60 | 39 | 4.4 | 24 | 85 | 61 | 6.9 | 31 | 55 | 39 | 4.4 | 20 |
| | Ages 75+ | 1 year | 92 | 79 | 21 | 47 | 47 | 40 | 11 | 24 | 94 | 83 | 28 | 52 | 47 | 41 | 14 | 26 |
| | Ages 75+ | 2 years | 92 | 72 | 12 | 37 | 46 | 36 | 5.9 | 18 | 94 | 77 | 17 | 45 | 44 | 37 | 8.2 | 21 |
| | Ages 75+ | 3 years | 90 | 67 | 9 | 31 | 44 | 32 | 4.3 | 15 | 93 | 74 | 12 | 38 | 42 | 34 | 5.4 | 17 |
| | Ages 75+ | 4 years | 89 | 63 | 6.9 | 28 | 42 | 29 | 3.2 | 13 | 91 | 71 | 9 | 32 | 39 | 31 | 3.9 | 14 |
| | Ages 75+ | 5 years | 87 | 59 | 5.2 | 24 | 39 | 27 | 2.3 | 11 | 89 | 69 | 7.3 | 27 | 37 | 29 | 3 | 11 |

**Table H-6: Summary of Race/Ethnicity-Specific Relative and Absolute Kidney Cancer Survival Used in the Model**

| Race/Ethnicity | Age at Diagnosis | Follow-Up Time | Females | | | | | | | | Males | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | |
| | | | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged |
| | Ages 75+ | 6 years | 85 | 56 | 4.2 | 23 | 37 | 24 | 1.8 | 10 | 89 | 64 | 6.4 | 23 | 35 | 25 | 2.5 | 8.9 |
| | Ages 75+ | 7 years | 84 | 54 | 4.1 | 22 | 35 | 22 | 1.7 | 9.1 | 86 | 61 | 6.1 | 21 | 32 | 22 | 2.2 | 7.7 |
| | Ages 75+ | 8 years | 82 | 52 | 4.1 | 19 | 32 | 21 | 1.6 | 7.6 | 84 | 58 | 5.9 | 20 | 28 | 20 | 2 | 7 |
| | Ages 75+ | 9 years | 77 | 49 | 3.1 | 17 | 29 | 18 | 1.2 | 6.4 | 83 | 56 | 4.6 | 17 | 26 | 18 | 1.4 | 5.5 |
| | Ages 75+ | 10 years | 75 | 44 | 2.9 | 17 | 26 | 15 | 1 | 6 | 82 | 55 | 3.8 | 16 | 24 | 16 | 1.1 | 4.7 |
| Non-Hispanic Black | Ages <15 | 1 year | 99 | 99 | 92 | - | 97 | 97 | 91 | - | 99 | 96 | 81 | - | 97 | 95 | 80 | - |
| | Ages <15 | 2 years | 99 | 96 | 88 | - | 97 | 95 | 87 | - | 99 | 94 | 69 | - | 97 | 93 | 68 | - |
| | Ages <15 | 3 years | 97 | 91 | 86 | - | 96 | 90 | 85 | - | 99 | 94 | 64 | - | 97 | 93 | 63 | - |
| | Ages <15 | 4 years | 95 | 89 | 81 | - | 94 | 88 | 80 | - | 99 | 94 | 64 | - | 97 | 93 | 63 | - |
| | Ages <15 | 5 years | 91 | 89 | 78 | - | 90 | 88 | 77 | - | 99 | 92 | 64 | - | 97 | 90 | 63 | - |
| | Ages <15 | 6 years | 91 | 89 | 78 | - | 90 | 88 | 77 | - | 97 | 92 | 64 | - | 95 | 90 | 62 | - |
| | Ages <15 | 7 years | 91 | 89 | 78 | - | 90 | 88 | 77 | - | 97 | 92 | 64 | - | 95 | 90 | 62 | - |
| | Ages <15 | 8 years | 91 | 89 | 78 | - | 90 | 88 | 77 | - | 97 | 92 | 59 | - | 95 | 90 | 58 | - |
| | Ages <15 | 9 years | 91 | 89 | 78 | - | 90 | 88 | 77 | - | 97 | 92 | 59 | - | 95 | 90 | 58 | - |
| | Ages <15 | 10 years | 91 | 89 | 78 | - | 90 | 88 | 77 | - | 97 | 92 | 59 | - | 94 | 90 | 58 | - |
| | Ages 15-39 | 1 year | 98 | 83 | 34 | - | 97 | 81 | 34 | - | 96 | 86 | 29 | - | 93 | 84 | 28 | - |

**Table H-6: Summary of Race/Ethnicity-Specific Relative and Absolute Kidney Cancer Survival Used in the Model**

| Race/Ethnicity | Age at Diagnosis | Follow-Up Time | Females | | | | | | | | Males | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | |
| | | | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged |
| | Ages 15-39 | 2 years | 98 | 77 | 20 | - | 96 | 76 | 20 | - | 95 | 70 | 15 | - | 92 | 67 | 15 | - |
| | Ages 15-39 | 3 years | 96 | 74 | 16 | - | 95 | 73 | 16 | - | 93 | 57 | 12 | - | 90 | 55 | 12 | - |
| | Ages 15-39 | 4 years | 95 | 70 | 14 | - | 94 | 69 | 14 | - | 92 | 51 | 9.4 | - | 89 | 49 | 9 | - |
| | Ages 15-39 | 5 years | 95 | 70 | 10 | - | 93 | 69 | 10 | - | 91 | 47 | 7.8 | - | 88 | 45 | 7.5 | - |
| | Ages 15-39 | 6 years | 94 | 70 | 10 | - | 93 | 69 | 10 | - | 90 | 41 | 5.9 | - | 86 | 40 | 5.6 | - |
| | Ages 15-39 | 7 years | 93 | 70 | 10 | - | 91 | 69 | 10 | - | 89 | 41 | 5.9 | - | 85 | 39 | 5.6 | - |
| | Ages 15-39 | 8 years | 92 | 70 | 10 | - | 90 | 69 | 10 | - | 89 | 41 | 5.9 | - | 84 | 39 | 5.6 | - |
| | Ages 15-39 | 9 years | 92 | 70 | 10 | - | 90 | 68 | 10 | - | 87 | 37 | 5.9 | - | 82 | 35 | 5.6 | - |
| | Ages 15-39 | 10 years | 90 | 70 | 10 | - | 88 | 68 | 10 | - | 87 | 37 | 5.9 | - | 82 | 35 | 5.6 | - |
| | Ages 40-64 | 1 year | 98 | 87 | 33 | 71 | 91 | 81 | 31 | 66 | 98 | 83 | 33 | 79 | 86 | 73 | 29 | 69 |
| | Ages 40-64 | 2 years | 96 | 78 | 23 | 64 | 88 | 71 | 21 | 58 | 96 | 77 | 19 | 67 | 84 | 67 | 17 | 58 |
| | Ages 40-64 | 3 years | 95 | 72 | 16 | 59 | 86 | 66 | 14 | 53 | 95 | 70 | 13 | 62 | 81 | 60 | 11 | 53 |
| | Ages 40-64 | 4 years | 93 | 68 | 12 | 53 | 84 | 62 | 11 | 47 | 93 | 66 | 8.6 | 57 | 79 | 56 | 7.3 | 48 |
| | Ages 40-64 | 5 years | 92 | 66 | 11 | 50 | 82 | 59 | 9.4 | 45 | 92 | 64 | 6.8 | 56 | 76 | 53 | 5.7 | 47 |

**Table H-6: Summary of Race/Ethnicity-Specific Relative and Absolute Kidney Cancer Survival Used in the Model**

| Race/Ethnicity | Age at Diagnosis | Follow-Up Time | Females | | | | | | | | Males | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | |
| | | | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged |
| | Ages 40-64 | 6 years | 91 | 62 | 9.5 | 48 | 80 | 55 | 8.4 | 42 | 90 | 60 | 6.2 | 54 | 74 | 50 | 5.1 | 44 |
| | Ages 40-64 | 7 years | 90 | 59 | 9.5 | 48 | 78 | 52 | 8.3 | 42 | 89 | 57 | 6 | 53 | 71 | 46 | 4.8 | 43 |
| | Ages 40-64 | 8 years | 89 | 57 | 9 | 48 | 77 | 49 | 7.8 | 41 | 87 | 51 | 5.7 | 52 | 69 | 40 | 4.5 | 41 |
| | Ages 40-64 | 9 years | 87 | 54 | 9 | 41 | 74 | 46 | 7.7 | 35 | 86 | 49 | 4.9 | 48 | 67 | 38 | 3.8 | 37 |
| | Ages 40-64 | 10 years | 87 | 52 | 9 | 41 | 73 | 44 | 7.6 | 35 | 84 | 48 | 4.9 | 43 | 64 | 37 | 3.7 | 32 |
| | Ages 65-74 | 1 year | 96 | 80 | 34 | 70 | 87 | 72 | 31 | 63 | 97 | 82 | 32 | 78 | 82 | 69 | 27 | 66 |
| | Ages 65-74 | 2 years | 95 | 74 | 21 | 58 | 83 | 65 | 19 | 51 | 95 | 76 | 20 | 70 | 78 | 62 | 16 | 57 |
| | Ages 65-74 | 3 years | 92 | 66 | 14 | 54 | 79 | 57 | 12 | 46 | 94 | 68 | 13 | 59 | 74 | 54 | 10 | 47 |
| | Ages 65-74 | 4 years | 90 | 58 | 10 | 52 | 75 | 49 | 8.7 | 43 | 92 | 64 | 10 | 56 | 69 | 48 | 7.7 | 42 |
| | Ages 65-74 | 5 years | 88 | 57 | 8.2 | 52 | 72 | 46 | 6.6 | 42 | 92 | 59 | 7.9 | 51 | 66 | 43 | 5.7 | 37 |
| | Ages 65-74 | 6 years | 86 | 56 | 7.4 | 52 | 68 | 44 | 5.9 | 41 | 91 | 59 | 6.2 | 37 | 63 | 41 | 4.3 | 25 |
| | Ages 65-74 | 7 years | 84 | 56 | 5.6 | 52 | 64 | 43 | 4.3 | 39 | 90 | 57 | 5.9 | 31 | 59 | 38 | 3.9 | 21 |
| | Ages 65-74 | 8 years | 83 | 56 | 5.6 | 35 | 61 | 41 | 4.2 | 26 | 88 | 52 | 5.2 | 28 | 55 | 32 | 3.3 | 18 |
| | Ages 65-74 | 9 years | 80 | 50 | 5.6 | 27 | 57 | 35 | 4 | 19 | 87 | 48 | 3.7 | 28 | 51 | 28 | 2.2 | 17 |

**Table H-6: Summary of Race/Ethnicity-Specific Relative and Absolute Kidney Cancer Survival Used in the Model**

| Race/Ethnicity | Age at Diagnosis | Follow-Up Time | Females | | | | | | | | Males | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | |
| | | | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged |
| | Ages 65-74 | 10 years | 80 | 47 | 5.6 | 27 | 54 | 32 | 3.8 | 18 | 85 | 48 | 2 | 28 | 47 | 27 | 1.1 | 16 |
| | Ages 75+ | 1 year | 90 | 65 | 20 | 58 | 47 | 34 | 11 | 30 | 87 | 73 | 27 | 49 | 43 | 36 | 13 | 24 |
| | Ages 75+ | 2 years | 88 | 60 | 14 | 41 | 44 | 30 | 6.9 | 20 | 87 | 59 | 19 | 43 | 41 | 27 | 8.8 | 20 |
| | Ages 75+ | 3 years | 85 | 53 | 10 | 32 | 41 | 26 | 4.8 | 15 | 87 | 54 | 10 | 37 | 38 | 24 | 4.5 | 17 |
| | Ages 75+ | 4 years | 83 | 47 | 8.9 | 29 | 39 | 22 | 4.2 | 14 | 82 | 48 | 8.4 | 27 | 34 | 20 | 3.5 | 11 |
| | Ages 75+ | 5 years | 80 | 43 | 8.3 | 24 | 36 | 19 | 3.7 | 11 | 80 | 41 | 6.4 | 27 | 32 | 16 | 2.5 | 11 |
| | Ages 75+ | 6 years | 75 | 36 | 8.3 | 21 | 32 | 16 | 3.6 | 9 | 78 | 40 | 6.4 | 24 | 29 | 15 | 2.4 | 8.8 |
| | Ages 75+ | 7 years | 69 | 35 | 8.3 | 19 | 28 | 14 | 3.4 | 7.9 | 73 | 38 | 5.2 | 14 | 25 | 13 | 1.8 | 4.7 |
| | Ages 75+ | 8 years | 64 | 35 | 8.3 | 19 | 25 | 13 | 3.2 | 7.5 | 71 | 38 | 3.7 | 14 | 22 | 12 | 1.2 | 4.3 |
| | Ages 75+ | 9 years | 61 | 31 | 8.3 | 19 | 22 | 11 | 3 | 7.1 | 70 | 38 | 3.7 | - | 20 | 11 | 1.1 | - |
| | Ages 75+ | 10 years | 60 | 30 | 4.8 | 19 | 20 | 10 | 1.6 | 6.7 | 70 | 36 | 3.7 | - | 19 | 9.4 | 1 | - |
| Hispanic | Ages <15 | 1 year | 98 | 99 | 90 | - | 98 | 99 | 89 | - | 100 | 100 | 85 | - | 99 | 99 | 84 | - |
| | Ages <15 | 2 years | 98 | 97 | 79 | - | 98 | 97 | 78 | - | 98 | 98 | 69 | - | 98 | 98 | 68 | - |
| | Ages <15 | 3 years | 98 | 97 | 77 | - | 98 | 97 | 77 | - | 98 | 98 | 67 | - | 97 | 98 | 66 | - |
| | Ages <15 | 4 years | 98 | 96 | 74 | - | 98 | 95 | 73 | - | 96 | 98 | 60 | - | 96 | 98 | 60 | - |
| | Ages <15 | 5 years | 98 | 96 | 74 | - | 98 | 95 | 73 | - | 95 | 98 | 58 | - | 94 | 98 | 57 | - |
| | Ages <15 | 6 years | 97 | 96 | 72 | - | 96 | 95 | 71 | - | 93 | 98 | 58 | - | 93 | 98 | 57 | - |
| | Ages <15 | 7 years | 97 | 94 | 72 | - | 96 | 93 | 71 | - | 93 | 98 | 58 | - | 93 | 98 | 57 | - |
| | Ages <15 | 8 years | 97 | 94 | 72 | - | 96 | 93 | 71 | - | 93 | 98 | 58 | - | 92 | 98 | 57 | - |

**Table H-6: Summary of Race/Ethnicity-Specific Relative and Absolute Kidney Cancer Survival Used in the Model**

| Race/Ethnicity | Age at Diagnosis | Follow-Up Time | Females | | | | | | | | Males | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | |
| | | | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged |
| | Ages <15 | 9 years | 97 | 94 | 72 | - | 96 | 93 | 71 | - | 93 | 95 | 58 | - | 92 | 94 | 57 | - |
| | Ages <15 | 10 years | 97 | 94 | 72 | - | 96 | 93 | 71 | - | 93 | 95 | 58 | - | 92 | 94 | 57 | - |
| | Ages 15-39 | 1 year | 99 | 89 | 53 | - | 99 | 88 | 53 | - | 99 | 93 | 49 | - | 98 | 92 | 48 | - |
| | Ages 15-39 | 2 years | 99 | 79 | 34 | - | 98 | 78 | 33 | - | 99 | 86 | 35 | - | 98 | 85 | 34 | - |
| | Ages 15-39 | 3 years | 98 | 72 | 23 | - | 97 | 71 | 23 | - | 99 | 74 | 25 | - | 98 | 73 | 25 | - |
| | Ages 15-39 | 4 years | 98 | 66 | 23 | - | 97 | 65 | 23 | - | 99 | 73 | 20 | - | 97 | 72 | 20 | - |
| | Ages 15-39 | 5 years | 98 | 66 | 14 | - | 97 | 65 | 14 | - | 98 | 71 | 19 | - | 96 | 70 | 18 | - |
| | Ages 15-39 | 6 years | 97 | 66 | 11 | - | 96 | 65 | 11 | - | 97 | 70 | 15 | - | 95 | 68 | 14 | - |
| | Ages 15-39 | 7 years | 96 | 66 | 11 | - | 95 | 65 | 11 | - | 96 | 70 | 15 | - | 94 | 68 | 14 | - |
| | Ages 15-39 | 8 years | 96 | 66 | 11 | - | 95 | 65 | 11 | - | 96 | 64 | 15 | - | 94 | 62 | 14 | - |
| | Ages 15-39 | 9 years | 96 | 66 | 11 | - | 95 | 65 | 11 | - | 96 | 60 | 15 | - | 93 | 58 | 14 | - |
| | Ages 15-39 | 10 years | 96 | 66 | 11 | - | 95 | 65 | 11 | - | 96 | 60 | 15 | - | 93 | 58 | 14 | - |
| | Ages 40-64 | 1 year | 99 | 91 | 43 | 79 | 95 | 87 | 42 | 76 | 98 | 92 | 46 | 77 | 92 | 86 | 43 | 72 |
| | Ages 40-64 | 2 years | 98 | 86 | 29 | 75 | 94 | 82 | 28 | 72 | 96 | 86 | 31 | 66 | 90 | 80 | 29 | 61 |

**Table H-6: Summary of Race/Ethnicity-Specific Relative and Absolute Kidney Cancer Survival Used in the Model**

| Race/Ethnicity | Age at Diagnosis | Follow-Up Time | Females | | | | | | | | Males | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | |
| | | | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged |
| | Ages 40-64 | 3 years | 97 | 82 | 21 | 70 | 93 | 78 | 20 | 67 | 95 | 82 | 24 | 60 | 88 | 76 | 22 | 56 |
| | Ages 40-64 | 4 years | 96 | 80 | 18 | 65 | 91 | 76 | 17 | 62 | 93 | 78 | 19 | 56 | 85 | 72 | 17 | 51 |
| | Ages 40-64 | 5 years | 94 | 78 | 16 | 63 | 89 | 74 | 15 | 60 | 92 | 73 | 16 | 52 | 83 | 67 | 14 | 47 |
| | Ages 40-64 | 6 years | 94 | 75 | 13 | 58 | 88 | 71 | 12 | 55 | 89 | 71 | 13 | 50 | 81 | 64 | 12 | 45 |
| | Ages 40-64 | 7 years | 92 | 70 | 12 | 58 | 87 | 66 | 11 | 54 | 88 | 67 | 11 | 45 | 79 | 60 | 10 | 40 |
| | Ages 40-64 | 8 years | 91 | 68 | 11 | 58 | 85 | 64 | 10 | 54 | 86 | 65 | 10 | 44 | 76 | 57 | 8.5 | 39 |
| | Ages 40-64 | 9 years | 90 | 66 | 10 | 54 | 83 | 61 | 9.1 | 50 | 86 | 61 | 8.9 | 42 | 75 | 53 | 7.8 | 37 |
| | Ages 40-64 | 10 years | 89 | 66 | 8 | 54 | 81 | 60 | 7.4 | 50 | 83 | 59 | 8.3 | 42 | 72 | 51 | 7.1 | 37 |
| | Ages 65-74 | 1 year | 98 | 90 | 37 | 62 | 93 | 85 | 35 | 59 | 97 | 92 | 40 | 66 | 88 | 84 | 37 | 60 |
| | Ages 65-74 | 2 years | 97 | 86 | 22 | 53 | 90 | 81 | 21 | 50 | 95 | 85 | 25 | 55 | 85 | 76 | 23 | 49 |
| | Ages 65-74 | 3 years | 95 | 77 | 18 | 53 | 88 | 71 | 16 | 49 | 93 | 78 | 18 | 51 | 81 | 68 | 16 | 45 |
| | Ages 65-74 | 4 years | 94 | 75 | 13 | 49 | 85 | 68 | 12 | 44 | 92 | 71 | 15 | 45 | 79 | 61 | 13 | 38 |
| | Ages 65-74 | 5 years | 93 | 74 | 11 | 44 | 83 | 66 | 10 | 39 | 90 | 65 | 12 | 39 | 75 | 54 | 10 | 32 |
| | Ages 65-74 | 6 years | 91 | 73 | 10 | 44 | 80 | 64 | 9.1 | 38 | 88 | 62 | 11 | 32 | 71 | 50 | 8.5 | 26 |

**Table H-6: Summary of Race/Ethnicity-Specific Relative and Absolute Kidney Cancer Survival Used in the Model**

| Race/Ethnicity | Age at Diagnosis | Follow-Up Time | Females | | | | | | | | Males | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | |
| | | | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged |
| | Ages 65-74 | 7 years | 89 | 69 | 10 | 44 | 76 | 59 | 8.2 | 38 | 87 | 59 | 10 | 26 | 68 | 46 | 7.8 | 20 |
| | Ages 65-74 | 8 years | 89 | 67 | 10 | 44 | 74 | 56 | 8 | 37 | 84 | 56 | 10 | 26 | 64 | 42 | 7.6 | 20 |
| | Ages 65-74 | 9 years | 87 | 64 | 10 | 35 | 71 | 52 | 7.8 | 28 | 83 | 54 | 10 | 25 | 61 | 40 | 7.3 | 18 |
| | Ages 65-74 | 10 years | 87 | 58 | 7.6 | 27 | 69 | 46 | 6.1 | 21 | 80 | 45 | 8.9 | 25 | 56 | 32 | 6.2 | 17 |
| | Ages 75+ | 1 year | 93 | 78 | 25 | 45 | 50 | 42 | 13 | 24 | 93 | 86 | 28 | 43 | 47 | 44 | 14 | 22 |
| | Ages 75+ | 2 years | 90 | 72 | 13 | 35 | 48 | 38 | 6.8 | 18 | 91 | 78 | 19 | 32 | 45 | 39 | 9.3 | 16 |
| | Ages 75+ | 3 years | 89 | 67 | 7.8 | 31 | 46 | 35 | 4 | 16 | 89 | 73 | 15 | 27 | 42 | 35 | 7.4 | 13 |
| | Ages 75+ | 4 years | 85 | 60 | 5.8 | 25 | 43 | 30 | 2.9 | 13 | 86 | 67 | 13 | 20 | 40 | 31 | 6.1 | 9.3 |
| | Ages 75+ | 5 years | 82 | 56 | 4.5 | 21 | 41 | 27 | 2.2 | 10 | 83 | 61 | 10 | 16 | 37 | 27 | 4.4 | 7 |
| | Ages 75+ | 6 years | 79 | 55 | 3.6 | 20 | 38 | 26 | 1.7 | 9.5 | 82 | 56 | 7.3 | 14 | 35 | 24 | 3.1 | 6 |
| | Ages 75+ | 7 years | 74 | 47 | 3.6 | 13 | 34 | 22 | 1.7 | 6.1 | 80 | 52 | 6.1 | 14 | 32 | 21 | 2.5 | 5.7 |
| | Ages 75+ | 8 years | 68 | 44 | 3.6 | 11 | 31 | 20 | 1.6 | 5.1 | 75 | 52 | 5 | 10 | 29 | 20 | 1.9 | 3.7 |
| | Ages 75+ | 9 years | 65 | 40 | 2.2 | 10 | 28 | 17 | 1 | 4.2 | 73 | 47 | 5 | 10 | 26 | 17 | 1.8 | 3.5 |
| | Ages 75+ | 10 years | 63 | 33 | 2.2 | 5.2 | 26 | 14 | 0.9 | 2.1 | 68 | 43 | 0 | 10 | 23 | 14 | 0 | 3.2 |
| Other | Ages <15 | 1 year | 99 | 99 | 92 | 100 | 99 | 98 | 91 | 99 | 99 | 99 | 88 | - | 99 | 98 | 88 | - |
| | Ages <15 | 2 years | 98 | 97 | 86 | 100 | 98 | 97 | 85 | 99 | 99 | 96 | 79 | - | 98 | 95 | 78 | - |
| | Ages <15 | 3 years | 98 | 95 | 83 | 96 | 97 | 94 | 82 | 96 | 97 | 95 | 76 | - | 96 | 95 | 75 | - |
| | Ages <15 | 4 years | 97 | 94 | 81 | 92 | 97 | 93 | 81 | 92 | 97 | 95 | 74 | - | 96 | 94 | 73 | - |

**Table H-6: Summary of Race/Ethnicity-Specific Relative and Absolute Kidney Cancer Survival Used in the Model**

| Race/Ethnicity | Age at Diagnosis | Follow-Up Time | Females | | | | | | | | Males | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | |
| | | | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged |
| | Ages <15 | 5 years | 97 | 93 | 80 | 92 | 96 | 93 | 79 | 92 | 97 | 94 | 73 | - | 96 | 93 | 72 | - |
| | Ages <15 | 6 years | 96 | 93 | 79 | 92 | 95 | 93 | 79 | 92 | 96 | 94 | 72 | - | 95 | 93 | 71 | - |
| | Ages <15 | 7 years | 95 | 93 | 79 | 87 | 95 | 92 | 79 | 86 | 96 | 94 | 71 | - | 95 | 93 | 70 | - |
| | Ages <15 | 8 years | 95 | 93 | 78 | 87 | 95 | 92 | 78 | 86 | 96 | 94 | 70 | - | 95 | 93 | 69 | - |
| | Ages <15 | 9 years | 95 | 93 | 78 | 87 | 95 | 92 | 78 | 86 | 96 | 92 | 69 | - | 95 | 91 | 68 | - |
| | Ages <15 | 10 years | 95 | 93 | 78 | 87 | 95 | 92 | 78 | 86 | 96 | 92 | 69 | - | 95 | 90 | 68 | - |
| | Ages 15-39 | 1 year | 99 | 93 | 50 | 90 | 99 | 92 | 49 | 89 | 99 | 92 | 42 | 91 | 97 | 90 | 41 | 89 |
| | Ages 15-39 | 2 years | 99 | 85 | 32 | 83 | 98 | 84 | 31 | 82 | 99 | 85 | 27 | 84 | 97 | 83 | 26 | 83 |
| | Ages 15-39 | 3 years | 98 | 80 | 24 | 77 | 97 | 79 | 24 | 76 | 98 | 78 | 20 | 83 | 96 | 76 | 19 | 81 |
| | Ages 15-39 | 4 years | 98 | 75 | 21 | 77 | 97 | 74 | 21 | 76 | 98 | 74 | 15 | 83 | 95 | 72 | 14 | 81 |
| | Ages 15-39 | 5 years | 97 | 73 | 16 | 77 | 96 | 72 | 16 | 76 | 97 | 71 | 12 | 79 | 94 | 69 | 12 | 77 |
| | Ages 15-39 | 6 years | 97 | 72 | 15 | 77 | 96 | 71 | 15 | 76 | 96 | 69 | 10 | 72 | 93 | 67 | 10 | 70 |
| | Ages 15-39 | 7 years | 97 | 71 | 14 | 77 | 95 | 70 | 14 | 76 | 95 | 68 | 8.9 | 69 | 92 | 65 | 8.7 | 67 |
| | Ages 15-39 | 8 years | 96 | 70 | 13 | 77 | 95 | 69 | 13 | 76 | 95 | 66 | 7.7 | 66 | 92 | 64 | 7.4 | 64 |
| | Ages 15-39 | 9 years | 96 | 69 | 13 | 77 | 94 | 68 | 12 | 76 | 94 | 65 | 7.7 | 66 | 91 | 62 | 7.4 | 63 |

**Table H-6: Summary of Race/Ethnicity-Specific Relative and Absolute Kidney Cancer Survival Used in the Model**

| Race/Ethnicity | Age at Diagnosis | Follow-Up Time | Females | | | | | | | | Males | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | |
| | | | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged |
| | Ages 15-39 | 10 years | 95 | 69 | 13 | 77 | 93 | 68 | 12 | 76 | 94 | 65 | 7.7 | 66 | 90 | 62 | 7.4 | 63 |
| | Ages 40-64 | 1 year | 99 | 91 | 43 | 73 | 94 | 87 | 40 | 70 | 99 | 92 | 46 | 78 | 90 | 84 | 42 | 71 |
| | Ages 40-64 | 2 years | 98 | 85 | 28 | 67 | 92 | 80 | 26 | 63 | 97 | 86 | 31 | 69 | 89 | 78 | 28 | 63 |
| | Ages 40-64 | 3 years | 97 | 80 | 21 | 64 | 91 | 75 | 19 | 60 | 96 | 81 | 23 | 64 | 87 | 73 | 20 | 58 |
| | Ages 40-64 | 4 years | 96 | 77 | 17 | 61 | 89 | 72 | 15 | 57 | 95 | 77 | 18 | 61 | 85 | 69 | 16 | 54 |
| | Ages 40-64 | 5 years | 95 | 74 | 14 | 60 | 88 | 69 | 13 | 55 | 94 | 74 | 14 | 58 | 83 | 65 | 13 | 51 |
| | Ages 40-64 | 6 years | 94 | 71 | 12 | 56 | 87 | 66 | 11 | 52 | 92 | 71 | 12 | 55 | 81 | 62 | 11 | 48 |
| | Ages 40-64 | 7 years | 93 | 69 | 11 | 55 | 85 | 63 | 10 | 50 | 91 | 68 | 11 | 52 | 79 | 58 | 9.2 | 45 |
| | Ages 40-64 | 8 years | 92 | 66 | 10 | 52 | 83 | 60 | 8.7 | 47 | 90 | 65 | 9.3 | 50 | 77 | 55 | 7.9 | 43 |
| | Ages 40-64 | 9 years | 91 | 64 | 8.6 | 50 | 82 | 57 | 7.7 | 45 | 89 | 63 | 8.6 | 48 | 75 | 53 | 7.2 | 40 |
| | Ages 40-64 | 10 years | 90 | 63 | 8.1 | 50 | 80 | 56 | 7.2 | 44 | 87 | 60 | 7.7 | 45 | 72 | 50 | 6.4 | 38 |
| | Ages 65-74 | 1 year | 98 | 89 | 38 | 66 | 90 | 82 | 35 | 61 | 98 | 90 | 41 | 67 | 87 | 80 | 37 | 60 |
| | Ages 65-74 | 2 years | 97 | 82 | 24 | 58 | 88 | 75 | 22 | 53 | 97 | 84 | 26 | 60 | 84 | 73 | 23 | 52 |
| | Ages 65-74 | 3 years | 95 | 76 | 17 | 53 | 85 | 68 | 16 | 47 | 95 | 78 | 19 | 54 | 80 | 66 | 16 | 45 |

**Table H-6: Summary of Race/Ethnicity-Specific Relative and Absolute Kidney Cancer Survival Used in the Model**

| Race/Ethnicity | Age at Diagnosis | Follow-Up Time | Females | | | | | | | | Males | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | |
| | | | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged |
| | Ages 65-74 | 4 years | 94 | 73 | 14 | 49 | 82 | 64 | 12 | 43 | 94 | 74 | 15 | 48 | 77 | 60 | 13 | 39 |
| | Ages 65-74 | 5 years | 92 | 69 | 11 | 47 | 79 | 59 | 9.4 | 40 | 92 | 70 | 12 | 44 | 73 | 55 | 10 | 35 |
| | Ages 65-74 | 6 years | 90 | 66 | 10 | 46 | 75 | 55 | 8 | 38 | 91 | 67 | 10 | 42 | 69 | 52 | 8 | 32 |
| | Ages 65-74 | 7 years | 88 | 63 | 8.1 | 44 | 72 | 51 | 6.6 | 36 | 89 | 65 | 9 | 37 | 65 | 48 | 6.6 | 27 |
| | Ages 65-74 | 8 years | 87 | 61 | 7.7 | 39 | 68 | 48 | 6 | 31 | 87 | 63 | 8.5 | 37 | 61 | 44 | 6 | 26 |
| | Ages 65-74 | 9 years | 85 | 57 | 7 | 35 | 65 | 43 | 5.3 | 27 | 86 | 61 | 7.8 | 34 | 58 | 41 | 5.3 | 23 |
| | Ages 65-74 | 10 years | 83 | 53 | 6.5 | 34 | 60 | 39 | 4.7 | 25 | 85 | 57 | 6.8 | 32 | 54 | 37 | 4.4 | 20 |
| | Ages 75+ | 1 year | 92 | 78 | 22 | 49 | 47 | 40 | 11 | 25 | 94 | 83 | 28 | 52 | 46 | 41 | 14 | 26 |
| | Ages 75+ | 2 years | 91 | 71 | 12 | 38 | 46 | 35 | 6.2 | 19 | 93 | 77 | 17 | 45 | 44 | 37 | 8.3 | 21 |
| | Ages 75+ | 3 years | 89 | 66 | 9.4 | 32 | 43 | 32 | 4.6 | 16 | 92 | 74 | 12 | 38 | 42 | 34 | 5.5 | 17 |
| | Ages 75+ | 4 years | 88 | 61 | 7.4 | 29 | 41 | 29 | 3.5 | 13 | 89 | 70 | 9.2 | 32 | 39 | 31 | 4 | 14 |
| | Ages 75+ | 5 years | 86 | 57 | 5.9 | 25 | 39 | 26 | 2.7 | 11 | 88 | 67 | 7.2 | 27 | 36 | 28 | 3 | 11 |
| | Ages 75+ | 6 years | 84 | 54 | 5 | 24 | 36 | 24 | 2.2 | 10 | 87 | 62 | 6.3 | 23 | 34 | 24 | 2.5 | 8.9 |
| | Ages 75+ | 7 years | 81 | 51 | 4.8 | 22 | 34 | 21 | 2 | 9 | 85 | 60 | 5.8 | 20 | 31 | 22 | 2.1 | 7.5 |
| | Ages 75+ | 8 years | 78 | 50 | 4.7 | 19 | 31 | 20 | 1.9 | 7.7 | 82 | 57 | 5.4 | 19 | 28 | 20 | 1.9 | 6.6 |
| | Ages 75+ | 9 years | 74 | 47 | 3.6 | 18 | 28 | 18 | 1.4 | 6.6 | 81 | 55 | 4.3 | 17 | 26 | 17 | 1.4 | 5.4 |

**Table H-6: Summary of Race/Ethnicity-Specific Relative and Absolute Kidney Cancer Survival Used in the Model**

| Race/Ethnicity | Age at Diagnosis | Follow-Up Time | Females | | | | | | | | Males | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | |
| | | | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged |
| | Ages 75+ | 10 years | 72 | 42 | 3.2 | 18 | 25 | 15 | 1.1 | 6.2 | 79 | 52 | 3.7 | 16 | 23 | 15 | 1.1 | 4.6 |

**Table H-7: Summary of All-Cause and Kidney Cancer Mortality Data Used in the Model**

| | Females | | | Males | | |
|---|---|---|---|---|---|---|
| | Rate per 100K | | | Rate per 100K | | |
| Age | All-Cause | Kidney Cancer | Percent Kidney Cancer | All-Cause | Kidney Cancer | Percent Kidney Cancer |
| <1 | 537 | 0.04 | 0.007 | 646 | 0.045 | 0.007 |
| 1-4 | 36 | 0.06 | 0.17 | 44 | 0.094 | 0.22 |
| 5-9 | 12 | 0.11 | 0.95 | 15 | 0.053 | 0.36 |
| 10-14 | 10 | 0.05 | 0.47 | 12 | 0.035 | 0.28 |
| 15-19 | 19 | 0.05 | 0.26 | 34 | 0.021 | 0.063 |
| 20-24 | 40 | 0.03 | 0.084 | 112 | 0.077 | 0.069 |
| 25-29 | 54 | 0.08 | 0.14 | 142 | 0.15 | 0.11 |
| 30-34 | 73 | 0.11 | 0.15 | 159 | 0.16 | 0.10 |
| 35-39 | 98 | 0.15 | 0.16 | 185 | 0.35 | 0.19 |
| 40-44 | 135 | 0.31 | 0.23 | 229 | 0.80 | 0.35 |
| 45-49 | 203 | 0.7 | 0.35 | 323 | 1.8 | 0.57 |
| 50-54 | 317 | 1.3 | 0.42 | 508 | 3.8 | 0.74 |
| 55-59 | 470 | 2.6 | 0.55 | 784 | 6.9 | 0.88 |
| 60-64 | 675 | 3.8 | 0.56 | 1136 | 11 | 0.95 |
| 65-69 | 987 | 6.2 | 0.63 | 1593 | 16 | 1.02 |
| 70-74 | 1533 | 8.9 | 0.58 | 2304 | 22 | 0.94 |
| 75-79 | 2481 | 13 | 0.51 | 3577 | 30 | 0.84 |
| 80-84 | 4171 | 17 | 0.41 | 5770 | 36 | 0.63 |
| 85+ | - | - | 0.31 | - | - | 0.49 |

**Table H-8: Summary of Race/Ethnicity-Specific All-Cause and Kidney Cancer Mortality Data Used in the Model**

| Race/Ethnicity | Age | Females | | | Males | | |
|---|---|---|---|---|---|---|---|
| | | Rate per 100K | | Percent Kidney Cancer | Rate per 100K | | Percent Kidney Cancer |
| | | All-Cause | Kidney Cancer | | All-Cause | Kidney Cancer | |
| Non-Hispanic White | <1 | 453 | 0.01 | 0.002 | 554 | 0.04 | 0.01 |
| | 1-4 | 33 | 0.03 | 0.08 | 41 | 0.08 | 0.19 |
| | 5-9 | 11 | 0.09 | 0.8 | 14 | 0.06 | 0.42 |
| | 10-14 | 8.5 | 0.06 | 0.69 | 12 | 0.02 | 0.21 |
| | 15-19 | 19 | 0.02 | 0.13 | 32 | 0.02 | 0.05 |
| | 20-24 | 41 | 0.02 | 0.05 | 103 | 0.02 | 0.02 |
| | 25-29 | 57 | 0.03 | 0.05 | 143 | 0.11 | 0.08 |
| | 30-34 | 80 | 0.09 | 0.11 | 166 | 0.1 | 0.06 |
| | 35-39 | 106 | 0.15 | 0.14 | 196 | 0.31 | 0.16 |
| | 40-44 | 143 | 0.26 | 0.18 | 238 | 0.81 | 0.34 |
| | 45-49 | 211 | 0.7 | 0.33 | 333 | 1.9 | 0.58 |
| | 50-54 | 324 | 1.4 | 0.44 | 516 | 3.9 | 0.76 |
| | 55-59 | 472 | 2.6 | 0.55 | 783 | 7.2 | 0.91 |
| | 60-64 | 668 | 3.9 | 0.59 | 1117 | 11 | 0.99 |
| | 65-69 | 985 | 6.5 | 0.66 | 1566 | 17 | 1.1 |
| | 70-74 | 1553 | 9.1 | 0.59 | 2298 | 22 | 0.96 |
| | 75-79 | 2537 | 13 | 0.51 | 3616 | 31 | 0.87 |
| | 80-84 | 4282 | 17 | 0.41 | 5894 | 38 | 0.64 |
| | 85+ | - | - | 0.31 | - | - | 0.5 |
| Non-Hispanic Black | <1 | 1042 | 0.03 | 0 | 1249 | 0.03 | 0.002 |
| | 1-4 | 59 | 0.09 | 0.15 | 70 | 0.09 | 0.13 |

**Table H-8: Summary of Race/Ethnicity-Specific All-Cause and Kidney Cancer Mortality Data Used in the Model**

| Race/Ethnicity | Age | Females | | | Males | | |
|---|---|---|---|---|---|---|---|
| | | Rate per 100K | | Percent Kidney Cancer | Rate per 100K | | Percent Kidney Cancer |
| | | All-Cause | Kidney Cancer | | All-Cause | Kidney Cancer | |
| | 5-9 | 18 | 0.18 | 1 | 24 | 0.03 | 0.12 |
| | 10-14 | 15 | 0.09 | 0.59 | 20 | 0.09 | 0.44 |
| | 15-19 | 23 | 0.15 | 0.63 | 50 | 0.03 | 0.06 |
| | 20-24 | 54 | 0.11 | 0.2 | 181 | 0.32 | 0.17 |
| | 25-29 | 76 | 0.25 | 0.32 | 220 | 0.39 | 0.18 |
| | 30-34 | 102 | 0.36 | 0.35 | 251 | 0.57 | 0.23 |
| | 35-39 | 152 | 0.29 | 0.19 | 288 | 0.81 | 0.28 |
| | 40-44 | 211 | 0.52 | 0.25 | 358 | 1.2 | 0.33 |
| | 45-49 | 316 | 0.83 | 0.26 | 483 | 2.4 | 0.49 |
| | 50-54 | 488 | 1.4 | 0.29 | 737 | 3.9 | 0.53 |
| | 55-59 | 725 | 3.1 | 0.42 | 1175 | 7.5 | 0.64 |
| | 60-64 | 1049 | 4.1 | 0.39 | 1783 | 11 | 0.64 |
| | 65-69 | 1457 | 6.4 | 0.44 | 2500 | 17 | 0.68 |
| | 70-74 | 2065 | 7.9 | 0.38 | 3375 | 23 | 0.68 |
| | 75-79 | 3073 | 12 | 0.4 | 4751 | 30 | 0.64 |
| | 80-84 | 4821 | 17 | 0.35 | 6991 | 34 | 0.49 |
| | 85+ | - | - | 0.31 | - | - | 0.41 |
| Hispanic | <1 | 435 | 0.05 | 0.01 | 513 | 0.07 | 0.01 |
| | 1-4 | 31 | 0.09 | 0.29 | 35 | 0.1 | 0.3 |
| | 5-9 | 11 | 0.14 | 1.3 | 12 | 0.05 | 0.45 |
| | 10-14 | 9 | 0 | 0 | 10 | 0.02 | 0.18 |

**Table H-8: Summary of Race/Ethnicity-Specific All-Cause and Kidney Cancer Mortality Data Used in the Model**

| Race/Ethnicity | Age | Females | | | Males | | |
|---|---|---|---|---|---|---|---|
| | | Rate per 100K | | Percent Kidney Cancer | Rate per 100K | | Percent Kidney Cancer |
| | | All-Cause | Kidney Cancer | | All-Cause | Kidney Cancer | |
| | 15-19 | 16 | 0.04 | 0.25 | 29 | 0.02 | 0.07 |
| | 20-24 | 31 | 0.02 | 0.07 | 97 | 0.07 | 0.08 |
| | 25-29 | 38 | 0.1 | 0.28 | 110 | 0.09 | 0.09 |
| | 30-34 | 46 | 0.02 | 0.05 | 111 | 0.12 | 0.1 |
| | 35-39 | 58 | 0.09 | 0.15 | 127 | 0.27 | 0.21 |
| | 40-44 | 82 | 0.38 | 0.46 | 159 | 0.67 | 0.43 |
| | 45-49 | 126 | 0.75 | 0.6 | 227 | 1.7 | 0.75 |
| | 50-54 | 193 | 1.2 | 0.6 | 365 | 3.5 | 0.97 |
| | 55-59 | 298 | 2.5 | 0.85 | 572 | 6.2 | 1.1 |
| | 60-64 | 461 | 3.6 | 0.79 | 854 | 11 | 1.3 |
| | 65-69 | 707 | 5.6 | 0.79 | 1230 | 16 | 1.3 |
| | 70-74 | 1118 | 9.8 | 0.87 | 1793 | 23 | 1.3 |
| | 75-79 | 1843 | 12 | 0.67 | 2774 | 22 | 0.78 |
| | 80-84 | 3174 | 17 | 0.54 | 4463 | 31 | 0.69 |
| | 85+ | - | - | 0.38 | - | - | 0.47 |
| Other | <1 | 409 | 0.22 | 0.05 | 498 | 0 | 0 |
| | 1-4 | 29 | 0.14 | 0.49 | 39 | 0.2 | 0.52 |
| | 5-9 | 12 | 0.07 | 0.57 | 14 | 0.07 | 0.48 |
| | 10-14 | 8.6 | 0 | 0 | 11 | 0.07 | 0.63 |
| | 15-19 | 15 | 0.07 | 0.45 | 26 | 0.07 | 0.26 |
| | 20-24 | 30 | 0 | 0 | 72 | 0 | 0 |

**Table H-8: Summary of Race/Ethnicity-Specific All-Cause and Kidney Cancer Mortality Data Used in the Model**

| Race/Ethnicity | Age | Females | | | Males | | |
|---|---|---|---|---|---|---|---|
| | | Rate per 100K | | Percent Kidney Cancer | Rate per 100K | | Percent Kidney Cancer |
| | | All-Cause | Kidney Cancer | | All-Cause | Kidney Cancer | |
| | 25-29 | 36 | 0.05 | 0.15 | 81 | 0.16 | 0.2 |
| | 30-34 | 44 | 0.05 | 0.11 | 85 | 0.05 | 0.06 |
| | 35-39 | 55 | 0.15 | 0.28 | 103 | 0.17 | 0.16 |
| | 40-44 | 74 | 0.16 | 0.21 | 132 | 0.47 | 0.36 |
| | 45-49 | 114 | 0.39 | 0.35 | 192 | 0.57 | 0.29 |
| | 50-54 | 181 | 0.68 | 0.37 | 310 | 2.3 | 0.74 |
| | 55-59 | 256 | 1.4 | 0.54 | 451 | 4.3 | 0.95 |
| | 60-64 | 373 | 1.7 | 0.46 | 641 | 6.1 | 0.95 |
| | 65-69 | 553 | 3.6 | 0.65 | 940 | 7.8 | 0.83 |
| | 70-74 | 895 | 6.1 | 0.68 | 1364 | 11 | 0.82 |
| | 75-79 | 1498 | 7.3 | 0.49 | 2206 | 18 | 0.82 |
| | 80-84 | 2648 | 9.6 | 0.36 | 3665 | 15 | 0.4 |
| | 85+ | - | - | 0.25 | - | - | 0.55 |

## H.4 Baseline Bladder Cancer Statistics

Table H-9 provides baseline bladder cancer incidence data used in the life-table model. Bladder cancer incidence rates per 100,000 range from 0.17 to 76 for females and from 0.11 to 357 for males. Bladder cancer incidence rates are highest for men in their 60s, 70s, and 80s, ranging from 67 per 100,000 to 357 per 100,000. Localized bladder cancers comprise 66%-90% of all bladder cancer incidence, whereas regional bladder cancers comprise 4.5%-8.6%, distant bladder cancers comprise 3.1%-14%, and unstaged bladder cancers comprise 0%-6.8% of all bladder cancer incidence.

**Table H-9: Summary of Baseline Bladder Cancer Incidence Data Used in the Model**

| Age | Females | | | | | Males | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Incidence per 100K | Percent of Incidence in Stage | | | | Incidence per 100K | Percent of Incidence in Stage | | | |
| | | Localized | Regional | Distant | Unstaged | | Localized | Regional | Distant | Unstaged |
| <1 | - | 77 | 4.5 | 14 | 4.5 | - | 66 | 23 | 11 | 0 |
| 1-4 | - | 77 | 4.5 | 14 | 4.5 | - | 66 | 23 | 11 | 0 |
| 5-9 | - | 77 | 4.5 | 14 | 4.5 | - | 66 | 23 | 11 | 0 |
| 10-14 | - | 77 | 4.5 | 14 | 4.5 | - | 66 | 23 | 11 | 0 |
| 15-19 | - | 82 | 8.2 | 5.1 | 4.9 | 0.11 | 90 | 4.8 | 3.1 | 2.5 |
| 20-24 | 0.17 | 82 | 8.2 | 5.1 | 4.9 | 0.30 | 90 | 4.8 | 3.1 | 2.5 |
| 25-29 | 0.26 | 82 | 8.2 | 5.1 | 4.9 | 0.51 | 90 | 4.8 | 3.1 | 2.5 |
| 30-34 | 0.50 | 82 | 8.2 | 5.1 | 4.9 | 1.1 | 90 | 4.8 | 3.1 | 2.5 |
| 35-39 | 0.89 | 82 | 8.2 | 5.1 | 4.9 | 2.1 | 90 | 4.8 | 3.1 | 2.5 |
| 40-44 | 1.5 | 83 | 8.6 | 6.1 | 2.7 | 4.2 | 85 | 7.4 | 4.9 | 2.5 |
| 45-49 | 2.9 | 83 | 8.6 | 6.1 | 2.7 | 8.8 | 85 | 7.4 | 4.9 | 2.5 |
| 50-54 | 6.6 | 83 | 8.6 | 6.1 | 2.7 | 19 | 85 | 7.4 | 4.9 | 2.5 |
| 55-59 | 11 | 83 | 8.6 | 6.1 | 2.7 | 38 | 85 | 7.4 | 4.9 | 2.5 |
| 60-64 | 18 | 83 | 8.6 | 6.1 | 2.7 | 67 | 85 | 7.4 | 4.9 | 2.5 |
| 65-69 | 29 | 84 | 7.9 | 5.6 | 2.8 | 114 | 86 | 6.7 | 4.3 | 2.9 |
| 70-74 | 43 | 84 | 7.9 | 5.6 | 2.8 | 176 | 86 | 6.7 | 4.3 | 2.9 |
| 75-79 | 58 | 80 | 7.1 | 5.8 | 6.8 | 245 | 85 | 6.2 | 4.1 | 5.2 |
| 80-84 | 71 | 80 | 7.1 | 5.8 | 6.8 | 315 | 85 | 6.2 | 4.1 | 5.2 |
| 85+ | 76 | 80 | 7.1 | 5.8 | 6.8 | 357 | 85 | 6.2 | 4.1 | 5.2 |

Table H-10 shows relative bladder cancer survival rates[53] by sex, age group at diagnosis, cancer stage, and the number of years post diagnosis. The relative bladder cancer survival ranges from 0% to 100%, and generally decreases as the number of years post-diagnosis increases. The table also shows the absolute survival probability, averaged over the age range for which the relative survival data were available; these probabilities are a product of general population survival probability and the relative bladder cancer survival probability by sex, age group at diagnosis, and the number of years post-diagnosis. The life-table model uses derived absolute survival probabilities to model all-cause mortality experience in bladder cancer populations for the baseline scenario and the regulatory alternative. Finally, Table H-11 shows all-cause and bladder cancer mortality rates used in the life-table model. Bladder cancer deaths <1% of all-cause mortality among females and <2% of all-cause mortality among males.

[53] Relative bladder cancer survival rate is the probability of being alive K years after diagnosis at age A divided by the general probability to survive K years for a person alive at age A without such a diagnosis.

**Table H-10: Summary of Relative and Absolute Bladder Cancer Survival Used in the Model**

| Age at Diagnosis | Follow-Up Time | Females | | | | | | | | Males | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | |
| | | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged |
| Ages 15-39 | 1 year | 98 | 79 | 20 | 90 | 97 | 79 | 20 | 90 | 99 | 85 | 46 | 100 | 97 | 83 | 45 | 98 |
| Ages 15-39 | 2 years | 97 | 58 | 4 | 83 | 96 | 57 | 4 | 83 | 99 | 67 | 23 | 97 | 96 | 65 | 22 | 95 |
| Ages 15-39 | 3 years | 96 | 47 | 0 | 80 | 95 | 46 | 0 | 79 | 98 | 60 | 14 | 95 | 96 | 58 | 13 | 92 |
| Ages 15-39 | 4 years | 95 | 39 | 0 | 80 | 94 | 39 | 0 | 79 | 97 | 58 | 11 | 91 | 95 | 56 | 11 | 89 |
| Ages 15-39 | 5 years | 95 | 32 | 0 | 80 | 93 | 32 | 0 | 79 | 96 | 56 | 11 | 91 | 94 | 54 | 11 | 89 |
| Ages 15-39 | 6 years | 94 | 28 | 0 | 80 | 93 | 27 | 0 | 79 | 96 | 56 | 9 | 91 | 93 | 54 | 9 | 89 |
| Ages 15-39 | 7 years | 94 | 28 | 0 | 80 | 92 | 27 | 0 | 79 | 96 | 56 | 7 | 91 | 93 | 54 | 7 | 88 |
| Ages 15-39 | 8 years | 93 | 28 | 0 | 80 | 92 | 27 | 0 | 78 | 95 | 56 | 7 | 91 | 92 | 54 | 7 | 88 |
| Ages 15-39 | 9 years | 93 | 28 | 0 | 80 | 91 | 27 | 0 | 78 | 94 | 52 | 5 | 91 | 91 | 51 | 4 | 88 |
| Ages 15-39 | 10 years | 93 | 28 | 0 | 80 | 91 | 27 | 0 | 78 | 93 | 52 | 5 | 85 | 90 | 50 | 4 | 82 |
| Ages 40-64 | 1 year | 97 | 73 | 34 | 84 | 92 | 69 | 32 | 80 | 98 | 78 | 36 | 85 | 90 | 72 | 33 | 78 |
| Ages 40-64 | 2 years | 95 | 53 | 15 | 81 | 90 | 50 | 14 | 76 | 96 | 57 | 16 | 79 | 87 | 52 | 15 | 72 |
| Ages 40-64 | 3 years | 94 | 45 | 9 | 77 | 88 | 42 | 9 | 72 | 94 | 48 | 11 | 75 | 85 | 43 | 10 | 67 |
| Ages 40-64 | 4 years | 93 | 40 | 7 | 76 | 87 | 37 | 7 | 70 | 93 | 43 | 9 | 73 | 83 | 38 | 8 | 65 |

**Table H-10: Summary of Relative and Absolute Bladder Cancer Survival Used in the Model**

| Age at Diagnosis | Follow-Up Time | Females | | | | | | | | Males | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | |
| | | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged |
| Ages 40-64 | 5 years | 92 | 37 | 5 | 74 | 85 | 34 | 5 | 69 | 91 | 40 | 8 | 71 | 81 | 35 | 7 | 63 |
| Ages 40-64 | 6 years | 91 | 36 | 5 | 74 | 84 | 33 | 5 | 68 | 90 | 38 | 7 | 68 | 79 | 33 | 7 | 60 |
| Ages 40-64 | 7 years | 90 | 34 | 4 | 73 | 82 | 31 | 4 | 66 | 89 | 37 | 7 | 66 | 77 | 32 | 6 | 57 |
| Ages 40-64 | 8 years | 89 | 32 | 4 | 71 | 80 | 29 | 4 | 64 | 88 | 36 | 7 | 64 | 75 | 30 | 6 | 54 |
| Ages 40-64 | 9 years | 88 | 31 | 4 | 70 | 79 | 28 | 3 | 63 | 87 | 35 | 7 | 61 | 73 | 29 | 6 | 51 |
| Ages 40-64 | 10 years | 87 | 31 | 4 | 70 | 77 | 27 | 3 | 62 | 86 | 34 | 7 | 61 | 71 | 28 | 6 | 51 |
| Ages 65-74 | 1 year | 95 | 67 | 25 | 72 | 88 | 62 | 24 | 66 | 97 | 74 | 32 | 81 | 86 | 66 | 29 | 72 |
| Ages 65-74 | 2 years | 92 | 48 | 11 | 67 | 83 | 44 | 10 | 61 | 94 | 55 | 16 | 75 | 82 | 48 | 13 | 65 |
| Ages 65-74 | 3 years | 90 | 38 | 8 | 63 | 80 | 34 | 7 | 57 | 92 | 47 | 11 | 72 | 77 | 39 | 9 | 60 |
| Ages 65-74 | 4 years | 88 | 34 | 6 | 60 | 77 | 30 | 5 | 52 | 89 | 42 | 8 | 69 | 73 | 34 | 6 | 56 |
| Ages 65-74 | 5 years | 86 | 31 | 5 | 58 | 73 | 26 | 5 | 50 | 88 | 39 | 6 | 66 | 70 | 31 | 5 | 52 |
| Ages 65-74 | 6 years | 85 | 28 | 5 | 56 | 71 | 23 | 4 | 47 | 86 | 36 | 6 | 64 | 66 | 27 | 4 | 49 |
| Ages 65-74 | 7 years | 84 | 27 | 4 | 54 | 68 | 22 | 3 | 44 | 84 | 34 | 5 | 61 | 62 | 25 | 4 | 45 |
| Ages 65-74 | 8 years | 82 | 25 | 4 | 52 | 64 | 20 | 3 | 41 | 82 | 32 | 5 | 57 | 58 | 23 | 4 | 40 |

**Table H-10: Summary of Relative and Absolute Bladder Cancer Survival Used in the Model**

| Age at Diagnosis | Follow-Up Time | Females | | | | | | | | Males | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | | Relative Survival by Stage (Percent) | | | | Absolute Survival (Average) by Stage (Percent) | | | |
| | | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged | Localized | Regional | Distant | Unstaged |
| Ages 65-74 | 9 years | 81 | 25 | 3 | 51 | 61 | 19 | 2 | 39 | 80 | 30 | 4 | 56 | 54 | 20 | 3 | 38 |
| Ages 65-74 | 10 years | 79 | 25 | 3 | 51 | 58 | 18 | 2 | 37 | 79 | 29 | 4 | 56 | 50 | 19 | 3 | 36 |
| Ages 75+ | 1 year | 86 | 48 | 17 | 39 | 44 | 25 | 9 | 20 | 92 | 60 | 22 | 59 | 45 | 30 | 11 | 29 |
| Ages 75+ | 2 years | 81 | 36 | 8 | 32 | 40 | 18 | 4 | 16 | 87 | 44 | 10 | 51 | 42 | 21 | 5 | 24 |
| Ages 75+ | 3 years | 77 | 30 | 6 | 27 | 38 | 15 | 3 | 13 | 84 | 38 | 7 | 45 | 38 | 17 | 3 | 21 |
| Ages 75+ | 4 years | 76 | 28 | 5 | 24 | 36 | 13 | 2 | 11 | 81 | 35 | 5 | 40 | 35 | 15 | 2 | 17 |
| Ages 75+ | 5 years | 73 | 26 | 4 | 22 | 33 | 12 | 2 | 10 | 79 | 33 | 5 | 37 | 33 | 14 | 2 | 15 |
| Ages 75+ | 6 years | 71 | 24 | 4 | 22 | 31 | 11 | 2 | 9 | 76 | 32 | 4 | 34 | 30 | 13 | 2 | 13 |
| Ages 75+ | 7 years | 69 | 22 | 3 | 20 | 29 | 9 | 1 | 8 | 74 | 29 | 3 | 31 | 27 | 11 | 1 | 11 |
| Ages 75+ | 8 years | 68 | 21 | 3 | 18 | 27 | 8 | 1 | 7 | 72 | 28 | 3 | 29 | 25 | 10 | 1 | 10 |
| Ages 75+ | 9 years | 66 | 21 | 2 | 18 | 25 | 8 | 1 | 7 | 70 | 28 | 3 | 26 | 22 | 9 | 1 | 8 |
| Ages 75+ | 10 years | 65 | 18 | 2 | 18 | 23 | 6 | 1 | 6 | 68 | 28 | 3 | 23 | 20 | 8 | 1 | 7 |

**Table H-11: Summary of All-Cause and Bladder Cancer Mortality Data Used in the Model**

| | Females | | | Males | | |
|---|---|---|---|---|---|---|
| | Rate per 100K | | | Rate per 100K | | |
| Age | All-Cause | Bladder Cancer | Percent Bladder Cancer | All-Cause | Bladder Cancer | Percent Bladder Cancer |
| <1 | 537 | 0 | 0 | 646 | 0.0090 | 0.0014 |
| 1-4 | 36 | 0 | 0 | 44 | 0 | 0 |
| 5-9 | 12 | 0 | 0 | 15 | 0 | 0 |
| 10-14 | 10 | 0 | 0 | 12 | 0.0086 | 0.070 |
| 15-19 | 19 | 0 | 0 | 34 | 0 | 0 |
| 20-24 | 40 | 0.0085 | 0.021 | 112 | 0.012 | 0.011 |
| 25-29 | 54 | 0.017 | 0.030 | 142 | 0.020 | 0.014 |
| 30-34 | 73 | 0.034 | 0.046 | 159 | 0.046 | 0.029 |
| 35-39 | 98 | 0.14 | 0.14 | 185 | 0.19 | 0.10 |
| 40-44 | 135 | 0.31 | 0.23 | 229 | 0.52 | 0.23 |
| 45-49 | 203 | 0.64 | 0.31 | 323 | 1.4 | 0.42 |
| 50-54 | 317 | 1.3 | 0.40 | 508 | 3.1 | 0.61 |
| 55-59 | 470 | 2.2 | 0.48 | 784 | 7.1 | 0.91 |
| 60-64 | 675 | 4.0 | 0.60 | 1136 | 12 | 1.1 |
| 65-69 | 987 | 6.5 | 0.66 | 1593 | 22 | 1.4 |
| 70-74 | 1533 | 12 | 0.77 | 2304 | 37 | 1.6 |
| 75-79 | 2481 | 22 | 0.87 | 3577 | 70 | 1.9 |
| 80-84 | 4171 | 36 | 0.85 | 5770 | 123 | 2.1 |
| 85+ | - | - | 0.77 | - | - | 1.9 |

## H.5 RCC Valuation Data

EPA identified the study selected for use in evaluating potential medical costs avoided as a result of the PFAS regulatory alternatives, Ambavane et al. (2020), as part of a targeted kidney cancer valuation literature search. The scope of the search covered cost of illness (COI) and willingness-to-pay (WTP) literature published in English language peer reviewed sources during 2010-2021.[54] The searches were executed in the Google Scholar article database. EPA reviewed 153 references retrieved by the WTP-oriented searches and the top 348 references retrieved by the COI-oriented searches.[55]

The search did not identify any suitable kidney cancer WTP studies. However, there were seven additional studies containing COI information. Of those, four were cost-effectiveness studies that focused only on medication costs. The remaining three studies focused on the overall medical care costs but had methodological issues that prevented EPA from using them as the basis for kidney cancer morbidity valuation:

- Hollenbeak et al. (2011) reported 5-year RCC cost estimates based on Medicare data from early 2000s; however, even after adjusting for medical care price inflation, these RCC cost estimates were too low relative to the costs reported by more recent cost-effectiveness studies.
- Bhattacharjee et al. (2017) annual cost estimates were based on the Medical Expenditure Panel Survey 2002-2011 data for persons experiencing kidney cancer but included expenditures for conditions other than kidney cancer.
- Mitchell et al. (2020) reported Medicare costs for various first line kidney cancer treatment types, but not the frequency and duration with which these treatments were typically applied.

Detailed notes on the 8 studies reviewed by EPA are provided in Table H-12.

[54] The query terms used for WTP-oriented and COI-oriented searches are available upon request.

[55] EPA applied exclusion-term based automated screening to the raw Google Scholar result sets; exclusion terms are available upon request. The number of references listed in this document reflect the size of the result sets after the automated screening was applied. There were 153 references in the WTP-oriented search result set and 1,342 references in the COI-oriented search result set. The overall budget for manual review was approximately 500 references, with priority given to the WTP-oriented results set. Therefore, EPA reviewed all 153 references in the WTP-oriented results set and top 348 references in the COI-oriented results set. The references in the COI-oriented results set were prioritized using Okapi BM25 metric applied to article titles and Google Scholar ranks.

**Table H-12: Studies Reviewed Related to Kidney Cancer Medical Treatment Costs**

| Study Reference | Valuation Target | Focus | Result(s) Type & Quality | Geographic Scope & Scale | Population | Datasets | Data Collection Year | Methodology and Other Notes |
|---|---|---|---|---|---|---|---|---|
| Ambavane et al. (2020) | Lifetime treatment costs of several treatment sequences (first and second line drug costs, administration costs, disease management, and adverse effects management) | Incidence-based | Accounting for first and second line, drug costs + administration costs + disease management costs per month + single time AE management cost (not accounting for mean AE disutility/month) = $189,594.76/month + $48,122; annual cost = $2.3 million (without including monthly disutility). Dollar values reported in 2018$. | ~26% U.S.; ~35% Canada/Western Europe/North Europe; ~39% rest of world | 779, majority male and white with baseline median age of 62 years | Cohort data from the CheckMate 214 trial | Not stated | Discrete event simulation model estimates lifetime costs and survival among patients. Recent US-based costs; risk data are bias toward older white males and 26% of trial participants were from U.S.; provides costs but not information on baseline treatment frequencies. |
| Hollenbeak et al. (2011) | Payments made by Medicare for all-cause medical treatments including inpatient stays, emergency room visits, outpatient procedures, office visits, home health visits, durable medical | Prevalence-based, by year since diagnosis | Mean costs per patient per month (PPPM) in the first year were $3,673 for patients with RCC. PPPM costs were higher for RCC patients with more advanced stage (i.e., regional or distant) disease. Average cumulative total costs for RCC patients were $33,605 per patient | USA, individual scale | 4,938 patients with RCC and 9,876 non-HMO noncancer comparison group. The sample was limited to non-HMO patients aged 65 years or older who were | Surveillance, Epidemiology, and End Results Program (SEER)-Medicare database, which combines tumor registry data from the National Cancer Institutes (NCI) SEER | 1995-2002 | Estimated all-cause health care costs associated with RCC using SEER-Medicare data. Using the method of Bang et al. (2000), estimated cumulative costs at 1 and 5 years by estimating average costs for each patient in each month up to 60 months following diagnosis. Medicare population; costs |

**Table H-12: Studies Reviewed Related to Kidney Cancer Medical Treatment Costs**

| Study Reference | Valuation Target | Focus | Result(s) Type & Quality | Geographic Scope & Scale | Population | Datasets | Data Collection Year | Methodology and Other Notes |
|---|---|---|---|---|---|---|---|---|
| | equipment, and hospice care, but excluding outpatient prescription drugs | | in the first year following diagnosis and $59,397 per patient in the first 5 years following diagnosis. Costs available for first five years and separated by stage. | | diagnosed with a first primary RCC (SEER site recode 59, kidney and renal pelvis) between 1995 and 2002 | program for patients who are covered by Medicare with their Medicare billing records | | within 5-years of diagnosis; data from 2005. |
| Mitchell et al. (2020) | Medicare costs for first-line and maintenance treatment | Cost accounting-based | First-line treatments for kidney cancer range from $30,538 to $31,190, while maintenance treatments range from $7,722 to $8,997. These costs represent the average monthly cost of treatment. | USA, individual scale | Not specified | Medicare costs for first-line and maintenance treatments for cancers with the highest incidence in the US that had published National Comprehensive Cancer Network (NCCN) Evidence Blocks as of December 31, 2018; costs based on Medicare prices from the January 2019 | 2018 | Calculated Medicare costs for all first-line and maintenance treatments for 30 cancers with the highest incidence in the US that had published National Comprehensive Cancer Network (NCCN) Evidence Blocks as of December 31, 2018. Categorized each treatment as either "time-limited" or "time-unlimited." For time-unlimited treatments (all kidney cancer treatments fall into this category), calculated the average monthly cost |

**Table H-12: Studies Reviewed Related to Kidney Cancer Medical Treatment Costs**

| Study Reference | Valuation Target | Focus | Result(s) Type & Quality | Geographic Scope & Scale | Population | Datasets | Data Collection Year | Methodology and Other Notes |
|---|---|---|---|---|---|---|---|---|
| | | | | | | Medicare ASP file | | of treatment. No information on treatment duration. |
| Bhattacharjee et al. (2017) | Total healthcare expenditure, which includes inpatient, outpatient, emergency room, prescription drugs, home health agency, dental care, vision care, and other expenditures. The study included different sources of payment such as direct payments from individuals, private insurance, Medicare, | Prevalence-based | The annual average total healthcare expenditures ($15,078 vs. $8,182; P < .001) for adults with kidney cancer were significantly higher compared with propensity-score-matched adults with other forms of cancer. The average inpatient ($6755 vs. $1959) and prescription drug ($3485 vs. $1570) expenditures were significantly higher for adults with KC compared with matched controls. Dollar values reported in 2011$. | USA, individual scale | Adults aged 21 or older who did not die during the calendar year of MEPS data and had positive total healthcare expenditures (N = 541 for time-unlimited treatments, N = 845 for time-limited treatments—analysis includes ~30 cancer types). Cancer stage not specified. | Medical Expenditure Panel Survey | 2002-2011 | Used a retrospective, cross-sectional, propensity-score-matched, case-control study design using 2002 to 2011 MEPS data to determine impacts of health and functional status and co-occurring chronic conditions. Developed OLS regressions on log-transformed expenditures for total and subtypes of health expenditures. Calculated percentage change in expenditure. Very small sample of ~100 persons; non-incremental annual average healthcare expenditures among |

**Table H-12: Studies Reviewed Related to Kidney Cancer Medical Treatment Costs**

| Study Reference | Valuation Target | Focus | Result(s) Type & Quality | Geographic Scope & Scale | Population | Datasets | Data Collection Year | Methodology and Other Notes |
|---|---|---|---|---|---|---|---|---|
| | Medicaid, Workers' Compensation, and miscellaneous other sources. All expenditures inflated using medical CPI. | | | | | | | those with RCC that could include care for other health issues; no stage and no variation by time since diagnosis; focus on those with positive expenditures. |
| Wan et al. (2019) | Compares cost-effectiveness of kidney cancer treatments: nivolumab plus ipilimumab vs sunitinib | Incidence-based | Provides total cost of regimen, other values reported in ICER/QALY; cost effectiveness analysis of two different treatments for renal cell carcinoma | USA, individual scale | 1096 patients with mRCC from clinical trial modeled to receive the drug | CheckMate 214, Centers for Medicare & Medicaid Services | 2018 | A Markov model was developed to compare the lifetime cost and effectiveness of nivolumab plus ipilimumab vs sunitinib in the first-line treatment of mRCC using outcomes data from the CheckMate 214 phase 3 randomized clinical trial, which included 1096 patients with mRCC (median age, 62 years) and compared nivolumab plus ipilimumab vs sunitinib as first-line treatment of mRCC. In the analysis, |

**Table H-12: Studies Reviewed Related to Kidney Cancer Medical Treatment Costs**

| Study Reference | Valuation Target | Focus | Result(s) Type & Quality | Geographic Scope & Scale | Population | Datasets | Data Collection Year | Methodology and Other Notes |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | | patients were modeled to receive sunitinib or nivolumab plus ipilimumab for 4 doses followed by nivolumab monotherapy. provides costs of treatment but does not provide the frequency with which these treatments are applied in the general population. |
| Reinhorn et al. (2019) | Compares cost-effectiveness of kidney cancer treatments: nivolumab and ipilimumab versus sunitinib | Incidence-based | Cost effectiveness analysis of two different treatments for renal cell carcinoma; study centered on specific drug cost and was limited by data availability | USA, individual scale | Markov model-simulated population with each model cycle representing 1 month over a 10-year time horizon | CheckMate 214 | 2017 | A Markov model was developed to compare the costs and effectiveness of nivolumab and ipilimumab with those of sunitinib in the first-line treatment of intermediate- to poor-risk advanced RCC. Health outcomes were measured in life-years and quality-adjusted life-years (QALYs). Drug costs were based on Medicare |

**Table H-12: Studies Reviewed Related to Kidney Cancer Medical Treatment Costs**

| Study Reference | Valuation Target | Focus | Result(s) Type & Quality | Geographic Scope & Scale | Population | Datasets | Data Collection Year | Methodology and Other Notes |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | | reimbursement rates in 2017. Study extrapolated survival beyond the trial closure using Weibull distribution. Model robustness was addressed in univariable and probabilistic sensitivity analyses. Provides costs of treatment but does not provide the frequency with which these treatments are applied in the general population |
| Perrin et al. (2015) | Compares cost-effectiveness of kidney cancer treatments: everolimus vs axitinib; provides costs per patient from simulated data | Incidence-based | Cost effectiveness analysis of two different treatments for renal cell carcinoma | USA, individual scale | Simulated population of advanced RCC patients | MarketScan Commercial Claims and Encounters and Medicare Supplemental database | 2004-2011 | A Markov model was developed to simulate a cohort of sunitinib-refractory advanced RCC patients and estimate the cost of treating patients with everolimus vs axitinib. The following health states were included: stable disease without adverse events (aEs), stable disease with aEs, |

**Table H-12: Studies Reviewed Related to Kidney Cancer Medical Treatment Costs**

| Study Reference | Valuation Target | Focus | Result(s) Type & Quality | Geographic Scope & Scale | Population | Datasets | Data Collection Year | Methodology and Other Notes |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | | disease progression (PD), and death. The model included the following resources: active treatments, post-progression treatments, aEs, physician and nurse visits, scans and tests, and palliative care. Resource utilization inputs were derived from a US claims database analysis. Additionally, a 3% annual discount rate was applied to costs, and the robustness of the model results was tested by conducting sensitivity analyses, including those on dosing scheme and post-progression treatment costs. Provides costs of treatment but does not provide the frequency with which these treatments are applied in the general population. |

**Table H-12: Studies Reviewed Related to Kidney Cancer Medical Treatment Costs**

| Study Reference | Valuation Target | Focus | Result(s) Type & Quality | Geographic Scope & Scale | Population | Datasets | Data Collection Year | Methodology and Other Notes |
|---|---|---|---|---|---|---|---|---|
| Racsa et al. (2015) | Compares cost-effectiveness of kidney cancer treatments: two tyrosine kinase inhibitors; provides original dollar estimates for different medications | Incidence-based | Cost effectiveness analysis of two different treatments for renal cell carcinoma | USA, individual scale | 1,438 RCC patients aged 19 to 89 years, with medical and pharmacy insurance through commercial or Medicare plans | Humana Research Database | 2009-2012 | Study used claims data to conduct an observational, retrospective cohort study of individuals aged 19 to 89 years, with commercial or Medicare insurance, advanced RCC, and at least one pharmacy claim for sunitinibor pazopanib between 1 November 2009 and 31 December 2012. Treatment characteristics (treatment interruption, adherence, duration, and discontinuation), survival, and costs were measured up to 12 months. Statistical models were adjusted for age, gender, geographic region, race, and RxRisk-Vscore. Provides costs of treatment but does not provide the frequency with which these treatments are |

**Table H-12: Studies Reviewed Related to Kidney Cancer Medical Treatment Costs**

| Study Reference | Valuation Target | Focus | Result(s) Type & Quality | Geographic Scope & Scale | Population | Datasets | Data Collection Year | Methodology and Other Notes |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | | applied in the general population; addresses a younger population. |

Abbreviations: AE – Adverse Effects; CPI – Consumer Price Index; HMO – Health Maintenance Organization; MEPS – Medical Expenditure Panel Survey; mRCC metastatic Renal Cell Carcinoma; NCCN – National Comprehensive Cancer Network; NC I– National Cancer Institute; OLS – Ordinary Least Squares; PD – Disease Progression; PPPM – Per Patient Per Month; QALYs – Quality Adjusted Life Years; RCC – Renal Cell Carcinoma; SEER – Surveillance, Epidemiology, and End Results Program.

# Appendix I. Trihalomethane Co-Removal Model Details and Analysis

## I.1 Data Analysis

EPA analyzed Information Collection Rule Treatment Study Database (ICR TSD) data to predict time-based removal efficacy of total organic carbon (TOC) and four regulated trihalomethanes (THM4) from pilot and rapid small-scale column tests (RSSCTs). In all, EPA extracted 182 datasets from the ICR TSD database, which included some quarterly RSSCTs and some long-term pilots. EPA used RSSCT scaling factors identified in the original datasets to scale predictions to expected full-scale operational time, rather than short duration experimental time.

This appendix focuses on estimates of THM4 production because it forms the basis of potential reductions in health risks resulting from reducing PFAS levels under various regulatory scenarios. Note that the same approaches described in this appendix were used to estimate TOC removal. EPA developed a Python program to standardize the data analysis and produce graphics. Figure I-1 shows example data from one study (SystemID 1003, RSSCT) to demonstrate the approach for estimating THM4 reduction. Each dataset provided influent and effluent concentrations for TOC and THM4 formation potential for a 10-min empty bed contact time (EBCT). Most datasets also included 20-min EBCT effluent concentrations. If data was not available for 20-min EBCT effluent concentrations, then only 10-min EBCT data was included in the analysis. For all datasets and EBCTs, EPA used a logistic function to estimate the expected breakthrough curve over time (effluent concentrations vs. time). Since the logistic function is non-linear, EPA used the Python function scipy.optimize.curve_fit to estimate equation parameters.

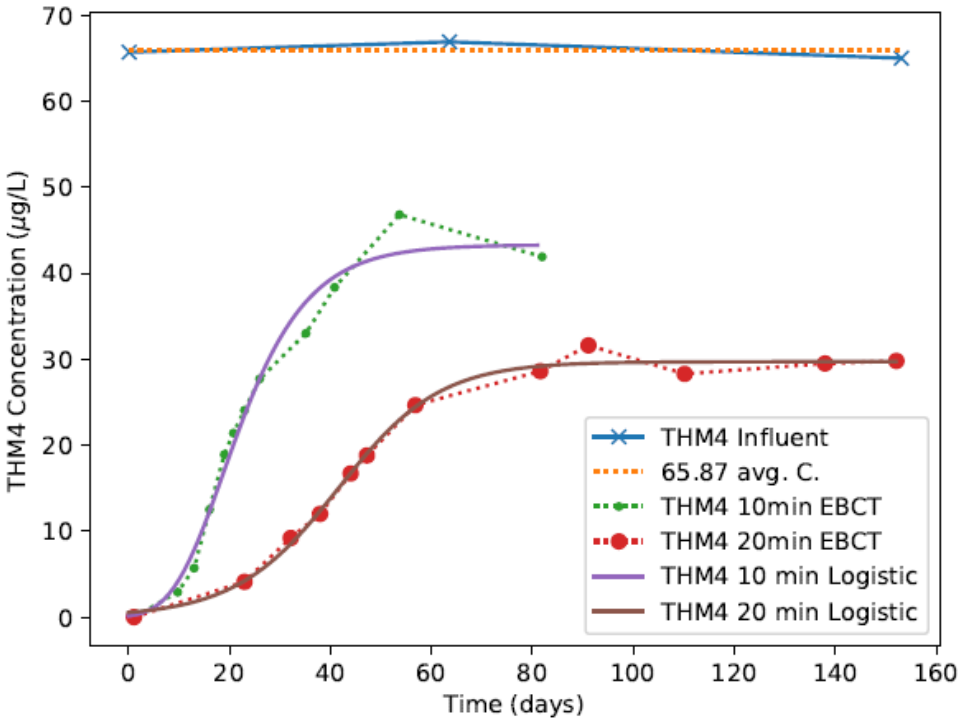



**Figure I-1: Example Breakthrough Curve for THM4 from the ICR Dataset with Logistic Fit Functions Shown.**

The logistic function is provided as:

Equation I-1:

$$C(t) = C_f(Ae^{-rt} + 1)^{-n+1}$$

where $C$ is effluent concentration, $C_f$ is the final concentration (concentration units), $A$, $r$ and $n$ are additional fit parameters and $t$ is time (in days). EPA generated a set of fit parameters for each of the datasets and EBCTs. The logistic function provides a continuous function throughout a period and can be used to estimate effective effluent concentrations beyond the original test period. This assumes that $C_f$ could be estimated effectively and represents the long-term effective removal after breakthrough (i.e., that an equilibrium removal was achieved). Figure I-2 shows the projected removal percentage for bed replacement intervals from 30 days (1 month) to 730 days (2 years). Percent removal for each data pair was calculated as:

Equation I-2:

$$\%Removal = 100 * (1 - \frac{C(t)}{C_{inf,avg}})$$

where, $C(t)$ is the result of the logistic function over time, and $C_{inf,avg}$ is the average influent concentration for each species.

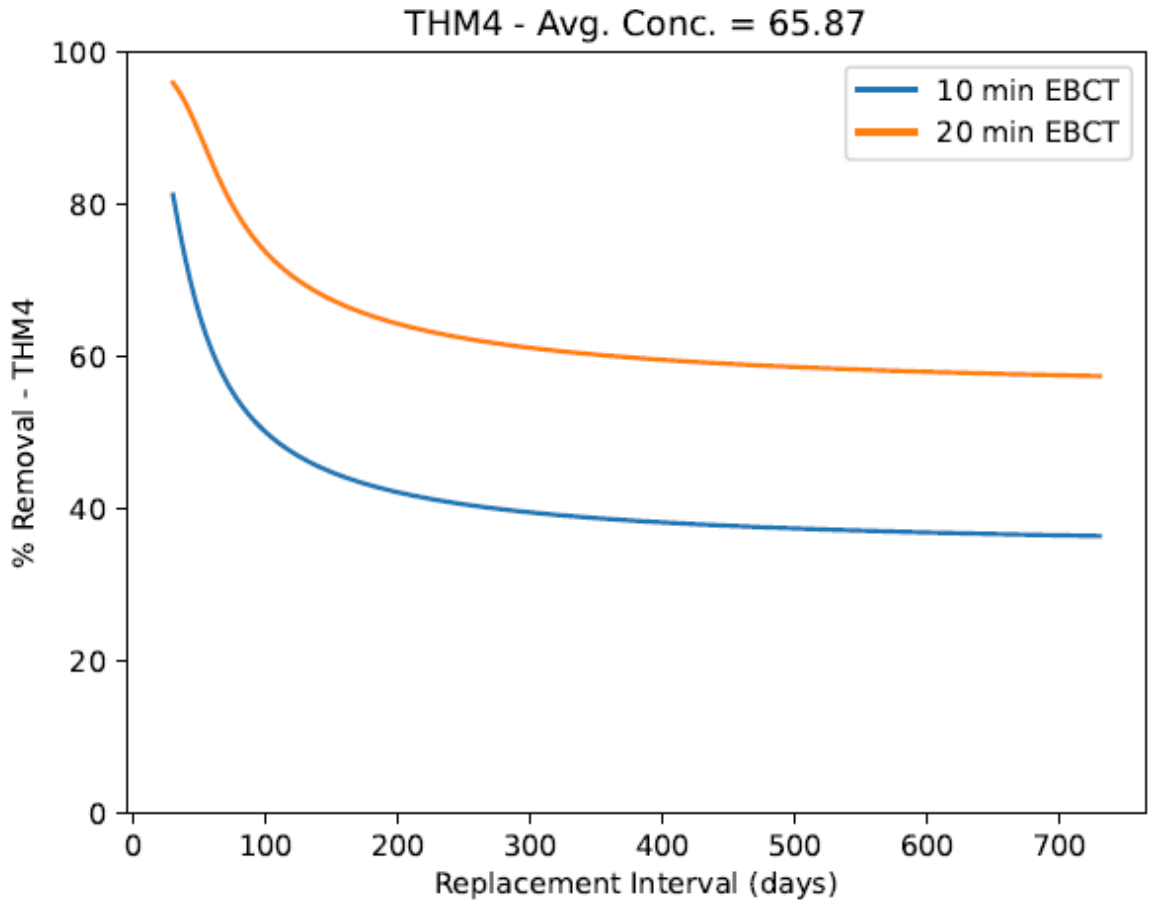



**Figure I-2: Example Percent Removal Results vs. Time based on Logistic Plots Shown in Figure I-1.**

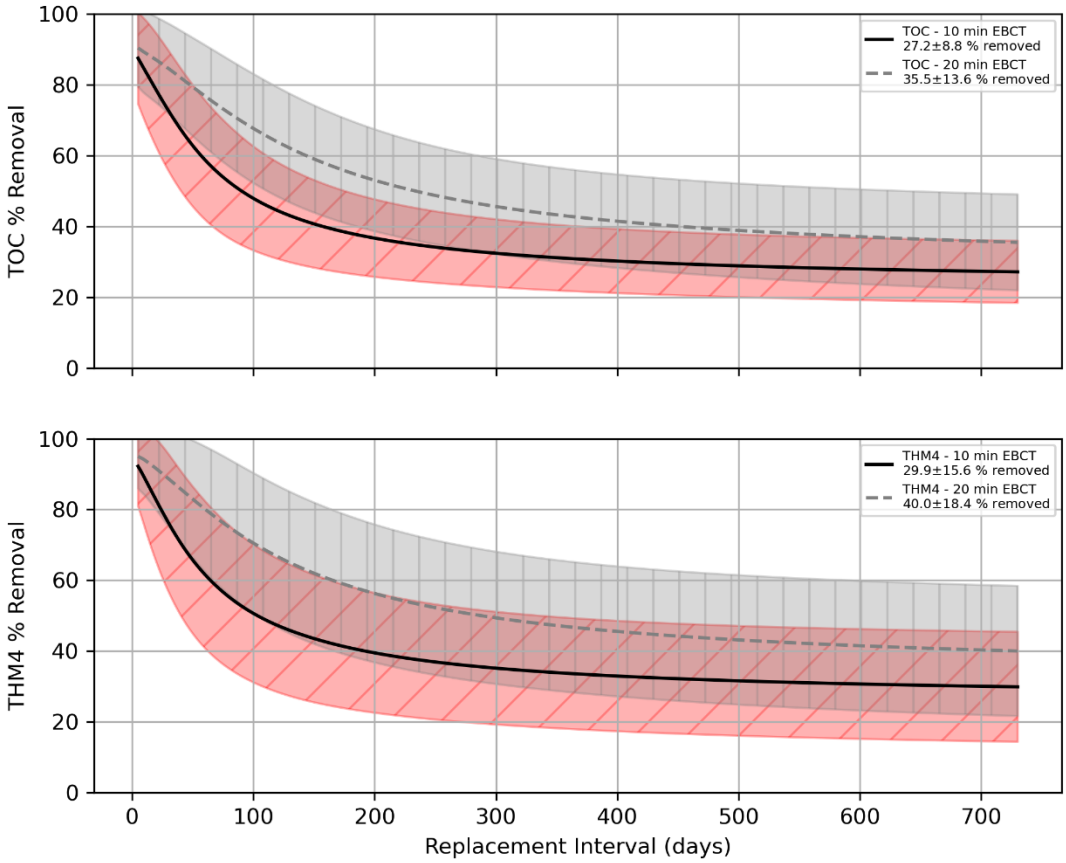



**Figure I-3: Mean Percentage Removal (Shaded Area ± 1 Standard Deviation)**

The percent removal formula provides a conservative estimate for removal over each EBCT. EPA assumes that the percent removal at the carbon removal day is the best removal that was achieved, where breakthrough curves demonstrate that additional removal may be achieved for earlier portions of the operational carbon life. For longer operational times, this early removal capacity for each species becomes a diminishingly small percentage of removal percentage.

EPA used the percentage removal at ½ year intervals for ½, 1, 1 ½, and 2 years in the co-removal benefits analysis. Information about the source water (pre-categorized type from the ICR, groundwater or surface water) and averages of influent concentrations of TOC, and THM4 were stored with results, which were used during further analyses.

Figure I-3 represents the mean percentage removal for TOC, THM4 over time with shaded areas representing mean ±1 standard deviation. Figure I-4 also shows a probability density function representation of concentration reduction following treatment after 2 years of carbon operations (i.e., GAC replacement time). These plots demonstrate the variability in the results.

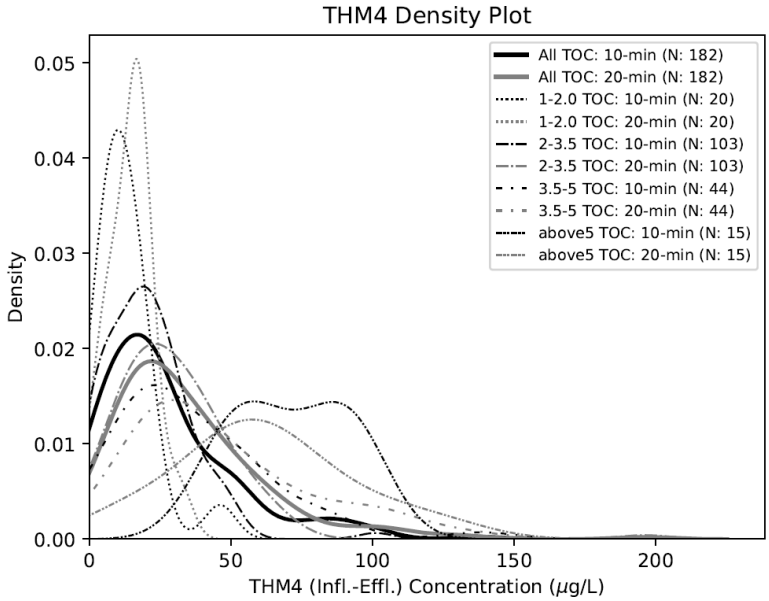



**Figure I-4: Probability Density Function of Concentration Difference at 2 years of Carbon Life (Subdivided by TOC level).**

## I.2 Discussion of Other Models

EPA explored another existing model to determine ΔTHM4 resulting from GAC treatment. The Water Treatment Plant model uses the ICR TSD data along with other datasets and includes specific process selection inputs such as GAC units (U.S. EPA, 2001). In contrast with the logistic model detailed in Section I.1, the Water Treatment Plant model cannot be run with the GAC unit in isolation. Within the Water Treatment Plant model, the GAC unit process equation relies on TOC and ultraviolet

absorbance (UVA) changes and does not directly predict THMs. Additional data needed to use the Water Treatment Plant model include types of chemicals used, dosing concentrations, contact times, and full process train information, which EPA did not have outside of the DBP ICR for national scale estimates. Comparing the models, the logistic equations for GAC treatment were generally in the same form. However, in this analysis EPA fit the THM4 results reported in the ICR dataset directly whereas the Water Treatment Plant model would need to have simulated all various treatment trains including GAC to calculate TOC levels (some uncertainty) followed by a conversion with then another model equation (with more uncertainty) to predict the ΔTHM4. While these equations result in the same shape of function to find predictions, the logistic model approach outlined in Section I.1 uses a singular step with singular uncertainty that was data driven.

## I.3 THM4 Reduction Results

All systems used free chlorine for the THM4 formation potential experiments in the ICR TSD. However, the hold time to replicate the distribution system varied based on the typical disinfectant used in the PWS. Table I-1 shows the THM4 removal (ΔTHM4) differences based on source water type, EBCTs, and disinfectant type of the parent system. Table I-2 to Table I-5 shows the ΔTHM4 differences based on GAC replacement intervals (1/2, 1, 1 ½, and 2 years), disinfectant type (free chlorine versus chloramine), source water type (ground versus surface water), and TOC range (1–2.0, 2–3.5, 3.5–5, and above 5 mg/L).

**Table I-1: ICR TSD Predictions for ΔTHM4 Based on Disinfectant**

| Disinfectant Type | Source Type | Pilot/ RSSCT Count | ΔTHM4 with 10 min EBCT (%) | ΔTHM4 with 20 min EBCT (%) | ΔTHM4 with 10 min EBCT (µg/L) | ΔTHM4 with 20 min EBCT (µg/L) |
|---|---|---|---|---|---|---|
| Chloramine | GW | 21 | 30.5 ± 10.5 | 29.6 ± 15.3 | 43.0 ± 32.2 | 38.1 ± 32.2 |
| Chloramine, Free Chlorine | SW | 102 | 26.6 ± 12.8 | 36.7 ± 14.5 | 29.0 ± 24.3 | 37.7 ± 26.2 |
| | GW | 16 | 34.7 ± 24.3 | 35.3 ± 17.6 | 18.8 ± 13.5 | 18.8 ± 10.7 |
| Free Chlorine | SW | 43 | 35.40 ± 17.8 | 54.7 ± 20.8 | 20.2 ± 17.5 | 32.9 ± 31.2 |

Abbreviations: EBCT – Empty Bed Contact Time; GW – Groundwater; RSSCT – Rapid Small-Scale Column Test; SW – Surface Water; THM4 – Four Regulated Trihalomethanes.

**Table I-2: ICR TSD Predictions for ΔTHM4 for ½ Year GAC Replacement Based on Disinfectant Type, EBCT, and Source Water Type**

| | Disinfectant Type | Source Water Type | TOC Range (mg/L) | Count (N) | ΔTHM4 with 10 min EBCT (%Reduction ± 1 Standard Deviation) | ΔTHM4 with 20 min EBCT (% Reduction ± 1 Standard Deviation) | ΔTHM4 with 10 min EBCT (µg/L Reduction ± 1 Standard Deviation) | ΔTHM4 with 20 min EBCT (µg/L Reduction ± 1 Standard Deviation) |
|---|---|---|---|---|---|---|---|---|
| ½ year | Chloramine | GW | 1-2.0 | 3 | 38.09 ± 14.59 | 48.46 ± 21.42 | 16.02 ± 6.77 | 20.42 ± 9.85 |
| | | | 2-3.5 | 4 | 51.61 ± 11.77 | 70.85 ± 1.40 | 31.79 ± 18.76 | 50.07 ± 43.63 |
| | | | 3.5-5 | 6 | 34.84 ± 4.41 | 39.33 ± 2.39 | 34.04 ± 17.05 | 42.42 ± 27.47 |
| | | | Above 5 | 8 | 33.41 ± 6.39 | 34.53 ± 14.62 | 86.59 ± 20.77 | 84.86 ± 30.12 |
| | | SW | 1-2.0 | 5 | 33.69 ± 27.18 | 43.68 ± 30.09 | 16.49 ± 8.62 | 22.78 ± 12.69 |
| | | | 2-3.5 | 59 | 36.87 ± 15.24 | 57.29 ± 17.23 | 29.15 ± 17.83 | 44.57 ± 23.77 |
| | | | 3.5-5 | 31 | 36.11 ± 11.62 | 52.84 ± 13.91 | 49.95 ± 33.55 | 72.35 ± 41.99 |
| | | | Above 5 | 7 | 40.79 ± 5.04 | 51.16 ± 8.68 | 73.81± 20.77 | 90.92 ± 21.64 |
| | Free chlorine | GW | 1-2.0 | 5 | 55.33 ± 22.41 | 59.13 ± 20.53 | 28.74 ± 19.06 | 25.74 ± 12.18 |
| | | | 2-3.5 | 10 | 33.81 ± 17.98 | 48.58 ± 19.85 | 18.95 ± 9.83 | 27.45 ± 12.81 |
| | | | 3.5-5 | 1 | 87.56 | 49.50 | 41.99 | 23.73 |
| | | SW | 1-2.0 | 7 | 60.83 ± 25.20 | 84.69 ± 25.89 | 13.91 ± 8.54 | 20.28 ± 12.94 |
| | | | 2-3.5 | 30 | 49.21 ± 19.68 | 74.65 ± 15.39 | 32.04 ± 23.71 | 50.60 ± 36.79 |
| | | | 3.5-5 | 6 | 42.78 ± 10.26 | 63.53 ± 17.68 | 30.57 ± 24.87 | 42.46 ± 31.69 |

Abbreviations: EBCT – Empty Bed Contact Time; GAC – granular activated carbon; ICR TSD – Information Collection Rule Treatment Study Database; THM4 – Four Regulated Trihalomethanes; TOC – total organic carbon.

**Table I-3: ICR TSD Predictions for ΔTHM4 for One Year GAC Replacement Based on Disinfectant Type, EBCT, and Source Water Type**

| | Disinfectant Type | Source Water Type | TOC Range (mg/L) | Count (N) | ΔTHM4 with 10 min EBCT (%Reduction ± 1 Standard Deviation) | ΔTHM4 with 20 min EBCT (%Reduction ± 1 Standard Deviation) | ΔTHM4 with 10 min EBCT (µg/L Reduction ± 1 Standard Deviation) | ΔTHM4 with 20 min EBCT (µg/L Reduction ± 1 Standard Deviation) |
|---|---|---|---|---|---|---|---|---|
| **1 year** | Chloramine | GW | 1-2.0 | 3 | 32.14 ± 14.75 | 33.55 ± 16.87 | 13.55 ± 6.76 | 14.16 ± 7.68 |
| | | | 2-3.5 | 4 | 39.39 ± 17.79 | 55.20 ± 7.81 | 21.38 ± 7.40 | 38.25 ± 32.05 |
| | | | 3.5-5 | 6 | 31.61 ± 4.48 | 32.56 ± 3.55 | 30.76 ± 15.12 | 33.06 ± 15.17 |
| | | | Above 5 | 8 | 31.33 ± 6.43 | 27.57 ± 16.09 | 81.10 ± 19.88 | 66.03 ± 35.55 |
| | | SW | 1-2.0 | 5 | 22.40 ± 16.25 | 33.48 ± 23.63 | 11.13 ± 6.38 | 17.24 ± 9.33 |
| | | | 2-3.5 | 59 | 29.59 ± 13.50 | 44.65 ± 15.02 | 23.82 ± 15.60 | 34.77 ± 18.39 |
| | | | 3.5-5 | 31 | 30.88 ± 12.05 | 42.95 ± 13.96 | 43.06 ± 30.99 | 58.76 ± 35.32 |
| | | | Above 5 | 7 | 36.90 ± 4.72 | 42.70 ± 9.72 | 66.85 ± 19.58 | 75.13 ± 18.43 |
| | Free Chlorine | GW | 1-2.0 | 5 | 45.26 ± 20.71 | 48.48 ± 18.62 | 23.75 ± 16.84 | 21.17 ± 10.73 |
| | | | 2-3.5 | 10 | 28.46 ± 17.25 | 36.76 ± 17.66 | 16.17 ± 9.50 | 21.35 ± 11.95 |
| | | | 3.5-5 | 1 | 93.04 | 49.50 | 44.61 | 23.73 |
| | | SW | 1-2.0 | 7 | 49.44 ± 21.75 | 73.99 ± 25.56 | 11.00 ± 6.30 | 17.02 ± 9.75 |
| | | | 2-3.5 | 30 | 39.04 ± 17.75 | 61.02 ± 16.94 | 25.33 ± 20.13 | 41.75 ± 34.79 |
| | | | 3.5-5 | 6 | 36.29 ± 14.08 | 55.21 ± 21.66 | 26.15 ± 20.67 | 35.33 ± 25.67 |

Abbreviations: EBCT – Empty Bed Contact Time; GAC – granular activated carbon; ICR TSD – Information Collection Rule Treatment Study Database; THM4 – Four Regulated Trihalomethanes; TOC – total organic carbon.

**Table I-4: ICR TSD Predictions for ΔTHM4 for 1 ½ Year GAC Replacement Based on Disinfectant Type, EBCT, and Source Water Type**

| | Disinfectant Type | Source Water Type | TOC Range (mg/L) | Count (N) | ΔTHM4 with 10 min EBCT (% reduction ± 1 standard deviation) | ΔTHM4 with 20 min EBCT (% reduction ± 1 standard deviation) | ΔTHM4 with 10 min EBCT (µg/L reduction ± 1 standard deviation) | ΔTHM4 with 20 min EBCT (µg/L reduction ± 1 standard deviation) |
|---|---|---|---|---|---|---|---|---|
| **1 ½ year** | Chloramine | GW | 1-2.0 | 3 | 30.17 ± 14.81 | 27.31 ± 13.19 | 12.73 ± 6.76 | 11.52 ± 6.02 |
| | | | 2-3.5 | 4 | 35.06 ± 20.01 | 48.68 ± 11.30 | 17.79 ± 5.62 | 33.79 ± 28.67 |
| | | | 3.5-5 | 6 | 30.54 ± 4.61 | 30.32 ± 5.21 | 29.67 ± 14.51 | 29.96 ± 11.22 |
| | | | Above 5 | 8 | 30.64 ± 6.45 | 25.26 ± 16.63 | 79.29 ± 19.61 | 59.80 ± 37.61 |
| | | SW | 1-2.0 | 5 | 18.19 ± 13.29 | 28.56 ± 19.06 | 9.21 ± 6.28 | 14.93 ± 8.17 |
| | | | 2-3.5 | 59 | 26.99 ± 13.11 | 39.59 ± 14.66 | 21.94 ± 14.98 | 30.94 ± 16.92 |
| | | | 3.5-5 | 31 | 29.14 ± 12.31 | 39.60 ± 14.37 | 40.78 ± 30.26 | 54.13 ± 33.41 |
| | | | Above 5 | 7 | 35.61 ± 4.79 | 39.86 ± 10.48 | 64.55 ± 19.30 | 69.85 ± 18.23 |
| | Free chlorine | GW | 1-2.0 | 5 | 41.91 ± 20.19 | 44.95 ± 17.99 | 22.10 ± 16.10 | 19.66 ± 10.25 |
| | | | 2-3.5 | 10 | 26.68 ± 17.09 | 32.73 ± 17.45 | 15.26 ± 9.44 | 19.27 ± 11.88 |
| | | | 3.5-5 | 1 | 94.96 | 49.50 | 45.53 | 23.73 |
| | | SW | 1-2.0 | 7 | 45.53 ± 21.01 | 68.48 ± 25.48 | 10.02 ± 5.61 | 15.42 ± 8.41 |
| | | | 2-3.5 | 30 | 35.66 ± 17.51 | 55.85 ± 18.31 | 23.10 ± 19.09 | 38.58 ± 34.59 |
| | | | 3.5-5 | 6 | 34.14 ± 15.63 | 52.45 ± 23.08 | 24.69 ± 19.35 | 32.96 ± 23.79 |

Abbreviations: EBCT – Empty Bed Contact Time; GAC – granular activated carbon; ICR TSD – Information Collection Rule Treatment Study Database; THM4 – Four Regulated Trihalomethanes; TOC – total organic carbon.

**Table I-5: ICR TSD Predictions for ΔTHM4 for Two Year GAC Replacement Based on Disinfectant Type, EBCT, and Source Water Type**

| | Disinfectant Type | Source Water Type | TOC Range (mg/L) | Count (N) | ΔTHM4 with 10 min EBCT (% reduction ± 1 standard deviation) | ΔTHM4 with 20 min EBCT (% reduction ± 1 standard deviation) | ΔTHM4 with 10 min EBCT (µg/L reduction ± 1 standard deviation) | ΔTHM4 with 20 min EBCT (µg/L reduction ± 1 standard deviation) |
|---|---|---|---|---|---|---|---|---|
| **2 year** | Chloramine | GW | 1-2.0 | 3 | 29.18 ± 14.84 | 24.02 ± 11.12 | 12.31 ± 6.75 | 10.13 ± 5.09 |
| | | | 2-3.5 | 4 | 32.87 ± 21.16 | 45.31 ± 13.18 | 15.99 ± 5.85 | 31.51 ± 27.06 |
| | | | 3.5-5 | 6 | 30.00 ± 4.69 | 29.20 ± 6.06 | 29.13 ± 14.21 | 28.40 ± 9.32 |
| | | | Above 5 | 8 | 30.30 ± 6.47 | 24.10 ± 16.91 | 78.37 ± 19.48 | 56.66 ± 38.69 |
| | | SW | 1-2.0 | 5 | 16.08 ± 12.47 | 26.09 ± 16.95 | 8.25 ± 6.42 | 13.76 ± 7.67 |
| | | | 2-3.5 | 59 | 25.69 ± 13.10 | 36.81 ± 14.64 | 21.00 ± 14.73 | 28.86 ± 16.36 |
| | | | 3.5-5 | 31 | 28.27 ± 12.46 | 37.92 ± 14.65 | 39.63 ± 29.92 | 51.80 ± 32.56 |
| | | | Above 5 | 7 | 34.97 ± 4.86 | 38.44 ± 10.92 | 63.39 ± 19.18 | 67.20 ± 18.30 |
| | Free chlorine | GW | 1-2.0 | 5 | 40.23 ± 19.94 | 43.17 ± 17.68 | 21.26 ± 15.73 | 18.90 ± 10.01 |
| | | | 2-3.5 | 10 | 25.79 ± 17.03 | 30.70 ± 17.46 | 14.79 ± 9.42 | 18.23 ± 11.89 |
| | | | 3.5-5 | 1 | 95.92 | 49.50 | 46.00 | 23.73 |
| | | SW | 1-2.0 | 7 | 43.57 ± 20.76 | 65.69 ± 25.67 | 9.52 ± 5.27 | 14.61 ± 7.76 |
| | | | 2-3.5 | 30 | 33.97 ± 17.48 | 53.22 ± 19.21 | 21.99 ± 18.59 | 36.97 ± 34.54 |
| | | | 3.5-5 | 6 | 33.06 ± 16.43 | 51.06 ± 23.81 | 23.95 ± 18.71 | 31.77 ± 22.87 |

Abbreviations: EBCT – Empty Bed Contact Time; GAC – granular activated carbon; ICR TSD – Information Collection Rule Treatment Study Database; THM4 – Four Regulated Trihalomethanes; TOC – total organic carbon.

## I.4 Sampling Points from the Fourth Six Year Review Plants with Granular Activated Carbon Treatment

To examine the Six Year Review 4 (SYR4) four regulated trihalomethanes (THM4) data, EPA extracted and matched sampling point IDs for the years that represent before and after GAC treatment. Only sampling point IDs with the same number of samples before and after GAC treatment were used to determine THM4 averages. To calculate a single location comparison, EPA selected one sampling point ID for each public water system identification (PWSID). Entry point (EP) sampling point types were used when available. When unavailable, EPA used the first sampling point type. Table I-6 shows an example of sampling point IDs, sampling point types, and number of samples available for one PWSID in the SYR4 dataset.

**Table I-6: Sampling Point IDs for each PWSID were Extracted and Matched for the Years that Represent Before/After GAC Treatment (Example: PWSID AL0000577)**

| Sampling Point ID | Sampling Point Type | # Of Samples (2017,2019) | ΔTHM4 (µg/L)[a] |
|---|---|---|---|
| 12967 | WS | 29 (4, 4) | 8.5 |
| 12970 | WS | 29 (4, 4) | 8.9 |
| 12972 | WS | 29 (4, 4) | 8.5 |
| 12974 | WS | 29 (4 ,4) | 9.3 |
| 12975 | EP | 32 (4, 4) | 5.7 |
| 12976 | WS | 29 (4, 4) | 15.8 |
| 12977 | DS | 32 (4, 4) | 10.4 |
| 12978 | WS | 28 (4, 4) | 9.4 |
| 12979 | WS | 29 (4, 4) | 9.8 |
| 12980 | DS | 24 (3, 0) | - |
| 12981 | DS | 26 (4, 0) | - |
| 12983 | DS | 26 (4, 0) | - |
| 13022 | WS | 25 (4, 4) | 11.9 |
| 13044 | DS | 6 (0, 4) | - |
| 13089 | MR | 2 (1, 0) | - |

Abbreviations: DS – distribution system; EP – entry point; MR – point of maximum residence; WS – water system facility point.
Notes:
[a] ΔTHM4 was not calculated for sampling point IDs that did not have sample data for the years that represent either before or after GAC treatment.

# Appendix J. Value of a Statistical Life Updating

EPA follows U.S. EPA (2010) to estimate the economic value of avoiding premature mortality. To obtain a value of a statistical life (VSL) suitable for valuation of mortality risk reductions during 2023-2104, EPA relies on the base value estimate of $4.8 million ($1990, 1990 income year), which is the central tendency of the VSL distribution recommended for use in EPA's regulatory impact analyses (U.S. EPA, 2010). EPA adjusted the base VSL estimate for inflation and income growth as follows:

Equation J-1:

$$V_{t,2021} = V_{1990,1990} \cdot \frac{P_{2021}}{P_{1990}} \cdot \left(\frac{Y_t}{Y_{1990}}\right)^{\epsilon}$$

Where:

| | |
|---|---|
| $V_{t,2021}$ | VSL value ($2021) updated for use in evaluation year $t$, $t = 2023 \ldots 2050$; |
| $V_{1990,1990}$ | Base VSL value of $4,800,000 ($1990, 1990 income year); |
| $P_{2021}$ | Gross Domestic Product (GDP) price deflator index value in 2021; |
| $P_{1990}$ | GDP price deflator index value in 1990; |
| $Y_t$ | Projected income per capita ($2012) in evaluation year $t$, $t = 2023 \ldots 2050$; |
| $Y_{1990}$ | Historical income per capita ($2012) in 1990; |
| $\epsilon$ | VSL income elasticity of 0.4 as recommended by U.S. EPA (U.S. EPA, 2010). |

EPA used disposable personal annual income to represent U.S. income per capita. Because the PFAS analysis spans a future time period 2023-2104, EPA relied on the long-term personal disposable income projections from the U.S. Energy Information Administration (2021). The long-term personal income projections are available annually from 2020 to 2050.

EPA's SafeWater model requires a single income growth factor to project the 2023 VSL value (in $2021) to future years (2024 through 2104). Based on the VSL estimates calculated using Equation J-1, EPA calculated the compound annual growth rate, $CAGR$, of VSL values from 2023 to 2050 as follows:

Equation J-2:

$$CAGR = \left(\frac{V_{2050,2021}}{V_{2023,2021}}\right)^{\left(\frac{1}{2050-2023}\right)} - 1$$

EPA used the calculated CAGR value to approximate VSL growth during the analysis period (2023 to 2104) based on the 2021 VSL value estimated using Equation J-1.

Equation J-3:

$$V_{t,2021} = V_{2023,2021} \cdot (1 + CAGR)^{t-2023}$$

Table J-1 summarizes the projected VSL estimates through 2050 and the approximated VSL estimates through 2104.

**Table J-1: Estimated VSL Series**

| Year | Historical Personal Disposable Income Per Capita (PDYPP, $2012) | Projected Personal Disposable Income Per Capita (PDYPP, $2012) | Income Growth Factor (Ratio of Projected PDYPP to Historical 1990 PDYPP to the Power of 0.4) | Projected VSL ($2021) | Approximated VSL ($2021) |
|---|---|---|---|---|---|
| 1990 | 30,327 | - | 1 | 8,929,233 | - |
| 2023 | - | 47,515 | 1.1967 | 10,686,015 | 10,686,015 |
| 2024 | - | 48,311 | 1.2047 | 10,757,230 | 10,752,695 |
| 2025 | - | 49,241 | 1.2140 | 10,839,662 | 10,819,792 |
| 2026 | - | 50,084 | 1.2222 | 10,913,510 | 10,887,308 |
| 2027 | - | 50,939 | 1.2305 | 10,987,592 | 10,955,245 |
| 2028 | - | 51,817 | 1.2390 | 11,062,980 | 11,023,605 |
| 2029 | - | 52,727 | 1.2476 | 11,140,284 | 11,092,393 |
| 2030 | - | 53,711 | 1.2569 | 11,223,004 | 11,161,609 |
| 2031 | - | 54,639 | 1.2655 | 11,300,154 | 11,231,258 |
| 2032 | - | 55,566 | 1.2741 | 11,376,490 | 11,301,341 |
| 2033 | - | 56,512 | 1.2827 | 11,453,543 | 11,371,861 |
| 2034 | - | 57,446 | 1.2911 | 11,528,885 | 11,442,821 |
| 2035 | - | 58,369 | 1.2994 | 11,602,639 | 11,514,225 |
| 2036 | - | 59,277 | 1.3074 | 11,674,522 | 11,586,073 |
| 2037 | - | 60,163 | 1.3152 | 11,744,001 | 11,658,370 |
| 2038 | - | 61,038 | 1.3228 | 11,812,021 | 11,731,119 |
| 2039 | - | 61,925 | 1.3305 | 11,880,357 | 11,804,321 |
| 2040 | - | 62,791 | 1.3379 | 11,946,526 | 11,877,980 |
| 2041 | - | 63,684 | 1.3455 | 12,014,214 | 11,952,098 |
| 2042 | - | 64,620 | 1.3534 | 12,084,516 | 12,026,680 |
| 2043 | - | 65,553 | 1.3612 | 12,154,071 | 12,101,726 |
| 2044 | - | 66,480 | 1.3688 | 12,222,510 | 12,177,241 |
| 2045 | - | 67,418 | 1.3765 | 12,291,208 | 12,253,227 |
| 2046 | - | 68,366 | 1.3842 | 12,360,002 | 12,329,687 |
| 2047 | - | 69,341 | 1.3921 | 12,430,265 | 12,406,624 |
| 2048 | - | 70,351 | 1.4002 | 12,502,317 | 12,484,041 |
| 2049 | - | 71,343 | 1.4080 | 12,572,559 | 12,561,942 |

**Table J-1: Estimated VSL Series**

| Year | Historical Personal Disposable Income Per Capita (PDYPP, $2012) | Projected Personal Disposable Income Per Capita (PDYPP, $2012) | Income Growth Factor (Ratio of Projected PDYPP to Historical 1990 PDYPP to the Power of 0.4) | Projected VSL ($2021) | Approximated VSL ($2021) |
|---|---|---|---|---|---|
| 2050 | - | 72,304 | 1.4156 | 12,640,072 | 12,640,328 |
| 2051 | - | - | - | - | 12,719,204 |
| 2052 | - | - | - | - | 12,798,572 |
| 2053 | - | - | - | - | 12,878,435 |
| 2054 | - | - | - | - | 12,958,796 |
| 2055 | - | - | - | - | 13,039,659 |
| 2056 | - | - | - | - | 13,121,027 |
| 2057 | - | - | - | - | 13,202,902 |
| 2058 | - | - | - | - | 13,285,288 |
| 2059 | - | - | - | - | 13,368,188 |
| 2060 | - | - | - | - | 13,451,606 |
| 2061 | - | - | - | - | 13,535,544 |
| 2062 | - | - | - | - | 13,620,006 |
| 2063 | - | - | - | - | 13,704,994 |
| 2064 | - | - | - | - | 13,790,514 |
| 2065 | - | - | - | - | 13,876,566 |
| 2066 | - | - | - | - | 13,963,156 |
| 2067 | - | - | - | - | 14,050,286 |
| 2068 | - | - | - | - | 14,137,960 |
| 2069 | - | - | - | - | 14,226,181 |
| 2070 | - | - | - | - | 14,314,952 |
| 2071 | - | - | - | - | 14,404,278 |
| 2072 | - | - | - | - | 14,494,160 |
| 2073 | - | - | - | - | 14,584,604 |
| 2074 | - | - | - | - | 14,675,612 |
| 2075 | - | - | - | - | 14,767,188 |
| 2076 | - | - | - | - | 14,859,335 |
| 2077 | - | - | - | - | 14,952,057 |
| 2078 | - | - | - | - | 15,045,358 |
| 2079 | - | - | - | - | 15,139,241 |
| 2080 | - | - | - | - | 15,233,710 |
| 2081 | - | - | - | - | 15,328,768 |
| 2082 | - | - | - | - | 15,424,420 |
| 2083 | - | - | - | - | 15,520,668 |
| 2084 | - | - | - | - | 15,617,517 |

**Table J-1: Estimated VSL Series**

| Year | Historical Personal Disposable Income Per Capita (PDYPP, $2012) | Projected Personal Disposable Income Per Capita (PDYPP, $2012) | Income Growth Factor (Ratio of Projected PDYPP to Historical 1990 PDYPP to the Power of 0.4) | Projected VSL ($2021) | Approximated VSL ($2021) |
|---|---|---|---|---|---|
| 2085 | - | - | - | - | 15,714,970 |
| 2086 | - | - | - | - | 15,813,032 |
| 2087 | - | - | - | - | 15,911,705 |
| 2088 | - | - | - | - | 16,010,994 |
| 2089 | - | - | - | - | 16,110,903 |
| 2090 | - | - | - | - | 16,211,435 |
| 2091 | - | - | - | - | 16,312,594 |
| 2092 | - | - | - | - | 16,414,385 |
| 2093 | - | - | - | - | 16,516,810 |
| 2094 | - | - | - | - | 16,619,875 |
| 2095 | - | - | - | - | 16,723,583 |
| 2096 | - | - | - | - | 16,827,939 |
| 2097 | - | - | - | - | 16,932,945 |
| 2098 | - | - | - | - | 17,038,606 |
| 2099 | - | - | - | - | 17,144,927 |
| 2100 | - | - | - | - | 17,251,912 |
| 2101 | - | - | - | - | 17,359,564 |
| 2102 | - | - | - | - | 17,467,887 |
| 2103 | - | - | - | - | 17,576,887 |
| 2104 | - | - | - | - | 17,686,567 |

Acronyms: PDYPP– Personal Disposable Income Per Capita; VSL– Value of a Statistical Life.

Table J-2 summarizes the data employed in updating the values used to monetize reductions in mortality and morbidity risks in the population exposed to PFOA and PFOS in drinking water. EPA uses the VSL to monetize reduced mortality benefits and uses the COI to monetize reduced morbidity benefits. The details on morbidity valuation for birth weight, CVD, RCC, and bladder cancer analyses are provided in the respective sections of the main document.

**Table J-2: Summary of Inputs and Data Sources Used for Valuation**

| Data Element | Modeled Variability | Data Source | Notes |
|---|---|---|---|
| Base VSL | None | U.S. EPA, 2010 | The base value of 4,800,000 ($1990) was used as recommended by the U.S. EPA Guidelines for Preparing Economic Analyses. |

**Table J-2: Summary of Inputs and Data Sources Used for Valuation**

| Data Element | Modeled Variability | Data Source | Notes |
|---|---|---|---|
| VSL income elasticity | None | U.S. EPA, 2010 | Income growth adjustments were done using income elasticity 0.4 per recommendations in the U.S. EPA Guidelines for Preparing Economic Analyses. |
| Medical Care CPI | Time: Annual, 1990..2021 | BLS 2022 (U.S. Bureau of Labor Statistics, 2020) | Medical cost inflation adjustments were done using annual CPI for medical care (U.S. city average, all urban consumers, series number CUUR0000SAM). |
| Employment Cost Index | Time: Quarterly, 2001..2021 | BLS 2022 (Bureau of Labor Statistics, 2022) | Opportunity cost inflation adjustments were done using quarterly index for total compensation for all civilian workers in all industries and occupations (series number CIS10100000000000I). |
| GDP Price Deflator Index | Time: Annual, 1990..2021 | BEA 2022 (U.S. Bureau of Economic Analysis, 2022) | VSL inflation adjustments were done using annual GDP price deflator index. |
| Historical income per capita | Time: Annual, 1990..2020 | BEA 2021 (U.S. Bureau of Economic Analysis, 2021) | Disposable personal annual income per capita (series number A229RC0A052NBEA). Data are in $2021. The series were converted to constant $2012 to align with US EIA 2021 projections using BLS 2020 CPI series. |
| Projected income per capita | Time: Annual, 2020..2050 | U.S. EIA 2021 (U.S. Energy Information Administration, 2021) | The U.S. EIA long-term projections focus on components of potential growth, fiscal balances and debt accumulation, domestic saving and investment balances, and external balances are covered and interest rates consistent with those projections. The projection horizon is 2050. EPA used the ratio of projected real disposable personal income (in constant $2012, series number 18-AEO2021.55.ref2021-d113020a) to project population size (series number 18-AEO2021.42.ref2021-d113020a). |

Abbreviations: BEA – Bureau of Economic Analysis; BLS – bureau of labor statistics; CPI – consumer price index; EIA – Energy Information Administration; GDP – gross domestic product; VSL – value of a statistical life.

# Appendix K. Benefits Sensitivity Analyses

This appendix provides details on the sensitivity analyses implemented by EPA to evaluate the impact of the exposure-response assumptions in the CVD benefits model and the impact of Perfluorononanoic Acid (PFNA) inclusion in the birth weight benefits model. Section K.1 describes hypothetical regulatory alternatives evaluated in the sensitivity analyses. Section K.2 provides details on estimation of blood serum PFOA, PFOS, and PFNA. Section K.3 summarizes the CVD exposure response scenarios and presents the associated results. Section K.4 summarizes the birth weight dose response scenarios and results. Section K.5 summarizes the RCC exposure response scenarios and results.

The sensitivity analyses described herein relied on methodology implemented in R software (R Core Team, 2021) and differ slightly from SafeWater MCBC methods. Specifically, SafeWater performs a set of pre-calculations to maximize computational efficiency and, as such, the order of analytical steps across R and SafeWater models differs; however, results across models are mathematically consistent. The R-based model version treats each integer age cohort between 85 and 99 separately, implements the CVD calculations for those aged 40-89 years only, and applies the ASCVD model-based annual incidence at age 80 years to ages 81-89 because the ASCVD model has been fit to those aged 40-80 years and predicts the 10-year probability of the first CVD event.

## K.1 Overview of the Hypothetical Exposure Reduction

Table K-1 shows the details of the two hypothetical exposure reductions developed by EPA for the sensitivity analyses. For both alternatives, EPA assumed the same population served size of 100,000 distributed over age-, sex-, and race-ethnicity categories using national-level demographic data (see Appendix B). Hypothetical exposure reduction 1 assumes a reduction of 1 ppt in PFOA and a reduction of 1 ppt in PFOS. Hypothetical exposure reduction 2 assumes a reduction of 1 ppt in PFNA,[56] in addition to the reductions specified for hypothetical exposure reduction 1. Additional sensitivity analysis assumptions (other than those pertaining to the exposure-response scenarios in Section K.3 and Section K.4), such as evaluation period, population growth, etc., align with those used in the Economic Analysis. EPA notes that uncertainty was not characterized for these sensitivity analysis scenarios. All parameters treated as uncertain in the Economic Analysis were set to their central estimate values (see Appendix L).

EPA notes that relative magnitudes of reductions in PFOA, PFOS, and PFNA may differ from those evaluated in the Economic Analysis. At entry points where PFOA and PFOS concentrations exceed their respective proposed MCLs, EPA expects reductions of 1 ppt or greater. Reductions in PFNA resulting from the proposed NPDWR are not predicted in this EA given the available occurrence data for PFNA at regulatory thresholds under consideration. However, multiple data sources, including UCMR 3 and state-collected finished drinking water data, demonstrate that PFNA has been detected between 0.22 ppt and 94.2 ppt. In UCMR 3, 0.28% of participating systems (14 total) had PFNA detections greater than/equal to the MRL (20 ppt), while state monitoring efforts showed that the number of systems in each state with PFNA detections ranged between 0.0% and 13.3%. EPA chose to evaluate unit reductions (i.e., 1

[56] Note that the inclusion of PFNA under Alternative 2 was only relevant to BW sensitivity analysis because there is evidence that PFNA reductions can improve BW. There is a lack of supporting evidence for an impact for CVD and RCC benefits.

ppt each) to demonstrate the effects of and make comparisons between unit changes in PFOA, PFOS, and PFNA exposure (U.S. EPA, 2023c). Caution should be exercised in quantifying the potential magnitude of change in the national benefits estimates based on the results of these sensitivity analyses, although conclusions about the directionality of these effects can be inferred.

**Table K-1: Overview of Hypothetical Exposure Reductions**

| Parameter Description | Hypothetical Exposure Reduction | |
|---|---|---|
| | 1 (PFOA+PFOS) | 2 (PFOA+PFOS+PFNA) |
| Population served at the start of the evaluation period | 100,000 | 100,000 |
| Reduction in PFOA concentration (ppt) | 1 | 1 |
| Reduction in PFOS concentration (ppt) | 1 | 1 |
| Reduction in PFNA concentration (ppt) | 0 | 1 |

Abbreviations: PFNA – perfluorononanoic acid; PFOA – perfluorooctanoic acid; PFOS – perfluorooctane sulfonic acid.

## K.2 Estimation of Blood Serum PFOA, PFOS, and PFNA

EPA used PFOA and PFOS drinking water concentrations as inputs to its Pharmacokinetic (PK) model to estimate blood serum PFOA and PFOS concentrations for adult males and females. In this analysis, the Agency used the September 18, 2021 PFOA/PFOS PK model version. See EPA's *Toxicity Assessments and Proposed Maximum Contaminant Level Goals for PFOA and PFOS in Drinking Water* for further information on the PFOA/PFOS model (U.S. EPA, 2023a; U.S. EPA, 2023b). Application of the PK model in the context of the benefits estimation is detailed in Section 6.3 of the Economic Analysis.

To estimate blood serum PFNA based on its drinking water concentration, EPA used a first-order single-compartment model whose behavior was previously demonstrated to be consistent with PFOA pharmacokinetics in humans (Bartell et al., 2010). Equation K-1–Equation K-4 summarize this model (Bartell, 2003; Bartell, 2017; Lu et al., 2020):

Equation K-1:

$$C_{\infty} = B + \frac{W * S}{1000}$$

Equation K-2:

$$C_t = C_{\infty} + (B - C_{\infty}) * e^{-kt}$$

Equation K-3:

$$k = ln(2) / t_{1/2}$$

Equation K-4:

$$S = \frac{f \cdot Q}{k \cdot V_d}$$

Where:

$C_\infty$ = steady-state serum PFNA concentration (ng/mL);

$C_t$ = serum concentration at time $t$ (ng/mL);

$t$ = time since beginning of / change in the water exposure (days);

$B$ = background serum PFNA concentration (ng/mL). EPA used an estimate of 0.411 ng/mL for 2017-2018 from Centers for Disease Control and Prevention (2022);

$W$ = drinking water PFNA concentration (ppt);

$S$ = steady-state serum/water concentration ratio (unitless);

$k$ = first order elimination rate constant for PFNA from serum (days$^{-1}$), defined as a function of half-life in Equation K-3 (Bartell, 2003);

$t_{1/2}$ = PFNA half-life in serum (days). Following Lu et al. (2020) model assumptions, EPA used an estimate of 3.9 years from Zhang et al. (2013) (weighted average estimate), after converting it to 1,424.5 days;

$f$ = fraction of PFNA absorbed (unitless). Following Lu et al. (2020) model assumptions, EPA used 100% absorption;

$Q$ = water intake (L/kg body weight per day). Consistent with assumptions used for serum PFOA and PFOS, EPA used a water intake of 0.013 L/kg of body weight per day (U.S. EPA, 2011b) in order to compute the PFNA dose from drinking water sources; and

$V_d$ = volume of distribution (L/kg body weight per day), a proportionality constant relating the total amount of a chemical in the body to the concentration in plasma (Hoffman et al., 2011). Following Lu et al. (2020) model assumptions, EPA used an estimate of 0.17 L/kg body weight from Zhang et al. (2013).

Using this model, EPA evaluated lifetime baseline and lifetime regulatory alternative exposure scenarios described in Section 6.3 of the Economic Analysis and used the difference between the two as an input to the downstream analysis of health effects.

## K.3 CVD Sensitivity Analyses

CVD sensitivity analyses rely on hypothetical exposure reduction 1 (i.e., 1 ppt reduction in PFOA and 1 ppt reduction in PFOS) to explore the impact of the following changes in the CVD exposure-response modeling:

- The use of single study-based TC effect estimates, rather than EPA meta-analysis-based effect estimates. To this end, EPA used estimates from a large NHANES study (Dong et al., 2019) and estimates from a longitudinal study of diabetes prevention program outcomes study (P.-I. D. Lin et al., 2019);
- Inclusion of HDLC effects from the CVD analysis; and,
- Exclusion of BP effects from the CVD analysis

Table K-2 summarizes the exposure-response scenarios, while Table K-3 provides details on the slope factors used in this sensitivity analysis.

**Table K-2: Overview of CVD Exposure-Response Scenarios**

| Exposure-Response Scenario | Scenario Definition |
|---|---|
| **1-EA** | Economic Analysis (EA) scenario using EPA meta-analysis for TC, Liao et al. (2020) for BP, and excluding HDLC impacts. |
| **2-Dong** | Scenario using Dong et al. (2019) for TC, Liao et al. (2020) for BP, and excluding HDLC impacts. |
| **3-Lin** | Scenario using P.-I. D. Lin et al. (2019) for TC, Liao et al. (2020) for BP, and excluding HDLC impacts. |
| **4-EA (+HDLC)** | Scenario using EPA meta-analysis for TC and HDLC, and Liao et al. (2020) for BP. |
| **5-Dong (+HDLC)** | Scenario using Dong et al. (2019) for TC and HDLC, and Liao et al. (2020) for BP. |
| **6-Lin (+HDLC)** | Scenario using P.-I. D. Lin et al. (2019) for TC and HDLC, and Liao et al. (2020) for BP. |
| **7-EA (–BP)** | Scenario using EPA meta-analysis for TC and excluding HDLC and BP impacts. This scenario is most comparable to the U.S. EPA (2021a) analysis implemented for the SAB review. |
| **8-Dong (–BP)** | Scenario using Dong et al. (2019) for TC and excluding HDLC and BP impacts. |
| **9-Lin (–BP)** | Scenario using P.-I. D. Lin et al. (2019) for TC and excluding HDLC and BP impacts. |
| **10-EA (–BP +HDLC)** | Scenario using EPA meta-analysis for TC and HDLC, and excluding BP impacts. |
| **11-Dong (–BP +HDLC)** | Scenario using Dong et al. (2019) for TC and HDLC, and excluding BP impacts. |
| **12-Lin (–BP +HDLC** | Scenario using P.-I. D. Lin et al. (2019) for TC and HDLC, and excluding BP impacts. |

Abbreviations: BP – blood pressure; CVD – cardiovascular disease; EA – economic analysis; HDLC – high-density lipoprotein cholesterol; PFOA – perfluorooctanoic acid; PFOS – perfluorooctane sulfonic acid; SAB – Science Advisory Board; TC – total cholesterol.

**Table K-3: Exposure-Response Information for CVD Biomarkers**

| Source | Contaminant | Linear Slope Estimate (mg/dL per 1 ng/mL) | | |
|---|---|---|---|---|
| | | TC | HDLC | BP |
| EPA meta-analysis[a] | Serum PFOA | 1.57 (CI95: 0.02,3.13) | 0.11 (CI95: -0.22, 0.43) | – |
| | Serum PFOS | 0.08 (CI95: –0.01,0.16) | 0.05 (CI95: –0.01, 0.11) | – |
| Dong et al. (2019) | Serum PFOA | 1.48 (CI95: 0.18, 2.78) | –0.03 (CI95: –0.44, 0.39) | – |
| | Serum PFOS | 0.40 (CI95: 0.13, 0.67) | 0.01 (CI95: –0.08, 0.11) | – |
| P.-I. D. Lin et al. (2019) | Serum PFOA | 1.63 (CI95: –0.84, 2.42) | –0.13 (CI95: –0.37,0.107) | – |
| | Serum PFOS | 0.13 (CI95: –0.005,0.27) | –0.02 (CI95: –0.06, 0.02) | – |
| Liao et al. (2020) | Serum PFOS | – | – | 0.044 (CI95: 0.006,0.083) |

Abbreviations: BP – systolic blood pressure; CI95 – 95% CI; CVD – cardiovascular disease; HDLC – high-density lipoprotein cholesterol; PFOA – perfluorooctanoic acid; PFOS – perfluorooctane sulfonic acid; TC – total cholesterol.
Notes:
[a] See Section 6.5.2 of the Economic Analysis.

Table K-4 shows the results of the CVD sensitivity analysis. EPA made the following observations:

- Relative to the annualized CVD benefits estimated using EPA meta-analysis-based slope factors, using the Dong et al. (2019) slope factors increases the annualized CVD benefits by 13%, while using the P.-I. D. Lin et al. (2019) slope factors increases the annualized CVD benefits by 7%.
- Inclusion of HDLC effects decreases annualized CVD benefits by 23%-25% if EPA meta-analysis slope factors are used. The use of Dong et al. (2019) and the P.-I. D. Lin et al. (2019) instead of the EPA meta-analysis slope factors decreases annualized benefits by 2.7%-3.0% and 20.1%-21.9%, respectively. The wide variation in the impact of HDLC inclusion may be explained by high variance in the slope factor estimates. EPA notes, however, that none of the PFOA/PFOS-HDLC slope factors are statistically significant at the 5% level.
- Exclusion of BP effects decreases annualized CVD benefits by 1.8%-2.2% if EPA meta-analysis slope factors are used. However, estimates decrease by 1.6%-1.9% and 1.7%-2.0% if the Dong et al. (2019) and the P.-I. D. Lin et al. (2019), respectively, slope factors are used.

The relative magnitudes of reductions in PFOA and PFOS used in this sensitivity analysis may differ from those implied by the regulatory alternatives evaluated in the Economic Analysis. Therefore, the potential magnitude of changes in national CVD benefits due to alternative TC/HDLC
exposure-response assumptions as well as exclusion of the BP effects may differ from the ones estimated in this sensitivity analyses.

**Table K-4: Summary of CVD Sensitivity Analysis for Hypothetical Exposure Reduction 1 (PFOA+PFOS)**

| Result Description[a] | Exposure-Response Scenario[b,c] | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **1-EA** | **2-Dong** | **3-Lin** | **4-EA (+HDLC)** | **5-Dong (+HDLC)** | **6-Lin (+HDLC)** | **7-EA (–BP)** | **8-Dong (–BP)** | **9-Lin (–BP)** | **10-EA (–BP +HDLC)** | **11-Dong (BP +HDLC)** | **12-Lin (–BP +HDLC)** |
| Average reduction in serum PFOA concentration (ng/mL) | 0.094 | 0.094 | 0.094 | 0.094 | 0.094 | 0.094 | 0.094 | 0.094 | 0.094 | 0.094 | 0.094 | 0.094 |
| Average reduction in serum PFOS concentration (ng/mL) | 0.086 | 0.086 | 0.086 | 0.086 | 0.086 | 0.086 | 0.086 | 0.086 | 0.086 | 0.086 | 0.086 | 0.086 |
| Average reduction in TC concentration (mg/dL) | 0.152 | 0.173 | 0.164 | 0.152 | 0.173 | 0.164 | 0.152 | 0.173 | 0.164 | 0.152 | 0.173 | 0.164 |
| Average reduction in HDLC concentration (mg/dL) | 0.000 | 0.000 | 0.000 | 0.015 | -0.002 | -0.014 | 0.000 | 0.000 | 0.000 | 0.015 | -0.002 | -0.014 |
| Average reduction in BP (mmHg) | 0.004 | 0.004 | 0.004 | 0.004 | 0.004 | 0.004 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| Non-fatal first MI (total cases avoided)[d] | 2.725 | 3.096 | 2.931 | 1.942 | 3.200 | 3.675 | 2.686 | 3.057 | 2.892 | 1.902 | 3.161 | 3.636 |
| Non-fatal first IS (total cases avoided)[d] | 4.091 | 4.649 | 4.401 | 3.078 | 4.783 | 5.363 | 4.030 | 4.587 | 4.339 | 3.016 | 4.722 | 5.302 |
| CVD deaths (total cases avoided)[d] | 0.849 | 0.966 | 0.913 | 0.690 | 0.986 | 1.064 | 0.825 | 0.941 | 0.889 | 0.665 | 0.962 | 1.040 |
| PDV, non-fatal first MI (3% discount rate, millions $2021) | 0.103 | 0.117 | 0.111 | 0.073 | 0.121 | 0.139 | 0.102 | 0.115 | 0.109 | 0.072 | 0.119 | 0.138 |
| PDV, non-fatal first IS (3% discount rate, millions $2021) | 0.043 | 0.049 | 0.047 | 0.032 | 0.051 | 0.057 | 0.043 | 0.049 | 0.046 | 0.032 | 0.050 | 0.057 |
| PDV, CVD deaths (3% discount rate, millions $2021) | 4.965 | 5.627 | 5.336 | 3.844 | 5.777 | 6.403 | 4.855 | 5.517 | 5.226 | 3.734 | 5.666 | 6.292 |
| PDV, total CVD benefits (3% discount rate, millions $2021) | 5.111 | 5.793 | 5.493 | 3.949 | 5.948 | 6.599 | 4.999 | 5.681 | 5.381 | 3.837 | 5.836 | 6.487 |
| **Annualized CVD benefits (3% discount rate, millions $2021)** | **0.168** | **0.191** | **0.181** | **0.130** | **0.196** | **0.217** | **0.165** | **0.187** | **0.177** | **0.126** | **0.192** | **0.214** |
| PDV, non-fatal first MI (7% discount rate, millions $2021) | 0.042 | 0.048 | 0.045 | 0.030 | 0.049 | 0.057 | 0.042 | 0.047 | 0.045 | 0.029 | 0.049 | 0.056 |
| PDV, non-fatal first IS (7% discount rate, millions $2021) | 0.018 | 0.020 | 0.019 | 0.013 | 0.021 | 0.024 | 0.018 | 0.020 | 0.019 | 0.013 | 0.021 | 0.024 |
| PDV, CVD deaths (7% discount rate, millions $2021) | 2.351 | 2.654 | 2.525 | 1.775 | 2.733 | 3.076 | 2.308 | 2.611 | 2.482 | 1.732 | 2.690 | 3.033 |

**Table K-4: Summary of CVD Sensitivity Analysis for Hypothetical Exposure Reduction 1 (PFOA+PFOS)**

| Result Description[a] | Exposure-Response Scenario[b,c] | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **1-EA** | **2-Dong** | **3-Lin** | **4-EA (+HDLC)** | **5-Dong (+HDLC)** | **6-Lin (+HDLC)** | **7-EA (–BP)** | **8-Dong (–BP)** | **9-Lin (–BP)** | **10-EA (–BP +HDLC)** | **11-Dong (BP +HDLC)** | **12-Lin (–BP +HDLC)** |
| PDV, total CVD benefits (7% discount rate, millions $2021) | 2.411 | 2.722 | 2.590 | 1.818 | 2.803 | 3.157 | 2.368 | 2.678 | 2.546 | 1.774 | 2.759 | 3.113 |
| **Annualized CVD benefits (7% discount rate, millions $2021)** | **0.169** | **0.191** | **0.182** | **0.128** | **0.197** | **0.222** | **0.166** | **0.188** | **0.179** | **0.125** | **0.194** | **0.219** |

Abbreviations: PFOA – perfluorooctanoic acid; PFOS – perfluorooctane sulfonic acid; TC – total cholesterol; HDLC – high-density lipoprotein cholesterol; BP – systolic blood pressure; CVD – cardiovascular disease; EA – economic analysis; SAB – science advisory board; MI – myocardial infarction; IS – ischemic stroke; PDV – present discounted value.

Notes:

[a]See Table K-1

[b]See Table K-3

[c]Negative values refer to increases in a particular result (e.g., the HDLC reduction of -0.002 mg/dL in Scenario 2-Dong refers to an increase in HDLC).

[d]Total over the period of analysis.

## K.4 Birth Weight Sensitivity Analyses

Birth weight sensitivity analyses rely on the two hypothetical exposure reductions described in Table K-1 to explore the impact of the following changes in the birth weight exposure-response modeling:

- **Early pregnancy birth weight effects** using first trimester estimates from Steenland et al. (2018) for PFOA and Dzierlenga, Crawford, et al. (2020) for PFOS; and
- **Inclusion of PFNA-birth weight effects** using estimates from two studies (Lenters et al., 2016; Valvi et al., 2017), in addition to the PFOA-birth weight and PFOS-birth weight effects analyzed in the Economic Analysis; inclusion of PFNA-birth weight effects using estimates from two studies (Lenters et al., 2016; Valvi et al., 2017), in addition to the PFOA-birth weight and PFOS-BW effects analyzed in the Economic Analysis.

Table K-5 summarizes the exposure-response scenarios, while Table K-6 provides details on the slope factors used in this sensitivity analysis.

**Table K-5: Overview of Birth Weight Exposure-Response Scenarios**

| Exposure-Response Scenario | Scenario Definition |
|---|---|
| **1-EA** | Economic Analysis (EA) scenario using Steenland et al. (2018) for PFOA, Dzierlenga, Crawford, et al. (2020) for PFOS |
| **2-First Trimester** | Scenario using first trimester estimates from Steenland et al. (2018) for PFOA and Dzierlenga, Crawford, et al. (2020) for PFOS |
| **3-EA+Lenters** | Scenario using Steenland et al. (2018) for PFOA, Dzierlenga, Crawford, et al. (2020) for PFOS, Lenters et al. (2016) for PFNA/PFDA |
| **4-EA+Valvi** | Scenario using Steenland et al. (2018) for PFOA, Dzierlenga, Crawford, et al. (2020) for PFOS, Valvi et al. (2017) for PFNA |

Abbreviations: PFDA – Perfluorodecanoic Acid; PFNA – perfluorononanoic acid; PFOA – perfluorooctanoic acid; PFOS – perfluorooctane sulfonic acid.

**Table K-6: Exposure-Response Information for Birth Weight**

| Source | Linear Slope Estimate (g birth weight per 1 ng/mL) | | |
|---|---|---|---|
| | **Serum PFOA** | **Serum PFOS** | **Serum PFNA** |
| Steenland et al. (2018) | –10.5 (CI95: –16.7, –4.4) | – | – |
| Dzierlenga, Crawford, et al. (2020) | – | –3.0 (CI95: –4.9, –1.1) | – |
| First trimester – Steenland et al. (2018) | –3.3 (CI95: –9.6, –3.0) | – | – |
| First trimester – Dzierlenga, Crawford, et al. (2020) | – | –1.35 (CI95: –2.3, –0.4) | – |
| Lenters et al. (2016) | – | – | –40.4 (CI95: –83.24, 2.43) |
| Valvi et al. (2017) | – | – | –60.07 (CI95: –154.47, 35.76) |

Abbreviations: CI95 – 95% confidence interval; PFNA – perfluorononanoic acid; PFOA – perfluorooctanoic acid; PFOS – perfluorooctane sulfonic acid.

Table K-7 shows the results of the birth weight sensitivity analysis. EPA made the following observations:

- Using early pregnancy study-based dose-response estimates could reduce annualized benefits by 66%.
- Inclusion of a 1 ppt PFNA reduction could increase annualized birth weight benefits 5.4-7.7-fold, relative to the scenario that quantifies a 1 ppt reduction in PFOA and a 1 ppt reduction in PFOS only.
- The range of estimated PFNA-related increases in benefits is driven by the exposure-response, with smaller estimates produced using the slope factors from Lenters et al. (2016), followed by Valvi et al. (2017). EPA notes that the PFNA slope factor estimates are orders of magnitude larger than the slope factor estimates used to evaluate the impacts of PFOA/PFOS reductions. EPA also notes that the PFNA slope factor estimates are not precise, with 95% CIs covering wide ranges that include zero (i.e., serum PFNA slope factor estimates are not statistically significant at 5% level).

The relative magnitudes of reductions in PFOA, PFOS, and PFNA used in this sensitivity analysis may differ from those implied by the regulatory alternatives evaluated in the Economic Analysis. Therefore, the potential magnitude of increase in the national birth weight benefits estimates due to inclusion of PFNA effects may differ from the one estimated in this sensitivity analyses.

## Table K-7: Summary of Birth Weight Sensitivity Analysis

| Result Description | Hypothetical Exposure Reduction[a] / Exposure-Response Scenario[b] | | | |
|---|---|---|---|---|
| | 1 (PFOA+PFOS) | | 2 (PFOA+PFOS+PFNA) | |
| | 1-EA | 2-First Trimester | 3-EA+Lenters | 4-EA+Valvi |
| Average reduction in serum PFOA concentration (ng/mL) | 0.092 | 0.092 | 0.092 | 0.092 |
| Average reduction in serum PFOS concentration (ng/mL) | 0.083 | 0.083 | 0.083 | 0.083 |
| Average reduction in serum PFNA concentration (ng/mL) | 0.000 | 0.000 | 0.139 | 0.139 |
| Total increase in birth weight (g) | 1.214 | 0.415 | 6.843 | 9.584 |
| Total number of births affected[c] | 95,263 | 95,263 | 95,263 | 95,263 |
| Total number of surviving births affected[c] | 94,831 | 94,830 | 94,833 | 94,835 |
| Birth weight-related deaths (total cases avoided)[c] | 0.592 | 0.203 | 3.324 | 4.647 |
| PDV, birth weight-related deaths (3% discount rate, millions $2021) | 2.337 | 0.799 | 12.951 | 18.091 |
| PDV, birth weight-related morbidity (3% discount rate, millions $2021) | 0.076 | 0.026 | 0.422 | 0.591 |
| PDV, total birth weight benefits (3% discount rate, millions $2021) | 2.414 | 0.825 | 13.373 | 18.682 |
| **Annualized birth weight benefits (3% discount rate, millions $2021)** | **0.079** | **0.027** | **0.440** | **0.615** |
| PDV, birth weight-related deaths (7% discount rate, millions $2021) | 0.848 | 0.290 | 4.612 | 6.436 |
| PDV, birth weight-related morbidity (7% discount rate, millions $2021) | 0.028 | 0.010 | 0.154 | 0.215 |
| PDV, total birth weight benefits (7% discount rate, millions $2021) | 0.877 | 0.299 | 4.766 | 6.651 |
| **Annualized birth weight benefits (7% discount rate, millions $2021)** | **0.062** | **0.021** | **0.335** | **0.467** |

Abbreviations: PDV – present discounted value; PFNA – perfluorononanoic acid; PFOA – perfluorooctanoic acid; PFOS – perfluorooctane sulfonic acid.
Notes:
[a]See Table K-1
[b]See Table K-5
[c]Total over the period of analysis.

## K.5 RCC Sensitivity Analyses

RCC sensitivity analyses rely on the first hypothetical exposure reduction described in Table K-1 to explore the impact of the following changes in the RCC exposure-response modeling:

- The use of the serum PFOA central tendency slope from Vieira et al. (2013), as derived by EPA/OST (U.S. EPA, 2023b); and
- The use of the serum PFOA central tendency slopes from Vieira et al. (2013) excluding a very high exposure group, as derived by EPA/OST (U.S. EPA, 2023b).

Table K-8 summarizes the exposure-response scenarios, while Table K-9 provides details on the slope factors used in this sensitivity analysis.

**Table K-8: Overview of RCC Exposure-Response Scenarios**

| Exposure-Response Scenario | Scenario Definition[a] |
|---|---|
| **1-EA** | Economic Analysis (EA) scenario using the serum PFOA central tendency slope from Shearer et al. (2021) |
| **2-Vieira** | Scenario using the serum PFOA central tendency slope from Vieira et al. (2013) |
| **3-Vieira$_{ExcludeHigh}$** | Scenario using the serum PFOA central tendency slope from Vieira et al. (2013), excluding a very high exposure group |

Abbreviations: PFOA – perfluorooctanoic acid; RCC – renal cell carcinoma.
Note:
[a]All exposure-response scenarios include the 3.94% PAF-based cap on the magnitude of relative risk reductions, as described in Section 6.6.

**Table K-9: Exposure-Response Information for RCC**

| Source | Linear Slope Estimate, Serum PFOA (per 1 ng/mL) |
|---|---|
| Shearer et al. (2021), as derived by EPA/OST (U.S. EPA, 2023b) | 0.00178 (CI95: 0.00005, 0.00352) |
| Vieira et al. (2013), as derived by EPA/OST (U.S. EPA, 2023b) | 0.00007 (CI95: 0.000001, 0.00014) |
| Vieira et al. (2013) excluding very high exposure group from Vieira et al. (2013), as derived by EPA/OST (U.S. EPA, 2023b) | 0.00025 (CI95: 0.00001, 0.00048) |

Abbreviations: CI95 – 95% CI; PFOA – perfluorooctanoic acid; RCC – renal cell carcinoma.

Table K-10 shows the results of the RCC sensitivity analysis. EPA made the following observations:

- Using the slope factor based on Vieira et al. (2013) could reduce annualized benefits by 96%;
- Using the slope factor based on Vieira et al. (2013) excluding a very high exposure group could reduce annualized benefits by 86%.

EPA also notes that the PAF-based cap of 3.94% on the RCC relative risk reductions associated with a 1 ppt reduction in PFOA is rarely binding for the Economic Analysis scenario presented below and never binding for the sensitivity analysis scenarios. For larger PFOA reduction magnitudes, the PAF-based cap could become binding, which would attenuate the differences across the sensitivity analysis scenarios.

**Table K-10: Summary of RCC Sensitivity Analysis**

| Result Description | Exposure-Response Scenario[a] | | |
|---|---|---|---|
| | **1-EA** | **2-Vieira** | **3- Vieira$_{ExcludeHigh}$** |
| Average reduction in serum PFOA concentration (ng/mL) | 0.088 | 0.088 | 0.088 |
| Non-fatal RCC (cases avoided) | 9.627 | 0.377 | 1.336 |
| RCC-related deaths (cases avoided)[b] | 3.887 | 0.152 | 0.539 |
| PDV, Non-fatal RCC (3% discount rate, millions $2021) | 1.569 | 0.061 | 0.218 |
| PDV, RCC-related deaths (3% discount rate, millions $2021) | 14.376 | 0.562 | 1.994 |
| PDV, total RCC benefits (3% discount rate, millions $2021) | 15.945 | 0.623 | 2.212 |
| **Annualized RCC benefits (3% discount rate, millions $2021)** | **0.525** | **0.021** | **0.073** |
| PDV, Non-fatal RCC (7% discount rate, millions $2021) | 0.483 | 0.019 | 0.067 |
| PDV, RCC-related deaths (7% discount rate, millions $2021) | 3.961 | 0.155 | 0.549 |
| PDV, total RCC benefits (7% discount rate, millions $2021) | 4.444 | 0.174 | 0.617 |
| **Annualized RCC benefits (7% discount rate, millions $2021)** | **0.312** | **0.012** | **0.043** |

Abbreviations: PDV – present discounted value; PFOA – perfluorooctanoic acid; RCC – renal cell carcinoma.
Notes:
[a]See Table K-8.
[b]Total over the period of analysis.

# Appendix L. Uncertainty Characterization Details and Input Data

## L.1 Cost Analysis Uncertainty Characterization

In addition to occurrence uncertainty, the national cost estimates reflect two additional sources of uncertainty. The first is the total organic carbon concentration, which affects PFAS treatment selection and is a factor for the DBP co-benefits analysis. The second is the unit cost curve selection. The following subsections provide additional details on EPA's approach to modeling these sources of uncertainty.

### *L.1.1 Total Organic Carbon Concentration Uncertainty*

For the national cost analysis, total organic carbon (TOC) is an input to the technology selection and design equations for granular activated carbon (GAC). Section 5.3.1.1 of the Economic Analysis provided a description of how TOC affects the decision tree for technology selection. The process design equations in Section 5.3.1.1.1 show the effect of TOC on the estimation of bed volumes for GAC.

As noted in Section 4.3.1.1 of the Economic Analysis, there is no national dataset of TOC values or ranges at PWSs. Some data are available at the system level in periodic data voluntarily provided by primacy agencies. EPA used the most recent data obtained in response to the ICR for the fourth Six-Year Review of drinking water regulations. EPA separated the systems into two groups – those with ground water sources and those with surface water sources – to reflect expected variations in TOC in different types of source water. Some of the systems provided TOC values at different facilities. Facilities can include water intakes or wells, treatment processes, and distribution system entry points. TOC levels at systems that have treatment may differ pre- and post-treatment.

EPA randomly assigned a TOC level to each entry point from the corresponding ground water or surface water distribution. EPA retained that value for each of the 4,000 uncertainty simulations. Thus, EPA's estimates reflect TOC uncertainty across entry points, but not TOC uncertainty interacted with PFAS uncertainty.

### *L.1.2 Compliance Technology Unit Cost Curve Selection Uncertainty*

Each WBS model includes an input that determines whether the cost estimate generated is a low, medium, or high cost estimate (U.S. EPA, 2023d). This input drives the selection of materials for items of equipment that can be constructed of different materials. For example, a low cost system might include fiberglass pressure vessels and PVC piping. A high cost system might include stainless steel pressure vessels and stainless steel piping. This input also drives other model assumptions that can affect the total cost including assumptions about building quality. High, medium, and low quality settings affect building costs for substructure, superstructure, exterior enclosure, interior finishes, and mechanical and electrical services.

For every technology, EPA generated cost curves for low-, medium-, and high-cost options. SafeWater MCBC randomly selects from these cost curves. EPA assigned a triangular distribution to the cost curve selection: 25% probability for low-cost, 50% probability for medium-cost, and 25% for high-cost.

## L.2 Benefits Analysis Uncertainty Characterization

EPA characterizes sources of uncertainty in its analysis of potential benefits resulting from changes in PFAS levels in drinking water. The analysis reports uncertainty bounds for benefits estimated in each category modeled for the proposed rule. Each lower (upper) bound value is the 5th (95th) percentile of the category-specific benefits estimate distribution represented by 4,000 Monte Carlo draws. Table L-1 provides the sources of uncertainty that EPA quantified in the benefits analysis that are specific to this analysis. In addition to these sources of uncertainty, reported uncertainty bounds also reflect the following upstream sources of uncertainty: baseline PFAS occurrence (Section 4.4 of the Economic Analysis), affected population size and demographic composition (Section 4.3 of the Economic Analysis), and the magnitude of PFAS concentration reduction (Section 4.4 of the Economic Analysis).

**Table L-1: Quantified Sources of Uncertainty in Benefits Estimates**

| Source | Description of Uncertainty |
|---|---|
| TC-serum PFOA slope factor; TC-serum PFOS slope factor | The slope factors that express the effects of PFOA and PFOS on serum lipid markers are based on 12 key studies with high-quality data and clearly defined PFAS-lipid level relationships (see Appendix F). EPA meta-analysis of these studies provides a central estimate and a standard error estimate for the slope factors. EPA uses a normal distribution with a mean set at the central slope factor estimate and a standard deviation set at the standard error estimate for the slope factor to characterize uncertainty surrounding these parameters. |
| BP-serum PFOS slope factor | The slope factor that expresses the effects of serum PFOS on systolic BP is from Liao et al. (2020) – a high confidence study conducted based on U.S. general population data from NHANES cycles 2003-2012. This study provides a central estimate and a standard error estimate for the slope factor. EPA uses a normal distribution with a mean set at the central slope factor estimate and a standard deviation set at the standard error estimate for the slope factor to characterize uncertainty surrounding this parameter. |
| BW-serum PFOA slope factor; BW-serum PFOS slope factor | The slope factors were obtained from meta-analyses of several studies on the subject: Steenland et al. (2018) for PFOA and an EPA reanalysis of Dzierlenga, Crawford, et al. (2020) for PFOS.[b] The meta-analyses provide a central estimate and a standard error estimate for the slope factors. EPA uses a normal distribution with a mean set at the central slope factor estimate and a standard deviation set at the standard error estimate for the slope factor to characterize uncertainty surrounding these parameters. |
| RCC-serum PFOA slope factor | The slope factor that expresses the effects of serum PFOA exposure on lifetime RCC risk is from Shearer et al. (2021), which estimated a higher slope factor for the impact of PFOA on RCC than previous estimates (Steenland et al., 2012; Vieira et al., 2013).[c] This study provides a central estimate and a standard error estimate for the slope factor. EPA uses a normal distribution with a mean set at the central slope factor estimate and a standard deviation set at the standard error estimate for the slope factor to characterize uncertainty surrounding this parameter. |
| Bladder cancer-THM4 slope factor | The slope factor that expresses the effect of co-occurring THM4 on bladder cancer is from Regli et al. (2015), who estimated a linear slope factor relating the lifetime bladder cancer risk associated with lifetime exposure to THM4 concentration in drinking water. This study provides a central estimate for the slope factor. EPA estimated a standard error for this slope factor based on the data reported in Regli et al. (2015). EPA uses a normal distribution with a mean set at the central slope factor estimate and a standard deviation set at the standard error estimate for the slope factor to characterize uncertainty surrounding this parameter. |
| RCC PAF to cap risk reductions for this endpoint | EPA developed a central tendency estimate and an uncertainty distribution for the PAF values to cap the relative risk estimates derived from the RCC exposure-response relationship. |

Abbreviations: ASCVD –Atherosclerotic Cardiovascular Disease; BW – birth weight; BP – blood pressure; CVD – cardiovascular disease; PAF – population attributable fraction; PFAS – per and polyfluoroalkyl substances; PFOA – perfluorooctanoic acid; PFOS – perfluorooctane sulfonic acid; RCC – renal cell carcinoma; TC – total cholesterol; THM4- four regulated trihalomethanes.

Notes:

[a]The slope factors contributing to the CVD benefits analysis include the relationship between total cholesterol and PFOA and PFOS, the relationship between high-density lipoprotein cholesterol and PFOA and PFOS, and the relationship between blood pressure and PFOS.

[b]In the original Dzierlenga, Crawford, et al. (2020) estimate, the authors duplicated an estimate from Chen et al. (2017) in the pooled estimate. EPA reran the analysis excluding the duplicated estimate.

[c]A sensitivity analysis of the RCC slope factor based on alternate estimates from Vieira et al. (2013) and pooled estimates of studies included in Shearer et al. (2021) and Vieira et al. (2013) is shown in Appendix K.

As described in Section 6.1 of the Economic Analysis, EPA did not characterize the following sources of potential uncertainty: U.S. population life tables (including standard and cause-eliminated life tables; See Section 6.1.3 of the Economic Analysis), annual all-cause and health

outcome-specific mortality rates, CVD risk model (Goff et al., 2014) predictors (e.g., share of smokers) estimated from health survey data, prevalence of CVD event history in the U.S. population, distribution of CVD events by type, the estimated infant mortality-birth weight slope factor (See Section 6.4.3.1 of the Economic Analysis), state-level distributions of infant births and infant deaths over discrete birth weight ranges, the 200-g cap on birth weight changes estimated under the rule, COI estimates for all modeled non-fatal health outcomes, the VSL reference value, the VSL income elasticity value used for VSL income growth adjustment, and the gross domestic product per capita projection used to for VSL income growth adjustment (see Appendix J). EPA expects that the sources listed in Table L-1, in addition to uncertainty surrounding about estimated PFAS occurrence, affected population size, and the magnitude of PFAS reduction, account for the largest portion of uncertainty in the benefits analysis.

## *L.2.1 Exposure-Response Function Uncertainty*

Table L-2 presents the central tendency estimates, 95% confidence interval bounds ($2.5^{th}$ and $97.5^{th}$ quantile), and standard errors for the slope factors used in EPA's assessment of benefits resulting from the PFAS NPDWR. This table also presents information on the uncertainty distribution used by EPA to characterize uncertainty for each slope factor.

**Table L-2: Standard Errors and Distributions for Benefits Model Exposure-Response Slope Factors**

| Pollutant | Health Benefits Analysis Category | Health Outcome | Exposure-Response Slope Factor | | | | | Uncertainty Distribution | Data Source |
|---|---|---|---|---|---|---|---|---|---|
| | | | Central Estimate | LCB | UCB | Standard Error | Units | | |
| PFOA | CVD | TC | 1.57 | 0.02 | 3.13 | 0.79 | mg/dL per ng/mL | Normal | EPA meta-analysis based on 12 studies (see Appendix F) |
| | BW | BW | -10.5 | –16.7 | –4.4 | 3.14 | g per ng/mL | Normal | Steenland et al. (2018) |
| | RCC | RCC | 0.00178 | 0.00005 | 0.00352 | 0.00 | per ng/mL | Normal | Shearer et al. (2021) |
| PFOS | CVD | TC | 0.08 | -0.01 | 0.16 | 0.04 | mg/dL per ng/mL | Normal | EPA meta-analysis based on 12 studies (see Appendix F) |
| | | BP | 0.044 | 0.006 | 0.083 | 0.02 | mmHg per ng/mL | Normal | Liao et al. (2020) |
| | BW | BW | -3.0 | –4.9 | –1.1 | 0.97 | g per ng/mL | Normal | EPA reanalysis of Dzierlenga, Crawford, et al. (2020) |
| THM4 | Bladder cancer | Bladder cancer | 0.00427 | 0.00331 | 0.00522 | 0.00 | per ug/L | Normal | Regli et al. (2015) |

Abbreviations: BW – birth weight; BP – blood pressure; CVD – cardiovascular disease; HDLC – high-density lipoprotein cholesterol; LCB – lower confidence bound, 2.5% quantile; PFAS – per and polyfluoroalkyl substances; PFOA – perfluorooctanoic acid; PFOS – perfluorooctane sulfonic acid; RCC – renal cell carcinoma; TC – total cholesterol; THM4- four regulated trihalomethanes; UCB – upper confidence bound, 97.5% quantile.

## *L.2.2 Population Attributable Fraction Uncertainty*

As described in Section 6.6 of the Economic Analysis and ICF (2022), EPA placed a PAF-based cap on the estimated RCC risk reductions associated with changes in serum PFOA exposure. EPA used a log-uniform distribution (also known as reciprocal) to approximate the distribution of PAF estimates given existing PAF estimates for other specific environmental exposures and other specific cancers (i.e., nitrate exposure in drinking water and colon cancer). The minimum of the distribution was set at the smallest identified PAF estimate (0.2%) and the maximum was set at the largest identified estimated PAF (17.9%). EPA used 3.94% (i.e., the mean of this log-uniform distribution) for as the central estimate of the PAF-based cap on the RCC relative risk reductions.

# Appendix M. Environmental Justice

This appendix provides additional detail on EPA's environmental justice (EJ) analysis. This includes discussion of results from EPA's EJ exposure analysis using EJScreen for PWS service areas in categories 4 and 5.

## M.1 Demographic Profile of Category 4 and 5 PWS Service Areas

Table M-1 summarizes the number of PWSs, size of PWSs, and population served for category 4 PWS service areas. There are 311 category 4 PWSs serving a population of 610,463, or 0.18% of the overall U.S. population; 98% of category 4 PWSs are small systems, serving 546,478 people. Table M-2 summarizes the demographic profile of category 5 PWS service areas. There are 148 category 5 PWSs serving a population of 578,751, or 0.17% of the overall U.S. population. 97% percent of category 5 PWSs are small systems, serving 519,924 people.

Table M-3 summarizes the demographic profile for category 4 and 5 PWS service areas combined and compares it to the demographic characteristics of the overall U.S. population. Population served by category 4 and 5 PWS service areas account for 0.2% of the U.S. population. Compared to the overall U.S. population, the population served by category 4 and 5 PWSs have lower percentages of American Indian or Alaska Native populations, Asian and Pacific Islander populations, Black populations, and Hispanic populations and populations with income less than twice the poverty level. Category 4 and 5 PWS service areas also have relatively higher percentages of non-Hispanic White populations and populations with income above twice the federal poverty level. Among category 4 and 5 PWS service areas, there are no Native American-owned community water systems.

## Table M-1: Number of Category 4 PWSs and Population Served by Size and State

| State | Number of Systems | Percent of Small PWSs | Total Population Served | Population Served in Small Systems[a] | Population Served in Medium and Large Systems |
|---|---|---|---|---|---|
| New Jersey | 311 | 98% | 610,463 | 546,478 | 63,985 |

Abbreviation: PWS – public water system.
Note:
[a]Small systems are defined as serving populations of 10,000 people or less.

## Table M-2: Number of Category 5 PWSs and Population Served by Size and State

| State | Number of Service Areas | Percent Small Service Areas | Total Population Served | Population Served in Small Systems[a] | Population Served in Medium and Large Systems |
|---|---|---|---|---|---|
| Alabama | 3 | 100% | 9,955 | 9,955 | - |
| Colorado | 24 | 96% | 94,604 | 83,737 | 10,867 |
| Illinois | 15 | 100% | 44,945 | 44,945 | - |
| Kentucky | 8 | 100% | 45,099 | 45,099 | - |
| Massachusetts | 7 | 86% | 42,807 | 31,044 | 11,763 |
| Michigan | 30 | 93% | 130,011 | 105,728 | 24,283 |
| New Hampshire | 7 | 100% | 14,795 | 14,795 | - |
| New Jersey | 5 | 100% | 4,177 | 4,177 | - |
| Ohio | 34 | 100% | 123,566 | 123,566 | - |
| South Carolina | 7 | 86% | 42,008 | 30,094 | 11,914 |
| Vermont | 8 | 100% | 26,784 | 26,784 | - |
| TOTAL | 148 | 97% | 578,751 | 519,924 | 58,827 |

Abbreviation: PWS – public water system.
Note:
[a]Small systems are defined as serving populations of 10,000 people or less.

**Table M-3: Population Served by Category 4 and 5 PWSs Compared to Percent of U.S. Population by Demographic Group**

| Results | Race and Ethnicity | | | | | Income | | Total Population Served |
|---|---|---|---|---|---|---|---|---|
| | American Indian or Alaska Native | Asian and Pacific Islander | Black | Hispanic | Non-Hispanic White | Below Twice the Poverty Level | Above Twice the Poverty Level | |
| Population Served | 3,281 | 27,098 | 68,682 | 96,511 | 976,596 | 290,466 | 898,748 | 1,189,214 |
| Percent of Total Population Served | 0.3% | 2.3% | 5.8% | 8.1% | 82.1% | 24.4% | 75.6% | *100%* |
| U.S. Population Percent by Demographic Group | 0.8% | 5.8% | 12.6% | 18.2% | 60.1% | 29.8% | 70.2% | *326,569,308* |
| Percent Difference Between Population Served and U.S. Population | -0.5% | -3.5% | -6.8% | -10.1% | 22.0% | -5.4% | 5.4% | - |

# M.2 Exposure Analysis Results

## *M.2.1 Baseline Scenario*

Table M-4 summarizes the population served by category 4 and 5 PWS service areas with PFAS occurrence above baseline thresholds based on Method 537.1 detection limits. The second set of rows in Table M-4 summarizes the percentage of the total population served by demographic group with modeled PFAS occurrence above these baseline thresholds. Percentages are bolded and italicized when the percentage of the population in a specific demographic group exposed to modeled PFAS above the baseline threshold is greater than the percentage of the total population served across all demographic groups exposed to modeled PFAS above this threshold (right-hand column). Higher percentages indicate higher PFAS exposure for a given demographic group compared to the percentage of the total population served across all demographic groups.

Notably, PFAS occurrence above the baseline thresholds is higher for Asian and Pacific Islander across all PFAS analytes compared to the total population served across all demographic groups. The difference in exposure in PFAS occurrence is even greater when compared to non-Hispanic White populations, or nearly 10% higher for PFOS and 15% higher for PFOA. PFAS occurrence above baseline thresholds is higher for Black and Hispanic populations for PFOS, PFHxS, and PFOA compared to the total population served across all demographic groups. When compared to non-Hispanic White populations instead of the total population served across all demographic groups, Black populations face over 10% greater PFOS exposure, while Hispanic populations face nearly 10% greater PFOA exposure. PFAS occurrence above the baseline threshold is higher for American Indian or Alaska Native populations for PFOS compared to the total population served across all demographic groups. However, for other PFAS analytes, exposure for American Indian or Alaska Native populations is less than or similar to occurrence rates for the total population served across all demographic groups. PFAS occurrence above the baseline thresholds is generally lower for populations with income below twice the federal poverty level compared to occurrence for the total population served across all demographic groups. Populations with income above the twice the poverty level have comparable but slightly higher occurrence in comparison to the total population served across all demographic groups.

Table M-5 expands on this analysis, showing average population-weighted PFAS concentrations across demographic groups in category 4 and 5 PWSs. Cells are highlighted in yellow when the average concentration for a given demographic group is higher than the average for the total population served across all demographic groups. These results are very similar to those of Table M-4, demonstrating again that Asian and Pacific Islander as well as Hispanic populations have higher average exposure than the total population served across all demographic groups in category 4 and 5 PWSs.

**Table M-4: Baseline Scenario: Population Served by Category 4 and 5 PWS Service Areas Above Baseline Thresholds and as a Percent of Total Population Served**

| Results | Analyte | Race and Ethnicity | | | | | Income | | Population Served |
|---|---|---|---|---|---|---|---|---|---|
| | | American Indian and Alaska Native | Asian and Pacific Islander | Black | Hispanic | Non-Hispanic White | Below Twice the Poverty Level | Above Twice the Poverty Level | |
| Population Served Above Baseline Threshold | PFOS | 688 | 7,690 | 20,061 | 23,785 | 184,981 | 56,145 | 181,620 | 237,765 |
| | PFHxS | 225 | 3,184 | 6,581 | 10,543 | 63,241 | 18,648 | 64,954 | 83,602 |
| | PFHpA | 65 | 4,297 | 2,666 | 8,486 | 85,439 | 18,059 | 83,652 | 101,711 |
| | PFOA | 724 | 11,316 | 23,956 | 35,861 | 259,752 | 74,091 | 260,928 | 335,019 |
| Population Served Above Baseline Threshold as a Percent of Total Population Served | PFOS | ***21.0%*** | ***28.4%*** | ***29.2%*** | ***24.6%*** | 18.9% | 19.3% | ***20.2%*** | 20.0% |
| | PFHxS | 6.9% | ***11.7%*** | ***9.6%*** | ***10.9%*** | 6.5% | 6.4% | ***7.2%*** | 7.0% |
| | PFHpA | 2.0% | ***15.9%*** | 3.9% | ***8.8%*** | ***8.7%*** | 6.2% | ***9.3%*** | 8.6% |
| | PFOA | 22.1% | ***41.8%*** | ***34.9%*** | ***37.2%*** | 26.6% | 25.5% | ***29.0%*** | 28.2% |

Abbreviations: PFHpA – Perfluoroheptanoic acid; PFHxS – Perfluorohexanesulfonic acid; PFOA – Perfluorooctanoic Acid PFOS – Perfluorooctanesulfonic Acid.

**Table M-5: Average PFAS Concentrations (ppt) by Demographic Group in the Baseline, Category 4 and 5 PWS Service Areas**

| PFAS | Race and Ethnicity | | | | | | Income | | Total Population Served |
|---|---|---|---|---|---|---|---|---|---|
| | American Indian or Alaska Native | Asian and Pacific Islander | Black | Hispanic | People of Color[a] | Non-Hispanic White | Below Twice the Poverty Level | Above Twice the Poverty Level | |
| PFOS | 0.94 | 1.97 | 1.71 | 1.93 | 1.68 | 1.37 | 1.41 | 1.43 | 1.42 |
| PFHxS | 0.25 | 0.72 | 0.41 | 0.57 | 0.49 | 0.39 | 0.38 | 0.42 | 0.41 |
| PFHpA | 0.06 | 0.61 | 0.12 | 0.36 | 0.29 | 0.27 | 0.17 | 0.31 | 0.27 |
| PFOA | 0.94 | 3.59 | 1.83 | 2.19 | 2.13 | 1.65 | 1.29 | 1.88 | 1.73 |

Abbreviations: PFHpA – perfluoroheptanoic acid; PFHxS – perfluorohexanesulfonic acid; PFOA – perfluorooctanoic acid; PFOS – perfluorooctanesulfonic acid.
Note:
[a]The demographic group people of color includes individuals who identify as Hispanic and/or a race other than White. It is calculated from EJScreen's percent minority indicator and is non-duplicative across race and ethnicity categories.

### *M.2.2 Hypothetical Regulatory Scenario #1: UCMR 5 MRLs*

Table M-6 summarizes the results for populations served by category 4 and 5 PWS service areas with PFAS occurrence above UCMR 5 MRL values. For this hypothetical regulatory scenario, EPA assumed that PWSs with PFAS system-level means above the MRL value will reduce PFAS levels to comply with the proposed rule. The first set of rows in Table M-6 summarizes population served by category 4 and 5 PWS service areas with modeled PFAS occurrence above the UCMR 5 MRLs. The second set of rows provides these estimates as a percentage of the total population served by PWS service areas included in EPA's analysis.

Percentages are bolded and italicized when the percentage of the population in a specific demographic group with PFAS occurrence above the MRL is greater than the percentage of the total population served across all demographic groups with PFAS occurrence above the MRL (right-hand column). Under this hypothetical regulatory scenario, where MCLs are assumed to be equal to UCMR 5 MRL values, these populations would be expected to experience reductions in PFAS exposure to below the hypothetical regulatory thresholds.

EPA's EJ exposure analysis shows that PFAS occurrence above the UCMR 5 MRL values is higher for Asian and Pacific Islander, Black, and Hispanic populations for particular PFAS analytes in comparison to occurrence over the MRL for the total population served across all demographic groups. Specifically, PFAS occurrence above the UCMR 5 MRL values is higher for Asian and Pacific Islander populations for all four PFAS analytes. Notably, for all PFAS analytes, occurrence above the MRL values for Asian and Pacific Islander populations are roughly two times the occurrence above the MRL values for the total population served across all demographic groups. PFAS occurrence above the UCMR 5 MRL values is higher for Hispanic populations for all four PFAS analytes. In each case, occurrence above the MRL values for Hispanic populations is more than 1% greater than PFAS occurrence for the total population served across all demographic groups. PFAS occurrence above the UCMR 5 MRL values is higher for Black populations for PFOS, PFHxS, and PFOA compared to the total population served across all demographic groups, with notable differences for PFHxS specifically. PFAS occurrence above UCMR 5 MRL values is lower for populations with income below twice the federal poverty level in comparison to PFAS occurrence for the total population served across all demographic groups.

Table M-7 presents average population-weighted PFAS reductions across demographic groups in category 4 and 5 PWSs under a hypothetical regulatory scenario where system-level means are reduced to UCMR 5 MRL values. Cells are highlighted when the average concentration for a given demographic group is higher than the average for the total population served across all demographic groups. These results suggest a very similar pattern to the findings of Table M-6. Nevertheless, Table M-7 suggests that reductions in PFOS and PFHxS are smaller for Black populations than for the total population served across all demographic groups, despite Black populations having a higher percent of potentially exposed population in category 4 and 5 PWSs.

### *M.2.3 Hypothetical Regulatory Scenario #2: 10.0 ppt*

Table M-8 summarizes the results of the population served by category 4 and 5 PWS service areas with PFAS occurrence above 10.0 ppt. For this hypothetical regulatory scenario, EPA assumed that PWSs with PFAS system-level means above 10.0 ppt will reduce PFAS levels to comply with the proposed rule. Percentages are bolded and italicized when the percentage of the population in a specific demographic group with PFAS occurrence above 10.0 ppt is greater than the percentage of the total population served across all demographic groups with PFAS occurrence above 10.0 ppt (right-hand column). Under this hypothetical regulatory scenario, where MCLs are assumed to be equal to 10.0 ppt, these populations would be expected to experience reductions in PFAS exposure to below the hypothetical regulatory thresholds.

EPA's EJ exposure analysis shows that PFAS occurrence above 10.0 ppt is higher for Asian and Pacific Islander, Hispanic, and non-Hispanic White populations for particular PFAS. Specifically, PFAS occurrence above 10.0 ppt is higher for Asian and Pacific Islander populations for PFOA and PFOS. Exceedances of 10.0 ppt for Asian and Pacific Islander populations are the highest of any demographic group, with PFOA occurrence in particular being roughly threefold the occurrence rate for the total population served across all demographic groups. PFAS occurrence above 10.0 ppt is higher for Hispanic individuals than for the total population served across all demographic groups for PFOA and PFOS. PFAS occurrence above 10.0 ppt is slightly higher for non-Hispanic White individuals than for the total population across all demographic groups for PFHxS, with a difference in occurrence of only 0.1%.PFAS occurrence above 10.0 ppt is generally somewhat lower for populations with income below twice the federal poverty level in comparison to the occurrence rate for the total population served across all demographic groups. One exception is for PFHxS occurrence for populations with income below twice the federal poverty level, which is 0.3% higher than occurrence for the total population served across all demographic groups.

Table M-9 presents average population-weighted PFAS reductions across demographic groups in category 4 and 5 PWSs under a hypothetical regulatory scenario where system-level means are reduced to 10.0 ppt. Cells are highlighted when the average concentration for a given demographic group is higher than the average for the total population served across all demographic groups. As in Table M-8, reductions in PFOA and PFOS are larger for Hispanic populations than the total population served across all demographic groups. Asian and Pacific Islander populations see the greatest reductions in PFOA of any demographic group. Notably, Table M-9 demonstrates that individuals with income below twice the poverty level have greater reductions in PFOS and PFHxS than the total population served across all demographic groups in category 4 and 5 PWSs.

**Table M-6: Hypothetical Regulatory Scenario #1: Demographic Breakdown of Population Served by Category 4 and 5 PWS Service Areas Above UCMR 5 MRL and as a Percent of Total Population Served**

| Results | Analyte | Race and Ethnicity | | | | | Income | | Population Served |
|---|---|---|---|---|---|---|---|---|---|
| | | American Indian and Alaska Native | Asian and Pacific Islander | Black | Hispanic | Non-Hispanic White | Below Twice the Poverty Level | Above Twice the Poverty Level | |
| Population Served Above UCMR 5 MRL | PFOS | 144 | 4,809 | 9,824 | 12,443 | 95,665 | 25,751 | 96,851 | 122,602 |
| | PFHxS | 120 | 2,623 | 5,731 | 7,877 | 39,317 | 12,786 | 42,843 | 55,629 |
| | PFHpA | 5 | 2,438 | 753 | 4,919 | 31,069 | 5,171 | 34,062 | 39,233 |
| | PFOA | 370 | 9,233 | 12,647 | 19,592 | 164,953 | 39,879 | 168,584 | 208,463 |
| Population Served Above UCMR 5 MRL as a Percent of Total Population Served | PFOS | 4.4% | ***17.7%*** | ***14.3%*** | ***12.9%*** | 9.8% | 8.9% | ***10.8%*** | 10.3% |
| | PFHxS | 3.7% | ***9.7%*** | ***8.3%*** | ***8.2%*** | 4.0% | 4.4% | ***4.8%*** | 4.7% |
| | PFHpA | 0.2% | ***9.0%*** | 1.1% | ***5.1%*** | 3.2% | 1.8% | ***3.8%*** | 3.3% |
| | PFOA | 11.3% | ***34.1%*** | ***18.4%*** | ***20.3%*** | 16.9% | 13.7% | ***18.8%*** | 17.5% |

Abbreviations: PFHpA – Perfluoroheptanoic acid; PFHxS – Perfluorohexanesulfonic acid; PFOA – Perfluorooctanoic Acid PFOS – Perfluorooctanesulfonic Acid.

**Table M-7: Reductions in Average PFAS Concentrations (ppt) by Demographic Group in a Hypothetical Regulatory Scenario with Maximum Contaminant Level at the UCMR 5 MRLs, Category 4 and 5 PWS Service Areas**

| PFAS | Race and Ethnicity | | | | | | Income | | Total Population Served |
|---|---|---|---|---|---|---|---|---|---|
| | American Indian or Alaska Native | Asian and Pacific Islander | Black | Hispanic | People of Color[a] | White, Non-Hispanic | Below Twice the Poverty Level | Above Twice the Poverty Level | |
| PFOS | 0.30 | 0.90 | 0.65 | 1.00 | 0.75 | 0.68 | 0.72 | 0.68 | 0.69 |
| PFHxS | 0.05 | 0.32 | 0.10 | 0.22 | 0.18 | 0.17 | 0.17 | 0.17 | 0.17 |
| PFHpA | 0.00 | 0.20 | 0.02 | 0.11 | 0.08 | 0.07 | 0.04 | 0.08 | 0.07 |
| PFOA | 0.26 | 1.97 | 0.63 | 0.97 | 0.92 | 0.76 | 0.48 | 0.89 | 0.79 |

Abbreviations: PFHpA – perfluoroheptanoic acid; PFHxS – perfluorohexanesulfonic acid; PFOA – perfluorooctanoic acid; PFOS – perfluorooctanesulfonic acid.
Note:
[a]The demographic group people of color includes individuals who identify as Hispanic and/or a race other than White. It is calculated from EJSCREEN's percent minority indicator and is non-duplicative across race and ethnicity categories.

**Table M-8: Hypothetical Regulatory Scenario #2: Demographic Breakdown of Population Served by Category 4 and 5 PWS Service Areas Above 10.0 ppt and as a Percent of Total Population Served**

| Results | Analyte | Race and Ethnicity | | | | | Income | | Population Served |
|---|---|---|---|---|---|---|---|---|---|
| | | American Indian and Alaska Native | Asian and Pacific Islander | Black | Hispanic | Non-Hispanic White | Below Twice the Poverty Level | Above Twice the Poverty Level | |
| Population Served Above 10.0 ppt | PFOS | 13 | 1,229 | 1,008 | 3,690 | 28,318 | 6,444 | 27,841 | 34,285 |
| | PFHxS | 6 | 29 | 251 | 223 | 5,870 | 2,400 | 4,008 | 6,408 |
| | PFHpA | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | PFOA | 26 | 3,145 | 935 | 4,838 | 41,674 | 5,658 | 45,205 | 50,863 |
| Population Served Above 10.0 ppt as a Percent of Total Population Served | PFOS | 0.4% | ***4.5%*** | 1.5% | ***3.8%*** | 2.9% | 2.2% | ***3.1%*** | 2.9% |
| | PFHxS | 0.2% | 0.1% | 0.4% | 0.2% | ***0.6%*** | ***0.8%*** | 0.4% | 0.5% |
| | PFHpA | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| | PFOA | 0.8% | ***11.6%*** | 1.4% | ***5.0%*** | 4.3% | 1.9% | ***5.0%*** | 4.3% |

Abbreviations: PFHpA – Perfluoroheptanoic acid; PFHxS – Perfluorohexanesulfonic acid; PFOA – Perfluorooctanoic Acid PFOS – Perfluorooctanesulfonic Acid.

**Table M-9: Reductions in Average PFAS Concentrations (ppt) by Demographic Group in a Hypothetical Regulatory Scenario with Maximum Contaminant Level at 10.0 ppt, Category 4 and 5 PWS Service Areas**

| PFAS | Race and Ethnicity | | | | | | Income | | Total Population Served |
|---|---|---|---|---|---|---|---|---|---|
| | American Indian or Alaska Native | Asian and Pacific Islander | Black | Hispanic | People of Color[a] | White, Non-Hispanic | Below Twice the Poverty Level | Above Twice the Poverty Level | |
| PFOS | 0.21 | 0.34 | 0.26 | 0.55 | 0.35 | 0.34 | 0.42 | 0.31 | 0.34 |
| PFHxS | 0.01 | 0.01 | 0.02 | 0.02 | 0.02 | 0.04 | 0.05 | 0.03 | 0.04 |
| PFHpA | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| PFOA | 0.01 | 0.71 | 0.09 | 0.35 | 0.28 | 0.26 | 0.12 | 0.31 | 0.26 |

Abbreviations: PFHpA – perfluoroheptanoic acid; PFHxS – perfluorohexanesulfonic acid; PFOA – perfluorooctanoic acid; PFOS – perfluorooctanesulfonic acid.
Note:
[a]The demographic group people of color includes individuals who identify as Hispanic and/or a race other than White. It is calculated from EJScreen's percent minority indicator and is non-duplicative across race and ethnicity categories.

# Appendix N. Supplemental Cost Analyses

Section N.1 discusses the approach EPA used to estimate the costs of the rule for PWSs serving more than 1 million people. Section N.2 discusses the potential impact on national costs if PWSs must dispose of treatment residuals as hazardous waste. Section N.3 explores the potential impact of limited PFAS occurrence data on national cost estimates.

## N.1 Cost Analysis for Very Large Systems

EPA identified 25 PWS that serve more than one million people based on retail population estimates in SDWIS/Fed. All of these systems are CWS with multiple entry points; most are surface water systems (see Table N-1).

**Table N-1: Characteristics of PWSs Serving a Retail Population Greater than One Million**

| PWSID | Name | SDWIS/Fed Retail Population | Water Source | Entry Points |
|---|---|---|---|---|
| AZ0407025 | Phoenix, City Of | 1,579,000 | SW | 20 |
| CA0110005 | East Bay Municipal Utility District | 1,405,000 | SW | 5 |
| CA1910067 | Los Angeles-City, Dept. Of Water & Power | 4,041,284 | SW | 11 |
| CA3710020 | San Diego - City Of | 1,394,515 | SW | 3 |
| CA4310011 | San Jose Water | 1,007,514 | SW | 3 |
| CO0116001 | Denver Water Board | 1,362,071 | SW | 3 |
| FL4130871 | Miami-Dade Water and Sewer Department - Main System | 2,300,000 | GW | 3 |
| GA1210001 | Atlanta | 1,089,893 | SW | 2 |
| IL0316000 | Chicago | 2,700,000 | SW | 2 |
| MA6000000 | Massachusetts Water Resources Authority | 2,550,000 | SW | 2 |
| MD0150005 | Washington Suburban Sanitary Commission | 1,800,000 | SW | 2 |
| MD0300002 | Baltimore City | 1,600,000 | SW | 3 |
| MO6010716 | Missouri American St Louis County St Charles County | 1,100,000 | SW | 4 |
| NC0160010 | Charlotte Water | 1,093,901 | SW | 2 |
| NV0000090 | Las Vegas Valley Water District | 1,502,604 | SW | 10 |
| NY5110526 | Suffolk County Water Authority | 1,100,000 | GW | 236 |
| NY7003493 | New York City System | 8,271,000 | SW | 4 |
| OH1801212 | Cleveland Public Water System | 1,308,955 | SW | 4 |
| OH2504412 | Columbus Public Water System | 1,233,879 | SW | 3 |
| PA1510001 | Philadelphia Water Department | 1,600,000 | SW | 3 |
| TX0150018 | San Antonio Water System | 1,999,472 | SW | 38 |
| TX0570004 | Dallas Water Utility | 1,286,380 | SW | 3 |
| TX1010013 | City of Houston | 2,221,706 | SW | 41 |
| TX2270001 | City of Austin Water & Wastewater | 1,044,405 | SW | 3 |
| VA6059501 | Fairfax County Water Authority | 1,074,422 | SW | 2 |

Abbreviations: GW – ground water; PWS – public water system; SDWIS/Fed – Safe Drinking Water Information System Federal Data Warehouse; SW – surface water.

Rather than model treatment costs using the PFAS occurrence values simulated from the MCMC model, EPA reviewed UCMR3 data and recent system consumer confidence reports to obtain entry point PFAS values. EPA used these values to determine which entry points at these systems exceed the MCLs and/or HI for the proposed rule and alternative options.

PFOA and PFOS levels at multiple entry points for two systems exceeded one or more MCLs for the proposed option and alternative options (no HI exceedances occurred). EPA used these reported PFAS values as the baseline occurrence estimates for the cost analysis. EPA applied the cost estimating methods described in Chapter 5 to these systems to derive point estimate of the costs to meet each MCL. EPA also estimated the corresponding affected entry point service population.

System 1 has multiple entry points with existing GAC treatment. EPA determined that meeting PFAS MCLs would reduce GAC bed life, thereby increasing O&M costs associated with more frequent media change-outs and disposal. To estimate service population and average flow rates at these entry points, EPA divided total system population by the number of entry points. This is the same assumption made for all systems serving less than one million and, therefore, introduces the same type of uncertainty to the cost analysis.

System 2 also has multiple entry points that would need to be treated to meet the proposed rule and alternatives. Because source water quality makes GAC infeasible and the high entry point flow rates result in impractical quantities of IX pressure vessels, EPA assumed that the system would install RO processes and estimated the removal rates and blending rates, which vary with baseline PFAS levels across entry points and reduction targets across regulatory options. EPA obtained the design and average flows data for the existing treatment plants. Based on relative average flow rates, EPA proportionately allocated the system service population across the entry points (e.g., allocating 25% of system population to an entry point accounting for 25% of total system average flow).

## N.2 Hazardous Waste Disposal Cost Impacts

The national cost analysis reflects the assumption that PFAS-contaminated wastes are not considered hazardous wastes. As a general matter, EPA notes that such wastes are not currently regulated under federal law as a hazardous waste. To address stakeholder concerns, including those raised during the SBREFA process, EPA conducted a sensitivity analysis with an assumption of hazardous waste disposal for illustrative purposes only. As part of this analysis, EPA generated a second full set of unit cost curves that are identical to the curves used for the national cost analysis with the exception that spent GAC and spent IX resin are considered hazardous. EPA acknowledges that if federal authorities later determine that PFAS-contaminated wastes require handling as hazardous wastes, the residuals management costs are expected to be higher.

For GAC, the national cost analysis assumes the spent media is reactivated off-site under current RCRA non-hazardous waste regulations. Under this scenario, the WBS model uses a unit cost for reactivation that includes transportation to the reactivation facility and back to the treatment plant. To account for losses in the reactivation and replacement process, it also adds the cost of replacing 30 percent of the spent GAC with virgin media. The hazardous waste sensitivity analysis assumes spent GAC is disposed off-site as a hazardous waste in a RCRA Subtitle C landfills and replaced with virgin GAC (i.e., single use operation). Under this scenario, the WBS model incorporates the cost of hazardous waste disposal, transportation to a hazardous waste facility 200 miles away, a minimum charge per hazardous waste shipment, and replacement of 100 percent of the spent GAC with virgin media. This scenario provides an upper bound on other options that might emerge under future air quality regulations that prevent reactivation of PFAS-

contaminated GAC (i.e., spent GAC must be disposed off-site as a non-hazardous waste and replaced with virgin GAC) or RCRA hazardous waste regulations (i.e., off-site reactivation remains feasible, but process wastes require hazardous waste disposal).

For IX, the national cost analysis assumes the spent resin is incinerated off-site under current RCRA non-hazardous waste regulations. Under this scenario, the WBS model uses a unit cost for non-hazardous incineration that includes transportation to the incineration facility. The hazardous waste sensitivity analysis assumes spent resin is incinerated off-site as a hazardous waste and replaced with virgin resin. Under this scenario, the WBS model incorporates the cost of hazardous waste incineration, transportation to a hazardous waste facility 200 miles away, and a minimum charge per hazardous waste shipment. Both scenarios incorporate the cost of replacing the spent resin with virgin resin. Because hazardous waste incineration costs more than disposal of spent resin in a hazardous waste landfill this hazardous waste scenario provides an upper bound on other options that might emerge under future air quality regulations (e.g., off-site disposal in a non-hazardous waste landfill) or RCRA hazardous waste regulations (e.g., off-site disposal in a hazardous waste landfill).

The potential impact on PWS treatment costs is shown in Table N-2 for the proposed option. At a 3 percent discount rate, the annualized cost would be $30M higher (4%) higher if hazardous waste disposal is required. At a 7 percent discount rate, PWS treatment costs would be $61 million (6%) higher if hazardous waste disposal is required. Note that these estimated costs do not include the costs associated with the storage, transportation and underground injection of the brine concentrate residuals from the RO/NF process that could possibly be required under a PFAS hazardous waste scenario.

**Table N-2: Annualized PWS Treatment Cost Associated with Non-Hazardous and Hazardous Residual Management Requirements, Proposed Option (PFOA and PFOS MCLs of 4.0 ppt and HI of 1.0) (Million $2021)**

| | 3% Discount Rate | | | 7% Discount Rate | | |
|---|---|---|---|---|---|---|
| | **5th Percentile** | **Mean** | **95th Percentile** | **5th Percentile** | **Mean** | **95th Percentile** |
| Non-Hazardous Disposal | $619 | $673 | $741 | $1,012 | $1,101 | $1,206 |
| Hazardous Disposal | $661 | $703 | $769 | $1,092 | $1,162 | $1,262 |
| **Increase due to Hazardous Disposal** | | $30 | | | $61 | |

Note: Percentiles cannot be subtracted.

## N.3 Incremental Treatment Cost of Other PFAS

To illustrate the potential incremental costs for removing PFAS compounds for which national occurrence data are not available, EPA used a model system approach. Table N-3 shows the characteristics (population served, number of entry points, and resulting design and average flows) of the ground water model systems in each of seven size categories. Table N-4 shows the same characteristics used to simulate surface water system costs. Surface water systems tend to have fewer entry points and, therefore, higher entry point flow rates and treatment costs.

**Table N-3: Model System Characteristics for Ground Water Systems**

| Parameter | | System Size Category (Population Served) | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | **25-500** | **501-3,300** | **3,301-10,000** | **10,001-50,000** | **50,001-100,000** | **100,001-500,000** | **>500,000** |
| System Population[a] | A | 110 | 1,140 | 5,476 | 18,660 | 66,549 | 163,947 | 826,664 |
| System Design Flow[b] (MGD) | B | 0.049 | 0458 | 2.051 | 6.617 | 22.296 | 56.683 | 314.128 |
| System Average Flow[b] (MGD) | C | 0.012 | 0.147 | 0.776 | 2.841 | 10.914 | 28.342 | 157.064 |
| Entry Points[c] | D | 1 | 2 | 2 | 4 | 10 | 12 | 39 |
| Entry Point Design Flow (MGD) | E = B/D | 0.049 | 0.229 | 1.025 | 1.654 | 2.230 | 4.724 | 8.055 |
| Entry Point Average Flow (MGD) | F = C/D | 0.012 | 0.074 | 0.388 | 0.710 | 1.091 | 2.362 | 4.027 |

Abbreviations: MGD – million gallons per day.
Notes:
[a] Median system populations are from USEPA Safe Drinking Water Information System Federal (SDWIS/Fed) fourth quarter 2021 "frozen" dataset that contains information reported through January 14, 2022.
[b] Flow estimates are based on regression equations that relate population and design or average flows, derived in U.S. EPA (2000b).
[c] Entry point data from 2006 Community Water System Survey (U.S. EPA, 2009), Table 13, values rounded to nearest whole number.

**Table N-4: Model System Characteristics for Surface Water Systems**

| Parameter | | System Size Category (Population Served) | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | 25-500 | 501-3,300 | 3,301-10,000 | 10,001-50,000 | 50,001-100,000 | 100,001-500,000 | >500,000 |
| System Population[a] | A | 110 | 1,140 | 5,476 | 18,660 | 66,549 | 163,947 | 826,664 |
| System Design Flow[b] (MGD) | B | 0.050 | 0.459 | 2.026 | 6.459 | 21.500 | 50.438 | 232.945 |
| System Average Flow[b] (MGD) | C | 0.015 | 0.156 | 0.748 | 2.538 | 9.017 | 22.155 | 111.175 |
| Entry Points[c] | D | 1 | 1 | 1 | 1 | 2 | 2 | 4 |
| Entry Point Design Flow (MGD) | E = B/D | 0.050 | 0.459 | 2.026 | 6.459 | 10.750 | 25.219 | 58.236 |
| Entry Point Average Flow (MGD) | F = C/D | 0.015 | 0.156 | 0.748 | 2.538 | 4.509 | 11.077 | 27.794 |

Abbreviations: MGD – million gallons per day.
Notes:
[a]Median system populations are from USEPA Safe Drinking Water Information System Federal (SDWIS/Fed) fourth quarter 2021 "frozen" dataset that contains information reported through January 14, 2022.
[b]Flow estimates are based on regression equations that relate population and design or average flows, derived in U.S. EPA (2000b).
[c]Entry point data from 2006 Community Water System Survey (U.S. EPA, 2009), Table 13, values rounded to nearest whole number.

Given these characteristics, EPA considered three types of systems:

- **Baseline System**: this model system has occurrence of all three potentially regulated PFAS included in the national analysis (PFOA, PFOS, and PFHxS). It reflects the costs that are covered in the national analysis and provides a basis for comparison.

- **System Type 1**: this model system has no detections of PFOA, PFOS, or PFHxS. However, it has occurrence of all the other PFAS included in the HI (HFPO-DA, PFBS, and PFNA). EPA considered two scenarios for this system type: high occurrence of the three PFAS and medium occurrence of the three PFAS. This system type represents additional systems that are not currently captured in the national costs but would incur treatment costs under the HI.

- **System Type 2**: this model system has occurrence of PFOA, PFOS, and PFHxS identical to the baseline system. It also has occurrence of all the other PFAS included in the HI (HFPO-DA, PFBS, and PFNA). Like System Type 1, EPA considered two scenarios: high occurrence of the three other PFAS and medium occurrence of those PFAS. This system type illustrates a range of potential incremental treatment costs for systems that are already treating to remove PFOA, PFOS, and/or PFHxS in the national cost analysis.

Table N-5 shows the occurrence assumptions for each system type. Concentrations for PFOA, PFOS, and PFHxS correspond to the median for each contaminant from the UCMR3 data, considering detected values only. Concentrations for the other PFAS are 95th percentile and median values based on EPA's analysis of state-level occurrence data.

**Table N-5: PFAS Occurrence Assumptions for Model System Analysis (ppt)**

| PFAS Compound | Baseline System[a] | System Type 1[a] | | System Type 2[a] | |
|---|---|---|---|---|---|
| | | High | Medium | High | Medium |
| PFOA | 30 | 0 | 0 | 30 | 30 |
| PFOS | 60 | 0 | 0 | 60 | 60 |
| PFHxS | 73 | 0 | 0 | 73 | 73 |
| HFPO-DA | 0 | 29.65 | 12.6 | 29.65 | 12.6 |
| PFBS | 0 | 25.285 | 5.2 | 25.285 | 5.2 |
| PFNA | 0 | 56.4 | 8.5 | 56.4 | 8.5 |

Abbreviations: HFPO-DA – Hexafluoropropylene oxide dimer acid; PFAS – Per- and polyfluoroalkyl substances; PFBS – Perfluorobutanesulfonic acid; PFHxS – Perfluorohexanesulfonic acid; PFNA - Perfluorononanoic acid; PFOA – Perfluorooctanoic Acid PFOS – Perfluorooctanesulfonic Acid.
Notes:
[a]Values of zero indicate no detection of that PFAS.

Given these occurrence assumptions and basic characteristics, EPA estimated a range of costs for model systems in each size category for each of the three treatment technologies (GAC, IX, and RO/NF). The range of costs reflects all combinations of two source waters (ground and surface) and two cost levels (low and high). For GAC and IX, the range of costs also incorporates two bed life scenarios corresponding to a range of influent water quality, as discussed below.

For GAC, the lower end of the cost range reflects a bed life corresponding to an influent TOC of 0.5 mg/L, which is a typical detection limit for TOC. The upper end of the range corresponds to an influent TOC of 2 mg/L, which is approximately the median for surface water systems and the 85th percentile for ground water systems. Beyond 2 mg/L influent TOC, GAC bed life may make GAC usage less practical, based on the linear equations from U.S. EPA (2023d). However, the maximum influent TOC value of 2 mg/L used in this analysis should not be regarded as a strict limit on the practicality of GAC. The bed life equations are based on pooled data from a limited number of studies and reflect central tendency results under varying water quality conditions. They should not be used in lieu of site-specific engineering analyses or pilot studies to estimate bed life or treatment costs for specific individual treatment systems. Individual systems might achieve longer GAC bed lives and lower treatment costs at higher influent TOC concentrations, particularly if their influent concentrations of PFAS are lower than the values assumed in this analysis.

For IX, the lower end of the cost range reflects a bed life corresponding to a total influent PFAS concentration that is the sum of the initial influent concentrations of the regulated PFAS shown in Table N-5 (i.e., the lower bound assumes that no other PFAS compounds are present). The upper end of the range assumes additional PFAS compounds are present such that total influent PFAS is approximately 7,000 ppt. Data are not available to estimate bed life for higher influent concentrations using the linear equations from U.S. EPA (2023d). IX costs are uncertain beyond this value, but it should not be regarded as a strict limit on the feasibility of the technology.

Sources of uncertainty in this analysis include the following:

- EPA does not have sufficient quantitative data to include PFNA in the linear equations used to estimate bed life for GAC and IX. For GAC, EPA assumes the bed life for these PFAS is the same as PFOS. For IX, EPA assumes the bed life is the same as PFOA. Given the chain length of PFNA, these assumptions likely underestimate the actual bed life and err on the side of higher costs for GAC and IX for model systems type 1 and 2.

- EPA does not have sufficient quantitative data to include HFPO-DA in the bed life estimates for IX. The IX costs for model system types 1 and 2 do not account for occurrence of HFPO-DA and, therefore, are underestimates.

Table N-6 shows the results for baseline model systems. The costs shown are in $1,000's per year ($2020) and reflect total capital costs annualized over the useful life of the technology utilizing a 7 percent cost of capital rate[57], plus annual O&M costs. The cost estimates for baseline systems form the basis of comparison for the other model systems. Given the PFAS concentrations shown in Table N-5, the baseline GAC costs are controlled by the removal requirements for PFHxS, IX costs are controlled by removal of PFOA, and RO/NF costs are controlled by removal of PFOS.

**Table N-6: Annualized Costs for Baseline Systems ($1,000's per year)**

| System Size (Population Served) | GAC | IX | RO/NF |
|---|---|---|---|
| 25-500 | $17 to $31 | $16 to $28 | $161 to $203 |
| 501-3,300 | $62 to $142 | $58 to $103 | $273 to $526 |
| 3,301-10,000 | $293 to $680 | $254 to $457 | $705 to $999 |
| 10,001-50,000 | $656 to $1,828 | $665 to $1,285 | $1,667 to $2,816 |
| 50,001-100,000 | $2,026 to $5,773 | $2,188 to $4,175 | $4,855 to $9,070 |
| 100,001-500,000 | $3,902 to $12,266 | $4,874 to $9,134 | $9,555 to $17,873 |
| >500,000 | $16,070 to $62,515 | $22,817 to $46,556 | $40,655 to $82,519 |

Abbreviations: GAC – granular activated carbon; IX – ion exchange; RO/NF – reverse osmosis/nanofiltration.

Table N-7 and Table N-8 show results for the type 1 model systems with high and medium occurrence, respectively. These results reflect potential costs at additional systems triggered into treatment and not captured in the national analysis of treatment costs. Overall, type 1 systems have estimated costs ranging from 0.70 to 1.77 times baseline system costs. These results vary by occurrence scenario and by technology, as discussed below.

Type 1 systems with high occurrence have estimated costs slightly lower to somewhat higher than systems captured in the national analysis (0.92 to 1.77 times baseline). These results vary by technology as follows:

[57] The 7 percent cost of capital represents the cost to systems for debt service associated with expenditures on capital equipment for treatment and is used in the annualization of engineering capital cost over the useful life of the technology. Note the use of 7 percent in this case is distinct from the 7 and 3 percent values used to adjust all national level costs and benefits to account for the differential timing of compliance costs and resultant benefit impacts.

- For GAC, removal of the other HI compounds results in a shorter bed life than required to remove PFHxS in the baseline scenario, with correspondingly higher costs. The impact of the shorter bed life increases with increasing system size, resulting in costs from 1.00 to 1.77 times baseline.

- For IX, removal of the other HI compounds results in a bed life that is not substantially different from that required to remove PFOA in the baseline scenario. As discussed in the body of this document, the WBS cost curves for IX differentiate at 20,000 bed volume increments. The difference in estimated bed life between baseline and type 1 systems with high occurrence is less than this increment, so cost results are coincidentally identical (1.00 times baseline). As discussed above, however, the IX costs in Table N-7 do not account for occurrence of HFPO-DA and, therefore, are underestimates.

- For RO/NF, the removal efficiency required for the other HI compounds is slightly lower than that required to remove PFOS in the baseline scenario. Correspondingly, costs are also slightly lower (0.92 to 1.00 times baseline).

Type 1 systems with medium occurrence have estimated costs that are the same as or somewhat lower than systems captured in the national analysis (0.70 to 1.00 times baseline). GAC costs are very similar (0.99 to 1.00 times baseline). Estimated costs for IX and RO/NF are lower than baseline (0.77 to 0.96 for IX, 0.70 to 0.98 for RO/NF). As discussed above, however, the IX costs in Table N-7 do not account for occurrence of HFPO-DA and, therefore, are underestimates.

**Table N-7: Results for Type 1 Systems for High PFAS Occurrence**

| System Size (Population Served) | GAC | IX | RO/NF |
|---|---|---|---|
| | **Annualized Cost ($1,000's per year)** | | |
| 25-500 | $17 to $38 | $16 to $28 | $161 to $202 |
| 501-3,300 | $63 to $201 | $58 to $103 | $269 to $521 |
| 3,301-10,000 | $296 to $902 | $254 to $457 | $682 to $920 |
| 10,001-50,000 | $666 to $2,703 | $665 to $1,285 | $1,622 to $2,740 |
| 50,001-100,000 | $2,063 to $9,195 | $2,188 to $4,175 | $4,714 to $8,819 |
| 100,001-500,000 | $3,995 to $21,084 | $4,874 to $9,134 | $9,229 to $17,396 |
| >500,000 | $16,539 to $110,936 | $22,817 to $46,556 | $39,203 to $80,018 |
| | **Ratio to Corresponding Baseline Cost** | | |
| 25-500 | 1.00 to 1.23 | 1.00 | 0.99 to 1.00 |
| 501-3,300 | 1.02 to 1.41 | 1.00 | 0.98 to 0.99 |
| 3,301-10,000 | 1.01 to 1.33 | 1.00 | 0.92 to 0.97 |
| 10,001-50,000 | 1.01 to 1.48 | 1.00 | 0.97 |
| 50,001-100,000 | 1.02 to 1.59 | 1.00 | 0.97 |
| 100,001-500,000 | 1.02 to 1.72 | 1.00 | 0.97 |
| >500,000 | 1.03 to 1.77 | 1.00 | 0.96 to 0.97 |

Abbreviations: GAC – granular activated carbon; IX – ion exchange; RO/NF – reverse osmosis/nanofiltration.

**Table N-8: Results for Type 1 Systems for Medium PFAS Occurrence**

| System Size (Population Served) | GAC | IX | RO/NF |
|---|---|---|---|
| | **Annualized Cost ($1,000's per year)** | | |
| 25-500 | $17 to $31 | $16 to $27 | $158 to $197 |
| 501-3,300 | $62 to $142 | $51 to $93 | $235 to $478 |
| 3,301-10,000 | $291 to $680 | $219 to $403 | $508 to $764 |
| 10,001-50,000 | $653 to $1,828 | $545 to $1,095 | $1,260 to $2,172 |
| 50,001-100,000 | $2,012 to $5,773 | $1,763 to $3,457 | $3,634 to $6,904 |
| 100,001-500,000 | $3,865 to $12,266 | $3,829 to $7,275 | $6,837 to $13,638 |
| >500,000 | $15,880 to $62,515 | $17,567 to $36,085 | $28,432 to $62,378 |
| | **Ratio to Corresponding Baseline Cost** | | |
| 25-500 | 1.00 | 0.96 | 0.97 to 0.98 |
| 501-3,300 | 0.99 to 1.00 | 0.87 to 0.91 | 0.86 to 0.91 |
| 3,301-10,000 | 0.99 to 1.00 | 0.86 to 0.88 | 0.72 to 0.76 |
| 10,001-50,000 | 0.99 to 1.00 | 0.82 to 0.85 | 0.76 to 0.77 |
| 50,001-100,000 | 0.99 to 1.00 | 0.81 to 0.83 | 0.75 to 0.76 |
| 100,001-500,000 | 0.99 to 1.00 | 0.79 to 0.80 | 0.72 to 0.76 |
| >500,000 | 0.99 to 1.00 | 0.77 to 0.78 | 0.70 to 0.76 |

Abbreviations: GAC – granular activated carbon; IX – ion exchange; RO/NF – reverse osmosis/nanofiltration.

Table N-9 and Table N-10 show results for type 2 model systems with high and medium occurrence, respectively. Comparing these costs to those in the baseline system costs in Table N-6 shows the potential additional costs at systems incurring treatment costs under the national analysis if additional PFAS occurrence data were available. Overall, the need to remove the other HI compounds could increase treatment costs by 0 to 77 percent on a per-system basis. These results vary by occurrence scenario and by technology, as discussed below.

For type 2 systems with high occurrence using GAC, treatment costs could increase by 0 to 77 percent. At the upper bound of the cost range, the high TOC influent combined with the need to remove the other HI compounds (particularly HFPO-DA) results in a shorter bed life. The impact of the shorter bed life on costs increases with increasing system size (23 to 77 percent increase in costs). At the lower bound of the cost range, the change in bed life is less significant with respect to other capital and operating costs, so the percent increase in cost is small (0 to 3 percent). For type 2 systems with medium occurrence, the change in GAC bed life is small, resulting in a relatively small increase in cost (0 to 9 percent).

For type 2 systems using IX in both occurrence scenarios, there is no increase in treatment cost. IX performance and cost remain controlled by removal of PFOA. As discussed above, however, the IX costs in Table N-9 and Table N-10 do not account for occurrence of HFPO-DA and, therefore, are underestimates. HFPO-DA removal could result in increased cost over baseline for type 2 systems.

For type 2 systems with high occurrence using RO/NF, the increase in removal efficiency needed to remove the other HI compounds is very small. The resulting increase in cost rounds to 0 percent (i.e., it is less than 0.5 percent). For type 2 systems with medium occurrence, RO/NF performance and cost remain controlled by PFOS, so there is no increase in treatment cost.

**Table N-9: Results for Type 2 Systems for High PFAS Occurrence**

| System Size (Population Served) | GAC | IX | RO/NF |
|---|---|---|---|
| | **Annualized Cost ($1,000's per year)** | | |
| 25-500 | $17 to $38 | $16 to $28 | $161 to $203 |
| 501-3,300 | $63 to $201 | $58 to $103 | $274 to $527 |
| 3,301-10,000 | $296 to $902 | $254 to $457 | $707 to $1,001 |
| 10,001-50,000 | $666 to $2,703 | $665 to $1,285 | $1,671 to $2,822 |
| 50,001-100,000 | $2,063 to $9,195 | $2,188 to $4,175 | $4,867 to $9,091 |
| 100,001-500,000 | $3,995 to $21,084 | $4,874 to $9,134 | $9,582 to $17,913 |
| >500,000 | $16,539 to $110,936 | $22,817 to $46,556 | $40,777 to $82,733 |
| | **Percent Increase from Baseline Cost** | | |
| 25-500 | 0% to 23% | 0% | 0% |
| 501-3,300 | 2% to 41% | 0% | 0% |
| 3,301-10,000 | 1% to 33% | 0% | 0% |
| 10,001-50,000 | 1% to 48% | 0% | 0% |
| 50,001-100,000 | 2% to 59% | 0% | 0% |
| 100,001-500,000 | 2% to 72% | 0% | 0% |
| >500,000 | 3% to 77% | 0% | 0% |

Abbreviations: GAC – granular activated carbon; IX – ion exchange; RO/NF – reverse osmosis/nanofiltration.

**Table N-10: Results for Type 2 Systems for Medium PFAS Occurrence**

| System Size (Population Served) | GAC | IX | RO/NF |
|---|---|---|---|
| | **Annualized Cost ($1,000's per year)** | | |
| 25-500 | $17 to $32 | $16 to $28 | $161 to $203 |
| 501-3,300 | $63 to $149 | $58 to $103 | $273 to $526 |
| 3,301-10,000 | $294 to $711 | $254 to $457 | $705 to $999 |
| 10,001-50,000 | $661 to $1,921 | $665 to $1,285 | $1,667 to $2,816 |
| 50,001-100,000 | $2,043 to $6,114 | $2,188 to $4,175 | $4,855 to $9,070 |
| 100,001-500,000 | $3,945 to $13,213 | $4,874 to $9,134 | $9,555 to $17,873 |
| >500,000 | $16,288 to $67,984 | $22,817 to $46,556 | $40,655 to $82,519 |
| | **Percent Increase from Baseline Cost** | | |
| 25-500 | 0% to 3% | 0% | 0% |
| 501-3,300 | 1% to 5% | 0% | 0% |
| 3,301-10,000 | 1% to 5% | 0% | 0% |
| 10,001-50,000 | 1% to 5% | 0% | 0% |
| 50,001-100,000 | 1% to 6% | 0% | 0% |
| 100,001-500,000 | 1% to 8% | 0% | 0% |
| >500,000 | 1% to 9% | 0% | 0% |

Abbreviations: GAC – granular activated carbon; IX – ion exchange; RO/NF – reverse osmosis/nanofiltration.

# Appendix O. Appendix References

Agency for Healthcare Research and Quality. (2011). *MEPS HC-128: 2009 Medical Conditions File. Medical Expenditure Panel Survey.* Retrieved from: https://www.meps.ahrq.gov/mepsweb/data_stats/download_data_files_detail.jsp?cboPufNumber=HC-128

Agency for Healthcare Research and Quality. (2012a). *MEPS HC-137: 2010 Medical Conditions File. Medical Expenditure Panel Survey.* Retrieved from: https://www.meps.ahrq.gov/mepsweb/data_stats/download_data_files_detail.jsp?cboPufNumber=HC-137

Agency for Healthcare Research and Quality. (2012b). *MEPS HC-139: Panel 14 Longitudinal Data File. Medical Expenditure Panel Survey.* Retrieved from: https://www.meps.ahrq.gov/mepsweb/data_stats/download_data_files_detail.jsp?cboPufNumber=HC-139

Agency for Healthcare Research and Quality. (2013a). *MEPS HC-146: 2011 Medical Conditions File. Medical Expenditure Panel Survey.* Retrieved from: https://www.meps.ahrq.gov/mepsweb/data_stats/download_data_files_detail.jsp?cboPufNumber=HC-146

Agency for Healthcare Research and Quality. (2013b). *MEPS HC-148: Panel 15 Longitudinal Data File. Medical Expenditure Panel Survey.* Retrieved from: https://www.meps.ahrq.gov/mepsweb/data_stats/download_data_files_detail.jsp?cboPufNumber=HC-148

Agency for Healthcare Research and Quality. (2014a). *MEPS HC-154: 2012 Medical Conditions File. Medical Expenditure Panel Survey.* Retrieved from: https://www.meps.ahrq.gov/mepsweb/data_stats/download_data_files_detail.jsp?cboPufNumber=HC-154

Agency for Healthcare Research and Quality. (2014b). *MEPS HC-156: Panel 16 Longitudinal Data File. Medical Expenditure Panel Survey.* Retrieved from: https://www.meps.ahrq.gov/mepsweb/data_stats/download_data_files_detail.jsp?cboPufNumber=HC-156

Agency for Healthcare Research and Quality. (2015a). *MEPS HC-162: 2013 Medical Conditions File. Medical Expenditure Panel Survey.* Retrieved from: https://www.meps.ahrq.gov/mepsweb/data_stats/download_data_files_detail.jsp?cboPufNumber=HC-162

Agency for Healthcare Research and Quality. (2015b). *MEPS HC-164: Panel 17 Longitudinal Data File. Medical Expenditure Panel Survey.* Retrieved from: https://www.meps.ahrq.gov/mepsweb/data_stats/download_data_files_detail.jsp?cboPufNumber=HC-164

Agency for Healthcare Research and Quality. (2016a). *MEPS HC-170: 2014 Medical Conditions File. Medical Expenditure Panel Survey.* Retrieved from: https://www.meps.ahrq.gov/mepsweb/data_stats/download_data_files_detail.jsp?cboPufNumber=HC-170

Agency for Healthcare Research and Quality. (2016b). *MEPS HC-172: Panel 18 Longitudinal Data File. Medical Expenditure Panel Survey.* Retrieved from: https://www.meps.ahrq.gov/mepsweb/data_stats/download_data_files_detail.jsp?cboPufNumber=HC-172

Agency for Healthcare Research and Quality. (2017a). *Healthcare Cost and Utilization Project*. Retrieved from: https://hcupnet.ahrq.gov

Agency for Healthcare Research and Quality. (2017b). *MEPS HC-180: 2015 Medical Conditions File. Medical Expenditure Panel Survey.* Retrieved from: https://www.meps.ahrq.gov/mepsweb/data_stats/download_data_files_detail.jsp?cboPufNumber=HC-180

Agency for Healthcare Research and Quality. (2017c). *MEPS HC-183: Panel 19 Longitudinal Data File. Medical Expenditure Panel Survey.* Retrieved from: https://www.meps.ahrq.gov/mepsweb/data_stats/download_data_files_detail.jsp?cboPufNumber=HC-183

Agency for Healthcare Research and Quality. (2018). *MEPS HC-193: Panel 20 Longitudinal Data File. Medical Expenditure Panel Survey.* Retrieved from: https://www.meps.ahrq.gov/mepsweb/data_stats/download_data_files_detail.jsp?cboPufNumber=HC-193

Agency for Healthcare Research and Quality. (2019a). *MEPS HC-190: 2016 Medical Conditions File. Medical Expenditure Panel Survey.* Retrieved from: https://www.meps.ahrq.gov/mepsweb/data_stats/download_data_files_detail.jsp?cboPufNumber=HC-190

Agency for Healthcare Research and Quality. (2019b). *MEPS HC-199: 2017 Medical Conditions File. Medical Expenditure Panel Survey.* Retrieved from: https://www.meps.ahrq.gov/mepsweb/data_stats/download_data_files_detail.jsp?cboPufNumber=HC-199

Agency for Healthcare Research and Quality. (2019c). *MEPS HC-202: Panel 21 Longitudinal Data File. Medical Expenditure Panel Survey.* Retrieved from: https://www.meps.ahrq.gov/mepsweb/data_stats/download_data_files_detail.jsp?cboPufNumber=HC-202

Agency for Toxic Substances and Disease Registry. (2018). *Toxicological Profile for Perfluoroalkyls*.

Ahrens, K. A., Rossen, L. M., Thoma, M. E., Warner, M., & Simon, A. E. (2017). Birth order and injury-related infant mortality in the U.S. *American Journal of Preventive Medicine, 53*(4), 412–420.

Alio, A. P., Mbah, A. K., Kornosky, J. L., Wathington, D., Marty, P. J., & Salihu, H. M. (2011). Assessing the impact of paternal involvement on racial/ethnic disparities in infant mortality rates. *Journal of Community Health, 36*, 63–68. doi:10.1007/s10900-010-9280-3

Almond, D., Chay, K. Y., & Lee, D. S. (2005). The costs of low birth weight. *The Quarterly journal of economics, 120*(3), 1031-1083. doi:10.1093/qje/120.3.1031

Ambavane, A., Yang, S., Atkins, M. B., Rao, S., Shah, A., Regan, M. M., . . . Michaelson, M. D. (2020). Clinical and economic outcomes of treatment sequences for intermediate- to poor-risk advanced renal cell carcinoma. *Immunotherapy, 12*(1), 37-51. doi:10.2217/imt-2019-0199

Anderson, R. N. (1999). *Method for constructing complete annual US life tables* (Vol. 129): National Ctr for Health Statistics.

Apelberg, B. J., Witter, F. R., Herbstman, J. B., Calafat, A. M., Halden, R. U., Needham, L. L., & Goldman, L. R. (2007). Cord serum concentrations of perfluorooctane sulfonate

(PFOS) and perfluorooctanoate (PFOA) in relation to weight and size at birth. *Children's Health, 115*(11), 1670-1676.

Arias, E., Heron, M., & Tejada-Vera, B. (2013). United States life tables eliminating certain causes of death, 1999-2001.

Arias, E., & Xu, J. (2019). *United States Life Tables, 2017.*

Arizona Department of Environmental Quality. (2021). *Public Water System PFAS Data*. Retrieved from https://static.azdeq.gov/wqd/pfas/liberty_results.pdf

Ashley-Martin, J., Dodds, L., Arbuckle, T. E., Bouchard, M. F., Fisher, M., Morriset, A. S., . . . Platt, R. W. (2017). Maternal concentrations of perfluoroalkyl substances and fetal markers of metabolic function and birth weight: the Maternal-Infant Research on Environmental Chemicals (MIREC) study. *American journal of epidemiology, 185*(3), 185-193. doi:10.1093/aje/kww213

Bach, C. C., Bech, B. H., Nohr, E. A., Olsen, J., Matthiesen, N. B., Bonefeld-Jorgensen E.C., . . . Henriksen, T. B. (2016). Perfluoroalkyl acids in maternal serum and indices of fetal growth: the Aarhus Birth Cohort. *Environmental health perspectives, 124*(6), 848-854. doi:10.1289/ehp.1510046.

Backes, C. H., Markham, K., Moorehead, P., Cordero, L., Nankervis, C. A., & Giannone, P. J. (2011). Maternal preeclampsia and neonatal outcomes. *Journal of pregnancy*.

Bang, H., & Tsiatis, A. A. (2000). Estimating medical costs with censored data. *Biometrika, 87*(2), 329-343.

Bartell, S. M. (2003). *Statistical Methods for Nonsteady State Exposure Inference using Biomarkers*. University of California–Davis, Davis, CA.

Bartell, S. M. (2017). Online serum PFOA calculator for adults. *Environmental health perspectives, 125*(10), 104502. doi:10.1289/EHP2820.

Bartell, S. M., Calafat, A. M., Lyu, C., Kato, K., Ryan, P. B., & Steenland, K. (2010). Rate of decline in serum PFOA concentrations after granular activated carbon filtration at two public water systems in Ohio and West Virginia. *Environ Health Perspect, 118*(2), 222-228. doi:10.1289/ehp.0901252

Beatty, A. L., Ku, I. A., Bibbins-Domingo, K., Christenson, R. H., DeFillippi, C. R., Ganz, P., . . . Whooley, M. A. (2015). Traditional risk factors versus biomarkers for prediction of secondary events in patients with stable Coronary Heart Disease: from the Heart and Soul Study. *Journal of the American Heart Association, 4*. doi:10.1161/JAHA.114.001646

Begg, C. B., & Mazumdar, M. (1994). Operating characteristics of a rank correlation test for publication bias. *Biometrics, 50*(4), 1088-1101. doi:https://doi.org/10.2307/2533446

Bell, E. M., Yeung, E. H., Ma, W., Kannan, K., Sundaram, R., Smarr, M. M., & Louis, G. M. B. (2018). Concentrations of endocrine disrupting chemicals in newborn blood spots and infant outcomes in the upstate KIDS study. *Environment international, 121*, 232-239.

Bhattacharjee, S., Gharaibeh, M., Kamal, M. U., & Riaz, I. B. (2017). Influence of Health and Functional Status and Co-occurring Chronic Conditions on Healthcare Expenditures Among Community-dwelling Adults With Kidney Cancer in the United States: A Propensity–score-matched Analysis. *Clinical Genitourinary Cancer, 15*(3), e357-e368. doi:https://doi.org/10.1016/j.clgc.2016.12.017

Bureau of Labor Statistics. (2022). *Employment Cost Index (NAICS). Total compensation for All Civilian workers in All industries and occupations, Index. Series ID: CIS1010000000000I*. Retrieved from: https://data.bls.gov/pdq/SurveyOutputServlet

Cadwallader, A., A. Greene, H. Holsinger, A. Lan, M. Messner, M. Simic, & Albert, R. (2022). A Bayesian hierarchical model for estimating national PFAS drinking water occurrence. *AWWA Water Science, e1284*.

California Division of Drinking Water. (2020). *Perfluorooctanoic acid (PFOA) and Perfluorooctanesulfonic acid (PFOS).* Retrieved from https://www.waterboards.ca.gov/drinking_water/certlic/drinkingwater/PFOA_PFOS.html

Callaghan, W. M., MacDorman, M. F., Shapiro-Mendoza, C. K., & Barfield, W. D. (2017). Explaining the recent decrease in US infant mortality rate, 2007–2013. *American journal of obstetrics and gynecology*, *216*(1), 73. e71-73. e78.

Callan, A. C., Rotander, A., Thompson, K., Heyworth, J., Meueller, J. F., Odland, J. O., & Hinwood, A. L. (2016). Maternal exposure to perfluoroalkyl acids measured in whole blood and birth outcomes in offspring. *Science of the total environment, 569-570*, 1107-1113. doi:10.1016/j.scitotenv.2016.06.177

Cao, W., Liu, X., Liu, X., Zhou, Y., Zhang, X., Tian, H., . . . Bhatti, P. (2018). Perfluoroalkyl substances in umbilical cord serum and gestational and postnatal growth in a Chinese birth cohort. *Environment international, 116*, 197-205.

Centers for Disease Control and Prevention. (2013a). *2011-2012 Data Documentation, Codebook, and Frequencies. Cholesterol - HDL (HDL_G). National Health and Nutrition Examination Survey.* Retrieved from: https://wwwn.cdc.gov/Nchs/Nhanes/2011-2012/HDL_G.XPT

Centers for Disease Control and Prevention. (2013b). *2011-2012 Data Documentation, Codebook, and Frequencies. Cholesterol - Total (TCHOL_G). National Health and Nutrition Examination Survey.* Retrieved from: https://wwwn.cdc.gov/Nchs/Nhanes/2011-2012/TDIQ_G.XPT

Centers for Disease Control and Prevention. (2013c). *2011-2012 Data Documentation, Codebook, and Frequencies. Diabetes (DIQ_G). National Health and Nutrition Examination Survey.*

Centers for Disease Control and Prevention. (2013d). *2011-2012 Data Documentation, Codebook, and Frequencies. Smoking - Cigarette Use (SMQ_G). National Health and Nutrition Examination Survey.* Retrieved from: https://wwwn.cdc.gov/Nchs/Nhanes/2011-2012/SMQ_G.XPT

Centers for Disease Control and Prevention. (2015a). *2011-2012 Data Documentation, Codebook, and Frequencies. Demographic Variables & Sample Weights (DEMO_G). National Health and Nutrition Examination Survey.* Retrieved from: https://wwwn.cdc.gov/Nchs/Nhanes/2011-2012/DEMO_G.XPT

Centers for Disease Control and Prevention. (2015b). *2013-2014 Data Documentation, Codebook, and Frequencies. Demographic Variables & Sample Weights (DEMO_H). National Health and Nutrition Examination Survey.* Retrieved from: https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/DEMO_H.XPT

Centers for Disease Control and Prevention. (2015c). *2013-2014 Data Documentation, Codebook, and Frequencies. Diabetes (DIQ_H). National Health and Nutrition Examination Survey.* Retrieved from: https://wwwn.cdc.gov/Nchs/Nhanes/2011-2012/DIQ_H.XPT

Centers for Disease Control and Prevention. (2015d). *2013-2014 Data Documentation, Codebook, and Frequencies. Smoking - Cigarette Use (SMQ_H). National Health and*

*Nutrition Examination Survey.* Retrieved from: https://wwwn.cdc.gov/Nchs/Nhanes/2011-2012/SMQ_H.XPT

Centers for Disease Control and Prevention. (2016a). *2013-2014 Data Documentation, Codebook, and Frequencies. Cholesterol - HDL (HDL_H). National Health and Nutrition Examination Survey.* Retrieved from: https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/HDL_H.XPT

Centers for Disease Control and Prevention. (2016b). *2013-2014 Data Documentation, Codebook, and Frequencies. Cholesterol - Total (TCHOL_H). National Health and Nutrition Examination Survey.* Retrieved from: https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/TCHOL_H.XPT

Centers for Disease Control and Prevention. (2016c, February 11). STDs During Pregnancy - CDC Detailed Fact Sheet. Retrieved from https://www.cdc.gov/std/pregnancy/stdfact-pregnancy-detailed.htm#r5

Centers for Disease Control and Prevention. (2017a). *2015-2016 Data Documentation, Codebook, and Frequencies. Cholesterol - HDL (HDL_I). National Health and Nutrition Examination Survey.* Retrieved from: https://wwwn.cdc.gov/Nchs/Nhanes/2015-2016/HDL_I.XPT

Centers for Disease Control and Prevention. (2017b). *2015-2016 Data Documentation, Codebook, and Frequencies. Cholesterol - Total (TCHOL_I). National Health and Nutrition Examination Survey.* Retrieved from: https://wwwn.cdc.gov/Nchs/Nhanes/2015-2016/TCHOL_I.XPT

Centers for Disease Control and Prevention. (2017c). *2015-2016 Data Documentation, Codebook, and Frequencies. Demographic Variables & Sample Weights (DEMO_I). National Health and Nutrition Examination Survey.* Retrieved from: https://wwwn.cdc.gov/Nchs/Nhanes/2015-2016/DEMO_I.XPT

Centers for Disease Control and Prevention. (2017d). *2015-2016 Data Documentation, Codebook, and Frequencies. Diabetes (DIQ_I). National Health and Nutrition Examination Survey.* Retrieved from: https://wwwn.cdc.gov/Nchs/Nhanes/2015-2016/DIQ_I.XPT

Centers for Disease Control and Prevention. (2017e). *2015-2016 Data Documentation, Codebook, and Frequencies. Smoking - Cigarette Use (SMQ_I). National Health and Nutrition Examination Survey.* Retrieved from: https://wwwn.cdc.gov/Nchs/Nhanes/2015-2016/SMQ_I.XPT

Centers for Disease Control and Prevention. (2017f). *User Guide to the 2017 Period/2016 Cohort Linked Birth/Infant Death Public Use File*.

Centers for Disease Control and Prevention. (2018). *User Guide to the 2018 Period/2017 Cohort Linked Birth/Infant Death Public Use File*.

Centers for Disease Control and Prevention. (2020a). Commit to Healthy Choices to Prevent Birth Defects. Retrieved from https://www.cdc.gov/ncbddd/birthdefects/prevention.html

Centers for Disease Control and Prevention. (2020b). Pregnancy Complications.

Centers for Disease Control and Prevention. (2020c). *Underlying Cause of Death, 1999-2020 on CDC WONDER Online Database, released in 2020. Data are from the Multiple Cause of Death Files, 1999-2019, as compiled from data provided by the 57 vital statistics jurisdictions through the Vital Statistics Cooperative Program.* Retrieved from: http://wonder.cdc.gov/ucd-icd10.html

Centers for Disease Control and Prevention. (2022). *National Report on Human Exposure to Environmental Chemicals. Updated March 2022.* Retrieved from https://www.cdc.gov/exposurereport/

Chang, H. Y., Nuyten, D. S. A., Sneddon, J. B., Hastie, T., Tibshirani, R., Sørlie, T., . . . van de Vijver, M. J. (2005). Robustness, scalability, and integration of a wound-response gene expression signature in predicting breast cancer survival. *Proc. Natl. Acad. Sci. U. S. A., 102*(10), 3738-3743. doi:10.1073/pnas.0409462102

Château-Degat, M.-L., Pereg, D., Dallaire, R., Ayotte, P., Dery, S., & Dewailly, É. (2010). Effects of perfluorooctanesulfonate exposure on plasma lipid levels in the Inuit population of Nunavik (Northern Quebec). *Environmental research, 110*(7), 710-717.

Chen, M. H., Ha, E. H., Wen, T. W., Su, Y. N., Lien, G. W., Chen, C. Y., . . . Hsieh, W. S. (2012). Perfluorinated compounds in umbilical cord blood and adverse birth outcomes. *PLoS One, 7*(8), e42474.

Chen, M. H., Ng, S., Hsieh, C. J., Lin, C. C., Hsieh, W. S., & Chen, P. C. (2017). The impact of prenatal perfluoroalkyl substances exposure on neonatal and child growth. *Science of the total environment, 607-608*, 669-675. doi:10.1016/j.scitotenv.2017.06.273

Chu, C., Zhou, Y., Li, Q.-Q., Bloom, M. S., Lin, S., Yu, Y.-J., . . . Yang, B.-Y. (2020). Are perfluorooctane sulfonate alternatives safer? New insights from a birth cohort study. *Environment international, 135*, 105365.

Cochran, W. G. (1954). The combination of estimates from different experiments. *Biometrics, 10*(1), 101-129. doi:https://doi.org/10.2307/3001666

Cole, T. J., Hey, E., & Richmond, S. (2010). The PREM score: A graphical tool for predicting survival in very preterm births. *Archives of Disease in Childhood-Fetal and Neonatal Edition, 95*(1), F14-F19.

Collins Jr, J. W., & David, R. J. (2009). Racial disparity in low birth weight and infant mortality. *Clinics in perinatology, 36*(1), 63-73.

Colorado Department of Public Health and Environment. (2020). *2020 PFAS Sampling Project*.

Convertino, M., Church, T. R., Olsen, G. W., Liu, Y., Doyle, E., Elcombe, C. R., . . . Evans, T. R. J. (2018). Stochastic Pharmacokinetic-Pharmacodynamic Modeling for Assessing the Systemic Health Risk of Perfluorooctanoate (PFOA). *Toxicological Sciences, 163*(1), 293-306. doi:10.1093/toxsci/kfy035

Cooke, R. W. I. (2010). *Does Neonatal and Infant Neurodevelopmental Morbidity of Multiples and Singletons Differ?* Paper presented at the Seminars in Fetal and Neonatal Medicine.

Crainiceanu, C. M., Stedinger, J. R., Ruppert, D., & Behr, C. T. (2003). Modeling the U.S. national distribution of waterborne pathogen concentrations with application to Cryptosporidium parvum. *Water Resources Research, 39*(9). doi:https://doi.org/10.1029/2002WR001664

D'Agostino, R. B., Grundy, S., Sullivan, L. M., Wilson, P., & Group, C. H. D. R. P. (2001). Validation of the Framingham coronary heart disease prediction scores: results of a multiple ethnic groups investigation. *Jama, 286*(2), 180-187. doi:10.1001/jama.286.2.180

D'Agostino, R. B., Russell, M. W., Huse, D. M., Ellison, R. C., Silbershatz, H., Wilson, P. W., & Hartz, S. C. (2000). Primary and subsequent coronary risk appraisal: new results from the Framingham study. *Am. Heart J., 139*(2 Pt 1), 272-281. doi:10.1067/mhj.2000.96469

D'Agostino, R. B., Vasan, R. S., Pencina, M. J., Wolf, P. A., Cobain, M., Massaro, J. M., & Kannel, W. B. (2008). General cardiovascular risk profile for use in primary care. *Circulation, 117*(6), 743-753.

D'Agostino, R. B., Wolf, P. A., Belanger, A. J., & Kannel, W. B. (1994). Stroke risk profile: adjustment for antihypertensive medication. The Framingham Study. *Stroke, 25*(1), 40-43. doi:10.1161/01.str.25.1.40

Darrow, L. A., Stein, C. R., & Steenland, K. (2013). Serum Perfluorooctanoic Acid and Perfluorooctane Sulfonate Concentrations in Relation to Birth Outcomes in the Mid-Ohio Valley, 2005–2010. *Environ. Health Perspect., 121*(10), 1207-1213. doi:10.1289/ehp.1206372

Deeks, J. J. (2002). Issues in the selection of a summary statistic for meta-analysis of clinical trials with binary outcomes. *Statistics in medicine, 21*(11), 1575-1600.

Delaware Office of Drinking Water. (2021). *Delaware Drinking Water Watch Data*. Retrieved from: https://drinkingwater.dhss.delaware.gov/

DerSimonian, R., & Laird, N. (1986). Meta-analysis in clinical trials. *Controlled clinical trials, 7*(3), 177-188.

Donahue, S. M., Kleinman, K. P., Gillman, M. W., & Oken, E. (2010). Trends in birth weight and gestational length among singleton term births in the United States: 1990–2005. *Obstetrics and gynecology, 115*(2 Pt 1), 357.

Dong, Z., Wang, H., Yu, Y. Y., Li, Y. B., Naidu, R., & Liu, Y. (2019). Using 2003–2014 US NHANES data to determine the associations between per-and polyfluoroalkyl substances and cholesterol: Trend and implications. *Ecotoxicology and environmental safety, 173*, 461-468.

Duval, S., & Tweedie, R. (2000a). A nonparametric "trim and fill" method of accounting for publication bias in meta-analysis. *J Am Stat Assoc, 95*(449), 89-98. doi:10.1080/01621459.2000.10473905

Duval, S., & Tweedie, R. (2000b). Trim and fill: A simple funnel-plot–based method of testing and adjusting for publication bias in meta-analysis. *Biometrics, 56*(2), 455-463. doi:10.1111/j.0006-341X.2000.00455.x

Dzierlenga, M., Allen, B., Clewell, H., & Longnecker, M. (2020). Pharmacokinetic bias analysis of an association between clinical thyroid disease and two perfluoroalkyl substances. *Environ Int, 141: 105784*.

Dzierlenga, M., Crawford, L., & Longnecker, M. (2020). Birth weight and perfluorooctane sulfonic acid: a random-effects meta-regression analysis. *Environmental Epidemiology, 4*(3).

Egger, M., Smith, G., Schneider, M., & Minder, C. (Eds.). (2008). *Systematic reviews in health care: Meta-analysis in context*. London, UK: BMJ Publishing Group.

Egger, M., Smith, G. D., Schneider, M., & Minder, C. (1997). Bias in meta-analysis detected by a simple, graphical test. *BMJ, 315*(7109), 629-634. doi:https://doi.org/10.1136/bmj.315.7109.629

Ely, D. M., & Driscoll, A. K. (2020). *Infant Mortality in the United States, 2018: Data From the Period Linked Birth/Infant Death File*. Retrieved from https://www.cdc.gov/nchs/data/nvsr/nvsr69/NVSR-69-7-508.pdf

Engels, E. A., Schmid, C. H., Terrin, N., Olkin, I., & Lau, J. (2000). Heterogeneity and statistical significance in meta-analysis: an empirical study of 125 meta-analyses. *Statistics in medicine, 19*(13), 1707-1728.

Eriksen, K. T., Raaschou-Nielsen, O., McLaughlin, J. K., Lipworth, L., Tjønneland, A., Overvad, K., & Sørensen, M. (2013). Association between plasma PFOA and PFOS levels and total cholesterol in a middle-aged Danish population. *PLoS One, 8*(2), e56969.

Fan, Y., Li, X., Xu, Q., Zhang, Y., Yang, X., Han, X., . . . Lu, C. (2020). Serum albumin mediates the effect of multiple per-and polyfluoroalkyl substances on serum lipid levels. *Environmental pollution*, *266*, 115138.

Fei, C., McLaughlin, J. K., Tarone, R. E., & Olsen, J. (2007). Perfluorinated Chemicals and Fetal Growth: A Study within the DanishNational Birth Cohort. *Environmental health perspectives*, *115*(11), 1677-1682.

Fisher, M., Arbuckle, T. E., Wade, M., & Haines, D. A. (2013). Do perfluoroalkyl substances affect metabolic function and plasma lipids?—Analysis of the 2007–2009, Canadian Health Measures Survey (CHMS) Cycle 1. *Environmental research*, *121*, 95-103.

Fitz-Simon, N., Fletcher, T., Luster, M. I., Steenland, K., Calafat, A. M., Kato, K., & Armstrong, B. (2013). Reductions in serum lipids with a 4-year decline in serum perfluorooctanoic acid and perfluorooctanesulfonic acid. *Epidemiology (Cambridge, Mass.)*, *24*(4), 569.

Fragki, S., Dirven, H., Fletcher, T., Grasl-Kraupp, B., Bjerve Gützkow, K., Hoogenboom, R., . . . Luijten, M. (2021). Systemic PFOS and PFOA exposure and disturbed lipid homeostasis in humans: what do we know and what not? *Crit Rev Toxicol*, 141-164.

Fried, L. P., Borhani, N. O., Enright, P., Furberg, C. D., Gardin, J. M., Kronmal, R. A., . . . Newman, A. (1991). The cardiovascular health study: design and rationale. *Annals of epidemiology*, *1*(3), 263-276.

Friedman, G. D., Cutter, G. R., Donahue, R. P., Hughes, G. H., Hulley, S. B., Jacobs Jr, D. R., . . . Savage, P. J. (1988). CARDIA: study design, recruitment, and some characteristics of the examined subjects. *Journal of clinical epidemiology*, *41*(11), 1105-1116.

Fromme, H., Mosch, C., Morovitz, M., Alba-Alejandre, I., Boehmer, S., Kiranoglu, M., . . . Koletzko, B. (2010). Pre-and postnatal exposure to perfluorinated compounds (PFCs). *Environmental Science & Technology*, *44*(18), 7123-7129.

Fu, Y., Wang, T., Fu, Q., Wang, P., & Lu, Y. (2014). Associations between serum concentrations of perfluoroalkyl acids and serum lipid levels in a Chinese population. *Ecotoxicology and environmental safety*, *106*, 246-252.

Gabry, J., & Mahr, T. (2020). bayesplot: Plotting for Bayesian Models. Retrieved from https://mc-stan.org/bayesplot/

Gabry, J., Veen, D., Stan Development Team, Andreae, M., Betancourt, M., Carpenter, B., . . . Trangucci, R. (2018). *shinystan: Interactive Visual and Numerical Diagnostics and Posterior Analysis for Bayesian Models*. Retrieved from: https://cran.r-project.org/web/packages/shinystan/index.html

Gao, K., Zhuang, T., Liu, X., Fu, J., Zhang, J., Fu, J., . . . Song, M. (2019). Prenatal exposure to per-and polyfluoroalkyl substances (PFASs) and association between the placental transfer efficiencies and dissociation constant of serum proteins–PFAS complexes. *Environmental Science & Technology*, *53*(11), 6529-6538.

Georgia Environmnetal Protection Division. (2020). *EPA Sampling Report for Summerville*. Retrieved from https://epd.georgia.gov/pfoa-and-pfos-information

Goff, D. C., Lloyd-Jones, D. M., Bennett, G., Coady, S., D'Agostino, R. B., Gibbons, R., . . . Wilson, P. W. F. (2014). 2013 ACC/AHA guideline on the assessment of cardiovascular risk: A report of the American College of Cardiology/American Heart Association task force on practice guidelines. *Circulation*, *129*(25 suppl 2), 49-73.

Govarts, E., Remy, S., Bruckners, L., Hond, E. D., Sioen, I., Nelen, V., . . . Schoeters, G. (2016). Combined Effects of Prenatal Exposures to Environmental Chemicals on Birth Weight.

*International journal of environmental research and public health, 13*(495), 1-19. doi:10.3390/ijerph13050495

Hamm, M. P., Cherry, N. M., Chan, E., Martin, J. W., & Burstyn, I. (2010). Maternal exposure to perfluorinated acids and fetal growth. *Journal of Exposure Science and Environmental Epidemiology, 20*, 589-597. doi:1559-0631/10

He, X., Liu, Y., Xu, B., Gu, L., & Tang, W. (2018). PFOA is associated with diabetes and metabolic alteration in US men: National Health and Nutrition Examination Survey 2003–2012. *Science of the total environment, 625*, 566-574.

Higgins, J., Chandler, J., Cumpston, M., Page, M., & Welch, V. E. (2021). Cochrane Handbook for Systematic Reviews of Interventions version 6.2 (updated February 2021). *Cochrane*.

Higgins, J., Thomas, J., Chandler, J., Cumpston, M., Li, T., Page, M. J., & Welch, V. A. (2019). *Cochrane handbook for systematic reviews of interventions*: John Wiley & Sons.

Higgins, J., Thompson, S., Deeks, J., & Altman, D. (2003). Measuring inconsistency in meta-analyses. *BMJ, 327*(7414), 557-560. doi:https://doi.org/10.1136/bmj.327.7414.557

Hjermitslev, M. H., Long, M., Wielsøe, M., & Bonefeld-Jørgensen, E. C. (2020). Persistent organic pollutants in Greenlandic pregnant women and indices of foetal growth: The ACCEPT study. *Science of the total environment, 698*, 134118.

Hoffman, K., Webster, T. F., Bartell, S. M., Weisskopf, M. G., Fletcher, T., & Vieira, V. M. (2011). Private drinking water wells as a source of exposure to perfluorooctanoic acid (PFOA) in communities surrounding a fluoropolymer production facility. *Environmental health perspectives, 119*(1), 92-97.

Hollenbeak, C. S., Nikkel, L. E., Schaefer, E. W., Alemao, E., Ghahramani, N., & Raman, J. D. (2011). Determinants of Medicare All-Cause Costs Among Elderly Patients with Renal Cell Carcinoma. *Journal of Managed Care Pharmacy, 17*(8), 610-620. doi:10.18553/jmcp.2011.17.8.610

Horon, I., Munson, K.M. (2020). Discussion of the Merits of Using Singleton Data from the CDC to Develop a Relationship Between Birthweight and Infant Mortality. Email Correspondence 11/10/2020.

Huang, M., Jiao, J., Zhuang, P., Chen, X., Wang, J., & Zhang, Y. (2018). Serum polyfluoroalkyl chemicals are associated with risk of cardiovascular diseases in national US population. *Environment international, 119*, 37-46.

ICF. (2020). *Memorandum re: Trends in Infant Mortality by Birth Weight Categories, EPA Contract No. 68HE0C18D0001, TO 68HERC20F0107. Submitted to U.S. Environmental Protection Agency Office of Groundwater and Drinking Water July 30, 2020.* Retrieved from https://www.regulations.gov/docket/EPA-HQ-OW-2022-0114

ICF. (2021). *Memorandum re: Review of PFAS Lipids Study Quality. Submitted to U.S. Environmental Protection Agency Office of Groundwater and Drinking Water March 23, 2021.* Retrieved from https://www.regulations.gov/docket/EPA-HQ-OW-2022-0114

ICF. (2022). *Memorandum re: Literature Review of Population Attributable Fraction Estimates and Next Steps for Renal Cell Carcinoma PFAS Benefits Modeling. Submitted to U.S. Environmental Protection Agency Office of Groundwater and Drinking Water July 26, 2022.* Retrieved from

Illinois Environmental Protection Agency. (2021). *Illinois Drinking Water Watch*. Retrieved from: http://water.epa.state.il.us/dww/index.jsp

Institute of Medicine. (1985). *Preventing Low Birthweight*. Washington, DC: The National Academies Press.

Jacob, J. A. (2016). U.S. infant mortality rate declines but still exceeds other developed countries. *Journal of the American Medical Association, 315*(5), 451-452.

Jain, R. B., & Ducatman, A. (2019). Roles of gender and obesity in defining correlations between perfluoroalkyl substances and lipid/lipoproteins. *Science of the total environment, 653*, 74-81.

Johnson, P. I., Sutton, P., Atchley, D. S., Koustas, E., Lam, J., Sen, S., . . . Woodruff, T. J. (2014). The Navigation Guide—Evidence-Based Medicine Meets Environmental Health: Systematic Review of Human Evidence for PFOA Effects on Fetal Growth. *Environmental health perspectives, 122*(10), 1028-1039. doi:10.1289/ehp.1307893

Joyce, C., Goodman-Bryan, M., & Hardin, A. (2012). *Preterm Birth and Low Birth Weight*. Retrieved from The Urban Child Institute: http://www.urbanchildinstitute.org/sites/all/files/2010-10-01-PTB-and-LBW.pdf

Kannel, W. B., D'Agostino, R. B., Silbershatz, H., Belanger, A. J., Wilson, P. W., & Levy, D. (1999). Profile for estimating risk of heart failure. *Arch. Intern. Med., 159*(11), 1197-1204. doi:10.1001/archinte.159.11.1197

Kashino, I., Sasaki, S., Okada, E., Matsuura, H., Goudarzi, H., Miyashita, C., . . . Kishi, R. (2020). Prenatal exposure to 11 perfluoroalkyl substances and fetal growth: A large-scale, prospective birth cohort study. *Environment international, 136*, 105355.

Kassambara, A. (2020). *ggpubr: 'ggplot2' Based Publication Ready Plots*. Retrieved from: https://cran.r-project.org/web/packages/ggpubr/index.html

Kentucky Department for Environmental Protection. (2019). *Evaluation of Kentucky Community Drinking Water for Per- & Poly-Fluoroalkyl Substances*. Retrieved from https://eec.ky.gov/Documents%20for%20URLs/PFAS%20Drinking%20Water%20Report%20Final.pdf

Kiely, J. L., Brett, K. M., Yu, S., & Rowley, D. L. (1994). Low birth weight and intrauterine growth retardation. *Birth Outcomes*, 185-202.

Kim, S., Choi, K., Ji, K., Seo, J., Kho, Y., Park, J., . . . Giesy, J. P. (2011). Trans-Placental Transfer of Thirteen Perfluorinated Compounds and Relations with Fetal Thyroid Hormones. *Environmental Science & Technology, 45*(17), 7465-7472. doi:10.1021/es202408a

Kochanek, K. D., Murphy, S. L., Xu, J., & Arias, E. (2019). Deaths: Final data for 2017. *National vital statistics reports : from the Centers for Disease Control and Prevention, National Center for Health Statistics, National Vital Statistics System, 68(9), 1–77.*

Kwon, E. J., Shin, J. S., Kim, B. M., Shah-Kulkarni, S., Park, H., Kho, Y. L., . . . Ha, E. H. (2016). Prenatal Exposure to Perfluorinated Compounds Affects Birth Weight Through GSTM1 Polymorphism. *JOEM, 58*(6), e198-e205.

Lau, C., Ambalavanan, N., Chakraborty, H., Wingate, M. S., & Carlo, W. A. (2013). Extremely low birth weight and infant mortality rates in the United States. *Pediatrics, 131*(5), 855-860.

Lauritzen, H. B., Larose, T. L., Øien, T., Sandanger, T. M., Odland, J. O., van der Bor, M., & Jacobsen, G. W. (2017). Maternal serum levels of perfluoroalkyl substances and organochlorines and indices of fetal growth: a scandinavian case–cohort study. *Pediatric research, 81*(1), 33-42. doi:10.1038/pr.2016.187

Lee, E. S., Han, S., & Oh, J. E. (2016). Association between perfluorinated compound concentrations in cord serum and birth weight using multiple regression model. *Reproductive Toxicology, 59*, 53-59. doi:10.1016/j.reprotox.2015.10.020

Lenters, V., Portengen, L., Rignell-Hydbom, A., Jonsson, B. A. G., Lindh, C. H., Piersma, A. H., . . . Vermeulen, R. (2016). Prenatal Phthalate, Perfluoroalkyl Acid, and Organochlorine Exposures and Term Birth Weight in Three Birth Cohorts: Multi-Pollutant Models Based on Elastic Net Regression. *Environmental health perspectives, 124*, 365-372. doi:10.1289/ehp.1408933

Li, M., Zeng, Z. W., Qian, Z. M., Vaughn, M. G., Suauve, S., Paul, G., . . . Dong, G. H. (2017). Isomers of perfluorooctanesulfonate (PFOS) in cord serum and birth outcomes in China: Guangzhou Birth Cohort Study. *Environment international, 102*, 1-8. doi:10.1016/j.envint.2017.03.006

Li, S., Peng, Y., Wang, X., Qian, Y., Xiang, P., Wade, S. W., . . . Handelsman, Y. (2019). Cardiovascular events and death after myocardial infarction or ischemic stroke in an older Medicare population. *Clinical cardiology, 42*(3), 391-399.

Li, Y., Barregard, L., Xu, Y., Scott, K., Pineda, D., Lindh, C. H., . . . Fletcher, T. (2020). Associations between perfluoroalkyl substances and serum lipids in a Swedish adult population with contaminated drinking water. *Environmental Health, 19*(33).

Li, Y., Fletcher, T., Mucs, D., Scott, K., Lindh, C. H., Tallving, P., & Jakobsson, K. (2018). Half-lives of PFOS, PFHxS and PFOA after end of exposure to contaminated drinking water. *Occupational and environmental medicine, 75*(1), 46-51.

Liao, S., Yao, W., Cheang, I., Tang, X., Yin, T., Lu, X., . . . Li, X. (2020). Association between perfluoroalkyl acids and the prevalence of hypertension among US adults. *Ecotoxicology and environmental safety, 196*, 110589.

Lin, C. Y., Lee, H. L., Hwang, Y. T., & Su, T. C. (2020). The association between total serum isomers of per-and polyfluoroalkyl substances, lipid profiles, and the DNA oxidative/nitrative stress biomarkers in middle-aged Taiwanese adults. *Environmental research, 182*, 109064.

Lin, L., & Chu, H. (2018). Quantifying publication bias in meta-analysis. *Biometrics, 74*(3), 785-794.

Lin, P.-I. D., Cardenas, A., Hauser, R., Gold, D. R., Kleinman, K. P., Hivert, M.-F., . . . Horton, E. S. (2019). Per-and polyfluoroalkyl substances and blood lipid levels in pre-diabetic adults—longitudinal analysis of the diabetes prevention program outcomes study. *Environment international, 129*, 343-353.

Lind, D. V., Priskorn, L., Lassen, T. H., Nielsen, F., Kyhl, H. B., Kristensen, D. M., . . . Jensen, T. K. (2017). Prenatal exposure to perfluoroalkyl substances and anogenital distance at 3 months of age in a Danish mother-child cohort. *Reproductive Toxicology, 68*, 200-206.

Liu, H.-S., Wen, L.-L., Chu, P.-L., & Lin, C.-Y. (2018). Association among total serum isomers of perfluorinated chemicals, glucose homeostasis, lipid profiles, serum protein and metabolic syndrome in adults: NHANES, 2013–2014. *Environmental pollution, 232*, 73-79.

Lockwood, J. R., Schervish, M. J., Gurian, P., & Small, M. J. (2001). Characterization of arsenic occurrence in source waters of U.S. community water systems. *Journal of the American Statistical Association, 96*(456), 1184-1193. doi:10.1198/016214501753381832

Louis, G. M. B., Zhai, S., Smarr, M. M., Grewal, J., Zhang, C., Grantz, K. L., . . . Honda, M. (2018). Endocrine disruptors and neonatal anthropometry, NICHD fetal growth studies-singletons. *Environment international, 119*, 515-526.

Lu, S., & Bartell, S. M. (2020). *Serum PFAS Calculator for Adults*. Retrieved from: www.ics.uci.edu/~sbartell/pfascalc.html

Ma, S., & Finch, B. K. (2010). Birth Outcome Measures and Infant Mortality. *Population Research and Policy Review, 29*(6), 865-891.

Mahmood, S. S., Levy, D., Vasan, R. S., & Wang, T. J. (2014). The Framingham Heart Study and the epidemiology of cardiovascular disease: a historical perspective. *The Lancet, 383*(9921), 999-1008.

Maine Department of Environmental Protection. (2020). *MAINE PFAS DATA (2007 - 2020)*. Retrieved from https://www1.maine.gov/dep/spills/topics/pfas/PFAS-current-results-10262020.pdf

Maisonet, M., Terrell, M. L., McGeehin, M. A., Christensen, K. Y., Holmes, A., Calafat, A. M., & Marcus, M. (2012). Maternal concentrations of polyfluoroalkyl compounds during pregnancy and fetal and postnatal growth in British girls. *Environmental health perspectives, 120*(10), 1432-1437.

Manzano-Salgado, C. B., Casas, M., Lopez-Espinosa, M.-J., Ballester, F., Iñiguez, C., Martinez, D., . . . Schettgen, T. (2017). Prenatal exposure to perfluoroalkyl substances and birth outcomes in a Spanish birth cohort. *Environment international, 108*, 278-284.

Marks, K. J., Cutler, A. J., Jeddy, Z., Northstone, K., Kato, K., & Hartman, T. J. (2019). Maternal serum concentrations of perfluoroalkyl substances and birth size in British boys. *International journal of hygiene and environmental health, 222*(5), 889-895.

Massachusetts Department of Energy and Environmental Affairs. (2021). Energy and Environmental Affairs Data Portal. In.

Mathews, T. (2013). Infant mortality statistics from the 2010 period linked birth/infant death data set. *National vital statistics reports : from the Centers for Disease Control and Prevention, National Center for Health Statistics, National Vital Statistics System, 62(8), 1–26*.

McCormick, M. C. (1985). The contribution of low birth weight to infant mortality and childhood morbidity. *New England Journal of Medicine, 312*(2), 82-90.

McIntire, D. D., Bloom, S. L., Casey, B. M., & Leveno, K. J. (1999). Birth weight in relation to morbidity and mortality among newborn infants. *New England Journal of Medicine, 340*(16), 1234-1238.

Meng, Q., Inoue, K., Ritz, B., Olsen, J., & Liew, Z. (2018). Prenatal exposure to perfluoroalkyl substances and birth outcomes; an updated analysis from the Danish National Birth Cohort. *International journal of environmental research and public health, 15*(9), 1832.

Michigan Environment, G. L., and Energy,. (2021). *Michigan Compliance Monitoring Data*. Retrieved from https://www.michigan.gov/pfasresponse/0,9038,7-365-95571_95577_106298---,00.html

Minatoya, M., Itoh, S., Miyashita, C., Araki, A., Sasaki, S., Miura, R., . . . Kishi, R. (2017). Association of prenatal exposure to perfluoroalkyl substances with cordblood adipokines and birth size: The Hokkaido Study on environment and children's health. *Environmental research, 156*, 175-182. doi:10.1016/j.envres.2017.03.033

Mishra, S., Ram, B., Singh, A., & Yadav, A. (2018). Birth order, stage of infancy and infant mortality in India. *Journal of biosocial science, 50*(5), 604-625.

Mitchell, A. P., Dey, P., Ohn, J. A., Tabatabai, S. M., Curry, M. A., & Bach, P. B. (2020). The Accuracy and Usefulness of the National Comprehensive Cancer Network Evidence Blocks Affordability Rating. *Pharmacoeconomics, 38*(7), 737-745. doi:10.1007/s40273-020-00901-x

Monroy, R., Morrison, K., Teo, K., Atkinson, S., Kubwabo, C., Stewart, B., & Foster, W. G. (2008). Serum levels of perfluoroalkyl compounds in human maternal and umbilicalcord blood samples. *Environmental research, 108*, 56-62. doi:10.1016/j.envres.2008.06.001

Mora, S. (2016). Nonfasting for Routine Lipid Testing: From Evidence to Action. *JAMA Intern Med, 176*, 1005-1006.

National Center for Health Statistics, H., MD. (2019). *Health, United States, 2018*. Retrieved from https://www.cdc.gov/nchs/data/hus/hus18.pdf

Negri, E., Metruccio, F., Guercio, V., Tosti, L., Benfenati, E., Bonzi, R., . . . Moretto, A. (2017). Exposure to PFOA and PFOS and fetal growth: a critical merging of toxicological and epidemiological data. *Critical reviews in toxicology, 10.1080/10408444.2016.1271972*, 489-515. doi:10.1080/10408444.2016.1271972

Nelson, J. W., Hatch, E. E., & Webster, T. F. (2010). Exposure to polyfluoroalkyl chemicals and cholesterol, body weight, and insulin resistance in the general US population. *Environmental health perspectives, 118*(2), 197-202.

New Hampshire Department of Environmental Services. (2021). One Stop Data Portal. In.

New Jersey Department of Environmental Protection. (2021). New Jersey Drinking Water Watch. In.

Ngui, E. M., Cortright, A. L., & Michalski, K. (2015). Relationship of paternity status, welfare reform period, and racial/ethnic disparities in infant mortality. *American Journal of Men's Health, 9*(5), 350-359. doi:10.1177/1557988314543906

North Dakota Department of Environmental Quality. (2020). *North Dakota Statewide 2020 Per- and Polyfluoroalkyl Substances (PFAS) Presence/Absence Survey*. Retrieved from https://deq.nd.gov/Publications/MF/PFAS_Report_2020.pdf?v=1

O'Sullivan, A. K., Rubin, J., Nyambose, J., Kuznik, A., Cohen, D. J., & Thompson, D. (2011). Cost estimation of cardiovascular disease events in the US. *Pharmacoeconomics, 29*(8), 693-704.

Occupational Safety and Health Administration. (2010). *Occupational Exposure to Respirable Crystalline Silica -- Review of Health Effects Literature and Preliminary Quantitative Risk Assessment*.

Ohio Department of Health. (2020). *Per- and Polyfluoroalkyl Substances (PFAS)*. Retrieved from: https://data-oepa.opendata.arcgis.com/datasets/pfas-sampling-results/explore

Osterman, M. J., Kochanek, K. D., MacDorman, M. F., Strobino, D. M., & Guyer, B. (2015). Annual summary of vital statistics: 2012–2013. *Pediatrics, 135*(6), 1115-1125.

Ott, W. R. (1995). *Environmental Statistics and Data Analysis* (1st ed.). New York: CRC Press, Lewis Publishers.

Palmer, T. M., & Sterne, J. A. C. (Eds.). (2016). *Meta-analysis in Stata: An updated collection from the Stata Journal* (2nd ed.). College Station, TX: Stata Press.

PEACE Trial Investigators. (2004). Angiotensin-converting–enzyme inhibition in stable coronary artery disease. *New England Journal of Medicine, 351*(20), 2058-2068.

Pencina, M. J., D'Agostino, R. B., Sr., Larson, M. G., Massaro, J. M., & Vasan, R. S. (2009). Predicting the 30-year risk of cardiovascular disease: the framingham heart study. *Circulation, 119*(24), 3078-3084. doi:10.1161/CIRCULATIONAHA.108.816694

Pencina, M. J., D'Agostino, R. B., Sr., & Steyerberg, E. W. (2011). Extensions of net reclassification improvement calculations to measure usefulness of new biomarkers. *Stat. Med., 30*(1), 11-21. doi:10.1002/sim.4085

Pennsylvania Department of Environmental Protection. (2020). *PFAS Phase 1 Results Summary*. Retrieved from http://files.dep.state.pa.us/Water/DrinkingWater/Perfluorinated%20Chemicals/SamplingResults/PFASPhase1ResultsSummary.pdf

Perrin, A., Sherman, S., Pal, S., Chua, A., Gorritz, M., Liu, Z., . . . Garrison, L. P. (2015). Lifetime cost of everolimus vs axitinib in patients with advanced renal cell carcinoma who failed prior sunitinib therapy in the US. *Journal of Medical Economics, 18*(3), 200-209.

Powers, D. A., Frisbie, W. P., Hummer, R. A., Pullum, S. G., & Solis, P. (2006). Race/ethnic differences and age-variation in the effects of birth outcomes on infant mortality in the US. *Demographic Research, 14*, 179-216.

Quah, S. R. (2016). *International Encyclopedia of Public Health*. Waltham, MA: Academic Press.

R Core Team. (2021). R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing.

Racsa, P. N., Whisman, T. R., & Worley, K. (2015). Comparing two tyrosine kinase inhibitors for treatment of advanced renal cell carcinoma in Medicare and commercially insured patients. *Current Medical Research and Opinion, 31*(10), 1933-1940.

Rappazzo, K. M., Coffman, E., & Hines, E. P. (2017). Exposure to perfluorinated alkyl substances and health outcomes in children: a systematic review of the epidemiologic literature. *International journal of environmental research and public health, 14*(7), 691.

Ratnasiri, A. W., Parry, S. S., Arief, V. N., DeLacy, I. H., Halliday, L. A., DiLibero, R. J., & Basford, K. E. (2018). Recent trends, risk factors, and disparities in low birth weight in California, 2005–2014: A retrospective study. *Maternal health, neonatology and perinatology, 4*(1), 1-13.

Raudenbush, S. W. (2009). Analyzing effect sizes: Random-effects models. *The handbook of research synthesis and meta-analysis, 2*, 295-316.

Ray, J. G., Park, A. L., & Fell, D. B. (2017). Mortality in infants affected by preterm birth and severe small-for-gestational-age birth weight. *Pediatrics, 140*(6).

Regli, S., Chen, J., Messner, M., Elovitz, M. S., Letkiewicz, F. J., Pegram, R. A., . . . Wright, J. M. (2015). Estimating potential increased bladder cancer risk due to increased bromide concentrations in sources of disinfected drinking waters. *Environmental Science & Technology, 49*(22), 13094-13102.

Reinhorn, D., Sarfaty, M., Leshno, M., Moore, A., Neiman, V., Rosenbaum, E., & Goldstein, D. A. (2019). A cost-effectiveness analysis of nivolumab and ipilimumab versus sunitinib in first-line intermediate-to poor-risk advanced renal cell carcinoma. *The oncologist, 24*(3), 366-371.

Rice, W. S., Goldfarb, S. S., Brisendine, A. E., Burrows, S., & Wingate, M. S. (2017). Disparities in infant mortality by race among Hispanic and non-Hispanic infants. *Maternal and child health journal, 21*(7), 1581-1588.

Robledo, C. A., Yeung, E., Mendola, P., Sundaram, R., Maisog, J., Sweeney, A. M., . . . Louis, G. M. B. (2015). Preconception maternal and paternal exposure to persistent organic pollutants and birth size: the LIFE study. *Environmental health perspectives, 123*(1), 88-94.

Rodríguez-Barranco, M., Tobías, A., Redondo, D., Molina-Portillo, E., & Sánchez, M. J. (2017). Standardizing effect size from linear regression models with log-transformed variables for meta-analysis. *BMC medical research methodology, 17*(1), 1-9.

Roger, V. L., Go, A. S., Lloyd-Jones, D. M., Benjamin, E. J., Berry, J. D., Borden, W. B., . . . Ford, E. S. (2012). Heart disease and stroke statistics—2012 update: a report from the American Heart Association. *Circulation, 125*(1), e2.

Rowley, D. L., & Hogan, V. (2012). Disparities in infant mortality and effective, equitable care: Are infants suffering from benign neglect? *Annual Review of Public Health, 33*, 75-87.

RStudio Team. (2020). RStudio: Integrated Development Environment for R. Retrieved from https://www.rstudio.com/

Rücker, G., Schwarzer, G., Carpenter, J., & Olkin, I. (2009). Why add anything to nothing? The arcsine difference as a measure of treatment effect in meta-analysis with zero cells. *Statistics in medicine, 28*(5), 721-738.

Russell, R. B., Petrini, J. R., Damus, K., Mattison, D. R., & Schwarz, R. H. (2003). The changing epidemiology of multiple births in the United States. *Obstetrics & Gynecology, 101*(1), 129-135.

Sagiv, S. K., Rifas-Shiman, S. L., Fleisch, A. F., Webster, T. F., Calafat, A. M., Ye, X., . . . Oken, E. (2018). Early-pregnancy plasma concentrations of perfluoroalkyl substances and birth outcomes in Project Viva: confounded by pregnancy hemodynamics? *American journal of epidemiology, 187*(4), 793-802.

Savitz, D. A., Stein, C. R., Elston, B., Wellenius, G. A., Bartell, S. M., Shin, H.-M., . . . Fletcher, T. (2012). Relationship of perfluorooctanoic acid exposure to pregnancy outcome based on birth records in the mid-Ohio Valley. *Environ. Health Perspect., 120*(8), 1201-1207. doi:10.1289/ehp.1104752

Seo, S.-H., Son, M.-H., Choi, S.-D., Lee, D.-H., & Chang, Y.-S. (2018). Influence of exposure to perfluoroalkyl substances (PFASs) on the Korean general population: 10-year trend and health effects. *Environment international, 113*, 149-161.

Shearer, J. J., Callahan, C. L., Calafat, A. M., Huang, W. Y., Jones, R. R., Sabbisetti, V. S., . . . Hofmann, J. N. (2021). Serum concentrations of per- and polyfluoroalkyl substances and risk of renal cell carcinoma. *Journal of the National Cancer Institute, 113*(5), 580-587. doi:10.1093/jnci/djaa143

Shi, Y., Yang, L., Li, J., Lai, J., Wang, Y., Zhao, Y., & Wu, Y. (2017). Occurrence of perfluoroalkyl substances in cord serum and association with growth indicators in newborns from Beijing. *Chemosphere, 169*, 396-402. doi:10.1016/j.chemosphere.2016.11.050

Sidik, K., & Jonkman, J. N. (2005). A note on variance estimation in random effects meta-regression. *Journal of Biopharmaceutical Statistics, 15*(5), 823-838.

Singh, G. K., & Stella, M. Y. (2019). Infant mortality in the United States, 1915-2017: Large social inequalities have persisted for over a century. *International Journal of Maternal and Child Health and AIDS, 8*(1), 19.

Solis, P., Pullum, S. G., & Frisbie, W. P. (2000). Demographic models of birth outcomes and infant mortality: An alternative measurement approach. *Demography, 37*(4), 489-498.

South Carolina Department of Health and Environmental Control. (2020). *PFAS Sampling Results: Surface Water-Sourced Community Drinking Water Systems*. Retrieved from https://scdhec.gov/BOW/pfas-sampling-results

Stan Development Team. (2020). Stan. Retrieved from http://mc-stan.org/

Stan Development Team. (2021). Stan Modeling Language Users Guide and Reference Manual, Version 2.26. Retrieved from https://mc-stan.org/

Starling, A. P., Adgate, J. L., Hamman, R. F., Kechris, K., Calafat, A. M., Ye, X., & Dabelea, D. (2017). Perfluoroalkyl substances during pregnancy and offspring weight and adiposity at birth: examining mediation by maternal fasting glucose in the Healthy Start Study. *Environ Health Perspect, 125*, 067016-067011. doi:10.1289/EHP641

StataCorp. (2013a). *Stata 13 logit Command Reference Manual*. Retrieved from College Station, TX: https://www.stata.com/manuals13/rlogit.pdf

StataCorp. (2013b). *Stata 13 Margins Command Reference Manual*. Retrieved from College Station, TX: https://www.stata.com/manuals13/rmargins.pdf

StataCorp. (2019). *Stata Statistical Software: Release 16*. College Station, TX: StataCorp LP.

Steenland, K., Barry, V., & Savitz, D. (2018). *An Updated Meta-Analysis of the Association of Serum PFOA and Birthweight, with an Evaluation of Potential Biases.* Paper presented at the ISEE Conference Abstracts.

Steenland, K., Tinker, S., Frisbee, S., Ducatman, A., & Vaccarino, V. (2009). Association of perfluorooctanoic acid and perfluorooctane sulfonate with serum lipids among adults living near a chemical plant. *American journal of epidemiology, 170*(10), 1268-1278.

Steenland, K., & Woskie, S. (2012). Cohort mortality study of workers exposed to perfluorooctanoic acid. *American journal of epidemiology, 176*, 909–917.

Surveillance Research Program - National Cancer Institute. (2020a). *SEER*Stat software Incidence-Based Mortality - SEER Research Data, 18 Registries*. Retrieved from: seer.cancer.gov/seerstat

Surveillance Research Program - National Cancer Institute. (2020b). *SEER*Stat software Incidence - SEER Research Limited-Field Data, 21 Registries*. Retrieved from: seer.cancer.gov/seerstat

Thom, T., Kannel, W., Silbershatz, H., & D'Agostino, R. (2001). Cardiovascular diseases in the United States and prevention approaches. *Hurst's the heart, 1*, 3-17.

U.S. Bureau of Economic Analysis. (2021). *Disposable personal income: Per capita [A229RC0A052NBEA]*. Retrieved from: https://fred.stlouisfed.org/series/A229RC0A052NBEA

U.S. Bureau of Economic Analysis. (2022). *US BEA National Income and Product Accounts. Table 1.1.9. Implicit Price Deflators for Gross Domestic Product. [Index numbers, 2012=100]*.

U.S. Bureau of Labor Statistics. (2020). *CPI for All Urban Consumers (CPI-U) All items in U.S. city average, all urban consumers, not seasonally adjusted. Base period 1982-84-100. Series ID: CUUR0000SA0,CUUS0000SA0*. Retrieved from: https://beta.bls.gov/dataViewer/view/timeseries/CUUR0000SA0.

U.S. Census Bureau. (2017). *American Community Survey Single-Year Estimates. American Community Survey Demographic and Housing Estimates.* Retrieved from: https://data.census.gov/cedsci/

U.S. Census Bureau. (2020). *Annual County Resident Population Estimates by Age, Sex, Race, and Hispanic Origin: April 1, 2010 to July 1, 2019, downloaded at https://www2.census.gov/programs-surveys/popest/ on May 3, 2022*.

U.S. Energy Information Administration. (2021). Annual Energy Outlook 2021. Retrieved August 10, 2021 https://www.eia.gov/outlooks/aeo/

U.S. Environmental Protection Agency. (2000a). *Arsenic Occurrence in Public Drinking Water Supplies. EPA-815-D-00-001*. Washington, D.C.

U.S. Environmental Protection Agency. (2000b). *Geometries and Characteristics of Public Water Systems*. (EPA-815-R-00-24).

U.S. Environmental Protection Agency. (2001). *Water Treatment Plant Model Version 2.0*. Retrieved from https://www.epa.gov/sites/default/files/2017-03/documents/wtp_model_v._2.0_manual_508.pdf

U.S. Environmental Protection Agency. (2005). *Occurrence and Exposure Assessment for the Final Long Term 2 Enhanced Surface Water Treatment Rule, EPA 815-R-06-002*. (EPA 815-R-06-002).

U.S. Environmental Protection Agency. (2008). *Final Ozone NAAQS Regulatory Impact Analysis*. (EPA 452/R-08-003). Research Triangle Park, North Carolina

U.S. Environmental Protection Agency. (2009). *Community Water System Survey, Volume II: Detailed Tables and Survey Methodology. EPA 815-R-09-002.* Retrieved from http://nepis.epa.gov/Exe/ZyPDF.cgi?Dockey=P1009USA.txt

U.S. Environmental Protection Agency. (2010). *Guidelines for Preparing Economic Analyses*.

U.S. Environmental Protection Agency. (2011a). *The Benefits and Costs of the Clean Air Act from 1990 to 2020. Final Report - Rev. A.* Retrieved from https://www.epa.gov/sites/default/files/2015-07/documents/fullreport_rev_a.pdf

U.S. Environmental Protection Agency. (2011b). *Exposure Factors Handbook, 2011 Edition (Final)*. (EPA-600-R-09-025F). U.S. Environmental Protection Agency, Washington, DC

U.S. Environmental Protection Agency. (2012). *Revisions to the Unregulated Contaminant Monitoring Regulation (UCMR 3) for Public Water Systems; Final Rule*. Federal Register Retrieved from https://www.federalregister.gov/documents/2012/05/02/2012-9978/revisions-to-the-unregulated-contaminant-monitoring-regulation-ucmr-3-for-public-water-systems

U.S. Environmental Protection Agency. (2015). *Benefit and Cost Analysis for the Effluent Limitations Guidelines and Standards for the Steam Electric Power Generating Point Source Category*. (EPA-821-R-15-005). US EPA, Office of Water, Washington DC 20460

U.S. Environmental Protection Agency. (2016a). *Health effects support document for Perfluorooctane Sulfonate (PFOS)*. (EPA 822-R-16-002). Retrieved from https://www.epa.gov/sites/production/files/2016-05/documents/pfos_hesd_final_508.pdf

U.S. Environmental Protection Agency. (2016b). *Health effects support document for Perfluorooctanoic Acid (PFOA)*. (EPA 822-R-16-003). Retrieved from https://www.epa.gov/sites/production/files/2016-05/documents/pfoa_hesd_final-plain.pdf

U.S. Environmental Protection Agency. (2017). *Monitoring Unregulated Drinking Water Contaminants: UCMR 3 (2013-2015) Occurrence Data*. Retrieved from https://www.epa.gov/dwucmr/occurrence-data-unregulated-contaminant-monitoring-rule#3

U.S. Environmental Protection Agency. (2019). *Benefit and Cost Analysis for the Proposed Revisions to the Effluent Limitations Guidelines and Standards for the Steam Electric Power Generating Point Source Category [DCN SE07401]*. (EPA-821-R-19-011). US EPA, Office of Water, Washington, DC 20460

U.S. Environmental Protection Agency. (2021a). *Analysis of Cardiovascular Disease Risk Reduction as a Result of Reduced PFOA and PFOS Exposure in Drinking Water*. (EPA

815-D-21-001). Retrieved from https://sab.epa.gov/ords/sab/f?p=100:19:9687145615924:::RP,19:P19_ID:963

U.S. Environmental Protection Agency. (2021b). *Safe Drinking Water Information System 2021 Quarter 4 Database*. Retrieved from https://www.epa.gov/ground-water-and-drinking-water/safe-drinking-water-information-system-sdwis-federal-reporting

U.S. Environmental Protection Agency. (2022). *Review of EPA's Analyses to Support EPA's National Primary Drinking Water Rulemaking for PFAS. EPA-SAB-22-008*. Washington, D.C. Retrieved from https://sab.epa.gov/ords/sab/f?p=100:18:16490947993:::RP,18:P18_ID:2601#report

U.S. Environmental Protection Agency. (2023a). *Public Comment Draft - Toxicity Assessment and Proposed Maximum Contaminant Level Goal for Perfluorooctane Sulfonic Acid (PFOS) in Drinking Water. EPA-822-P-23-007*. Washington, D.C.

U.S. Environmental Protection Agency. (2023b). *Public Comment Draft - Toxicity Assessment and Proposed Maximum Contaminant Level Goal for Perfluorooctanoic Acid (PFOA) in Drinking Water. EPA-822-P-23-005*. Washington, D.C.

U.S. Environmental Protection Agency. (2023c). Technical Support Document - Per- and Polyfluoroalkyl Substances (PFAS) Occurrence & Contaminant Background. EPA-822-P-23-010.

U.S. Environmental Protection Agency. (2023d). *Technical Support Document - Technologies and Cost for Removing Per- and Polyfluoroalkyl Substances (PFAS) from Drinking Water. EPA-822-P-23-011*.

Uno, H., Cai, T., Pencina, M. J., D'Agostino, R. B., & Wei, L. J. (2011). On the C-statistics for evaluating overall adequacy of risk prediction procedures with censored survival data. *Stat. Med., 30*(10), 1105-1117. doi:10.1002/sim.4154

Valvi, D., Oulhote, Y., Weihe, P., Dalgård, C., Bjerve, K. S., Steuerwald, U., & Grandjean, P. (2017). Gestational diabetes and offspring birth size at elevated environmental pollutant exposures. *Environment international, 107*, 205-215.

Vermont Department of Environmental Conservation. (2021). *Per and Polyfluoroalkyl Substances (PFAS) & Drinking Water*. Retrieved from https://dec.vermont.gov/water/drinking-water/water-quality-monitoring/pfas

Verner, M. A., Loccisano, A. E., Morken, N. H., Yoon, M., Wu, H., McDougall, R., . . . Longnecker, M. P. (2015). Associations of Perfluoroalkyl Substances (PFAS) with Lower Birth Weight: An Evaluation of Potential Confounding by Glomerular Filtration Rate Using a Physiologically Based Pharmacokinetic Model (PBPK). *Environmental health perspectives, 123*(12), 1317-1324. doi:10.1289/ehp.1408837

Vieira, V. M., Hoffman, K., Shin, H., Weinberg, J. M., Webster, T. F., & Fletcher, T. (2013). Perfluorooctanoic acid exposure and cancer outcomes in a contaminated community: A geographic analysis. *Environmental health perspectives, 121*(3), 318-323.

von Hippel, P. T. (2015). The heterogeneity statistic I 2 can be biased in small meta-analyses. *BMC medical research methodology, 15*(1), 1-8.

Wan, X., Zhang, Y., Tan, C., Zeng, X., & Peng, L. (2019). First-line nivolumab plus ipilimumab vs sunitinib for metastatic renal cell carcinoma: a cost-effectiveness analysis. *JAMA Oncology, 5*(4), 491-496.

Wang, Y., Adgent, M., Su, P.-H., Chen, H.-Y., Chen, P.-C., Hsiung, C. A., & Wang, S.-L. (2016). Prenatal exposure to perfluorocarboxylic acids (PFCAs) and fetal and postnatal

growth in the Taiwan Maternal and Infant Cohort Study. *Environmental health perspectives, 124*(11), 1794-1800.
Washino, N., Saijo, Y., Sasaki, S., Kato, S., Ban, S., Konishi, K., . . . Saito, K. (2009). Correlations between prenatal exposure to perfluorinated chemicals and reduced fetal growth. *Environmental health perspectives, 117*(4), 660-667.
Whitworth, K. W., Haug, L. S., Baird, D. D., Becher, G., Hoppin, J. A., Skjaerven, R., . . . Wilson, R. (2012). Perfluorinated compounds in relation to birth weight in the Norwegian Mother and Child Cohort Study. *American journal of epidemiology, 175*(12), 1209-1216.
Whooley, M. A., De Jonge, P., Vittinghoff, E., Otte, C., Moos, R., Carney, R. M., . . . Feldman, M. D. (2008). Depressive symptoms, health behaviors, and risk of cardiovascular events in patients with coronary heart disease. *Jama, 300*(20), 2379-2388.
Wickham, H. (2007). Reshaping Data with the reshape Package. *Journal of statistical software, 21*(12), 1 - 20. doi:10.18637/jss.v021.i12
Wickham, H. (2016). *ggplot2: elegant graphics for data analysis*: springer.
Wickham, H., François, R., & Henry, L. (2020). *dplyr: A Grammar of Data Manipulation*. Retrieved from: https://CRAN.R-project.org/package=dplyr
Wikström, S., Lin, P.-I., Lindh, C. H., Shu, H., & Bornehag, C.-G. (2020). Maternal serum levels of perfluoroalkyl substances in early pregnancy and offspring birth weight. *Pediatric research, 87*(6), 1093-1099.
Wikström, S., Lindh, C. H., Shu, H., & Bornehag, C.-G. (2019). Early pregnancy serum levels of perfluoroalkyl substances and risk of preeclampsia in Swedish women. *Sci. Rep., 9*(1), 9179. doi:10.1038/s41598-019-45483-7
Williams, O. (1989). The Atherosclerosis Risk in Communities (ARIC) study-design and objectives. *American journal of epidemiology, 129*(4), 687-702.
Wilson, P. W., D'Agostino, R. B., Levy, D., Belanger, A. M., Silbershatz, H., & Kannel, W. B. (1998). Prediction of coronary heart disease using risk factor categories. *Circulation, 97*(18), 1837-1847. doi:10.1161/01.cir.97.18.1837
Workman, C. E., Becker, A. B., Azad, M. B., Moraes, T. J., Mandhane, P. J., Turvey, S. E., . . . Wong, C. S. (2019). Associations between concentrations of perfluoroalkyl substances in human plasma and maternal, infant, and home characteristics in Winnipeg, Canada. *Environmental pollution, 249*, 758-766.
World Health Organization. (2014). *Global Nutrition Targets 2025: Low Birth Weight Policy Brief*. Retrieved from https://www.who.int/publications/i/item/WHO-NMH-NHD-14.5
World Health Organization. (2018). Preterm Birth: Key Facts. Retrieved from https://www.who.int/news-room/fact-sheets/detail/preterm-birth
Wu, K., Xu, X., Peng, L., Liu, J., Guo, Y., & Huo, X. (2012). Association between maternal exposure to perfluorooctanoic acid (PFOA) from electronic waste recycling and neonatal health outcomes. *Environment international, 48*, 1-8.
Xu, C., Yin, S., Liu, Y., Chen, F., Zhong, Z., Li, F., . . . Liu, W. (2019). Prenatal exposure to chlorinated polyfluoroalkyl ether sulfonic acids and perfluoroalkyl acids: Potential role of maternal determinants and associations with birth outcomes. *Journal of hazardous materials, 380*, 120867.
Yang, Q., Guo, X., Sun, P., Chen, Y., Zhang, W., & Gao, A. (2018). Association of serum levels of perfluoroalkyl substances (PFASs) with the metabolic syndrome (MetS) in Chinese male adults: A cross–sectional study. *Science of the total environment, 621*, 1542-1549. doi:10.1016/j.scitotenv.2017.10.074

Zhang, Y., Beesoon, S., Zhu, L., & Martin, J. W. (2013). Biomonitoring of perfluoroalkyl acids in human urine and estimates of biological half-life. *Environmental Science & Technology, 47*(18), 10619-10627.