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

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Acronyms and Abbreviations

AE	Adverse Events
AHRQ	Agency for Healthcare Research and Quality
ANGIDX	Angina, or Angina Pectoris, As Defined in the Medical Exposure Panel Survey
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
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
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 Ground Water 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	Per- and Polyfluoroalkyl Substances
PFBS	Perfluorobutane Sulfonic Acid
PFHxS	Perfluorohexanesulfonic Acid
PFHpA	Perfluoroheptanoic 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 Identification
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	Water Treatment Plant

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 the EPA to estimate national occurrence of per- and polyfluoroalkyl 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). The 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. The EPA has used similar hierarchical model structures to inform analyses in previous regulatory actions (U.S. EPA, 2000; U.S. EPA, 2005b).

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), the 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. The EPA anticipates that, if temporal trends are significant, the addition of more recent state data will only bias the results towards present day.

The EPA collected state occurrence data using broad internet searches[1] and downloaded publicly available monitoring data from state government websites as of May 2023. While comprehensive information about methods used and reporting was not fully available for all of the state monitoring programs, the vast majority 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, the 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, the 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, perfluorooctanoic acid (PFOA), perfluorooctanesulfonic acid (PFOS), perfluoroheptanoic acid (PFHpA), and perfluorohexanesulfonic acid (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, 28 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, Idaho, Illinois, Indiana, Iowa, Kentucky, Maine, Massachusetts, Michigan, Missouri, New Hampshire, New Jersey, New York, North Carolina, North Dakota, Ohio, Oregon, Pennsylvania, South Carolina, Tennessee, Vermont, Virginia, West Virginia, and Wisconsin (Arizona Department of Environmental Quality, 2021;Arizona Department of Environmental Quality, 2023; California Division of Drinking Water, 2023; Colorado Department of Public Health and Environment, 2020; Delaware Office of Drinking Water, 2021; Georgia Environmnetal Protection Division, 2020; Idaho Department of Environmental Quality, 2023; Indiana Department of Environmental Management, 2023; Kentucky Department for Environmental Protection, 2019; Maine Department of Environmental Protection, 2020; Maine Department of Health and Human Services, 2023; Missouri Department of Natural Resources, 2023; New Hampshire Department of Environmental Services, 2021; New York Department of Health, 2022; North Carolina Department of Environmental Quality, 2023; North Dakota Department of Environmental Quality, 2020; North Dakota Department of Environmental Quality, 2021; Oregon Health Authority, 2022; South Carolina Department of Health and Environmental Control, 2020; South Carolina Department of Health and Environmental Control, 2023; Tennessee Department of Environment and Conservation, 2023; Vermont Department of Environmental Conservation, 2023; Virginia Department of Health, 2021; West Virginia Department of Health and Human Resources, 2023; Wisconsin Department of Natural Resources, 2023). According to state websites, these state data represent samples collected between March 2016 through May 2023.

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,

[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).

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 18,091 PFOS samples, 18,082 PFOA samples, 14,458 PFHpA samples, and 14,906 PFHxS samples collected at systems that were included in UCMR 3. Of these samples, 7,156 (40%) were reported values for PFOS, 8,257 (46%) were reported values for PFOA, 4,496 (31%) were reported values for PFHpA, and 5,041 (34%) were reported values for PFHxS. The remainder were listed as being below their respective reporting limits.

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	4	202	201	11	11
CA	85	5372	5372	5179	5179
CO	52	95	95	95	95
DE	1	34	34	0	0
GA	1	2	2	2	2
IA	23	88	88	87	87
ID	2	7	7	7	7
IL	122	763	763	756	762
IN	8	10	10	10	10
KY	23	25	25	25	25
MA	128	3445	3446	3445	3445
ME	17	30	30	30	30
MI	61	550	528	491	520
MO	5	11	11	5	5
NC	29	99	99	0	0
ND	5	5	5	5	5
NH	20	323	323	166	318
NJ	148	5053	5061	2775	2776
NY	98	1059	1059	741	743
OH	145	232	232	0	232
OR	4	4	4	4	4
PA	51	91	91	91	91
SC	44	208	208	205	204

[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: System and Sample Counts for Contributions to the Supplemental State Dataset by State

State	Systems Included	PFOS Samples	PFOA Samples	PFHpA Samples	PFHxS Samples
TN	1	2	2	2	2
VA	9	14	14	14	14
VT	10	28	28	28	28
WI	59	308	313	284	311
WV	1	31	31	0	0

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, the 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 helps 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.

The 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, the 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 the EPA and others, including for arsenic and Cryptosporidium parvum, two contaminants with considerable occurrence below reporting limits (Crainiceanu et al., 2003; Lockwood et al., 2001; Ott, 1995).

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 (SDs), within-system SDs, and fixed factor shifts of system-level means. The 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. The EPA compared these model variants using 5-fold cross validation. The EPA selected the model that performed best in the 5-fold cross validation exercise (described below).

The 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, …, nsys , nsys 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 σB 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, …,nsamp, where nsamp 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 jth sample of contaminant k collected from system i. $mu_{i,k}$ represents the k th element of mu_i shown in Equation A-3, σ_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 σ_W.

Within-system standard deviations specific to small systems were fit for PFOS and PFOA. σ_{Wsm} replaces σ_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, the EPA used within-system standard deviations pooled across both system size categories for PFHxS and PFHpA.

A.3 Model Implementation

The 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 & Mahr, 2020; Kassambara, 2020; Wickham, 2016).

Stan uses Hamiltonian Monte Carlo No-U-Turn-Sampling for Markov chain Monte Carlo. The 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. The 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. The 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.

The 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). The EPA used weakly informative prior distributions. Prior distributions serve 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 PFAS. Table B-1 describes the data elements used to assess the affected population in the 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 SDWIS/Fed 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. The 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. The 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, the 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, the EPA took the following steps:

1. For PWSs for which the 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 the 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 the 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 the EPA's SDWIS Q4 in 2021. The 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+ Sex: males, females Race/Ethnicity: non-Hispanic White, non-Hispanic Black, Hispanic, other 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, Final Rule (PFOA and PFOS MCLs of 4.0 ppt each, PFHxS, PFNA, HFPO-DA MCLs of 10 ppt each and HI of 1) (Commercial Cost of Capital, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile
Private	Ground	Less than 100	$939	$1,267	$1,641
Private	Ground	100 to 500	$1,501	$2,061	$2,725
Private	Ground	500 to 1,000	$2,555	$3,691	$5,029
Private	Ground	1,000 to 3,300	$4,422	$6,565	$9,005
Private	Ground	3,300 to 10,000	$9,947	$17,274	$25,321
Private	Ground	10,000 to 50,000	$124,300	$154,480	$187,950
Private	Ground	50,000 to 100,000	$220,850	$408,390	$634,090
Private	Ground	100,000 to 1,000,000	$387,230	$684,490	$1,114,300
Private	Surface	Less than 100	$958	$1,487	$2,089
Private	Surface	100 to 500	$1,486	$2,238	$3,012
Private	Surface	500 to 1,000	$1,970	$3,701	$5,671
Private	Surface	1,000 to 3,300	$3,260	$6,293	$9,746
Private	Surface	3,300 to 10,000	$7,796	$16,964	$28,072
Private	Surface	10,000 to 50,000	$103,870	$132,270	$162,860
Private	Surface	50,000 to 100,000	$288,750	$400,440	$522,370
Private	Surface	100,000 to 1,000,000	$1,785,000	$2,089,900	$2,416,800
Public	Ground	Less than 100	$929	$1,333	$1,792
Public	Ground	100 to 500	$1,701	$2,389	$3,181
Public	Ground	500 to 1,000	$2,844	$4,057	$5,426
Public	Ground	1,000 to 3,300	$5,456	$7,887	$10,578
Public	Ground	3,300 to 10,000	$15,003	$21,291	$27,664
Public	Ground	10,000 to 50,000	$160,790	$176,300	$193,730
Public	Ground	50,000 to 100,000	$329,880	$411,810	$495,280
Public	Ground	100,000 to 1,000,000	$1,185,700	$1,501,800	$1,879,400
Public	Surface	Less than 100	$1,056	$1,667	$2,334
Public	Surface	100 to 500	$1,823	$2,582	$3,463

Table C-1: Mean Annualized Cost per CWSs, Final Rule (PFOA and PFOS MCLs of 4.0 ppt each, PFHxS, PFNA, HFPO-DA MCLs of 10 ppt each and HI of 1) (Commercial Cost of Capital, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile
Public	Surface	500 to 1,000	$2,785	$4,196	$5,825
Public	Surface	1,000 to 3,300	$5,442	$7,815	$10,645
Public	Surface	3,300 to 10,000	$15,106	$21,231	$28,498
Public	Surface	10,000 to 50,000	$135,520	$147,870	$160,150
Public	Surface	50,000 to 100,000	$277,760	$320,770	$366,610
Public	Surface	100,000 to 1,000,000	$786,610	$906,230	$1,036,800

Abbreviations: CWS – community water system.

Table C-2: Mean Annualized Cost per CWSs, Option 1a (PFOA and PFOS MCLs of 4.0 ppt) (Commercial Cost of Capital, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile
Private	Ground	Less than 100	$938	$1,266	$1,642
Private	Ground	100 to 500	$1,498	$2,059	$2,730
Private	Ground	500 to 1,000	$2,553	$3,685	$4,977
Private	Ground	1,000 to 3,300	$4,450	$6,553	$9,191
Private	Ground	3,300 to 10,000	$9,615	$17,224	$25,362
Private	Ground	10,000 to 50,000	$122,760	$152,720	$186,520
Private	Ground	50,000 to 100,000	$202,940	$383,200	$611,860
Private	Ground	100,000 to 1,000,000	$381,440	$676,770	$1,097,600
Private	Surface	Less than 100	$958	$1,486	$2,104
Private	Surface	100 to 500	$1,519	$2,235	$3,011
Private	Surface	500 to 1,000	$1,970	$3,695	$5,667
Private	Surface	1,000 to 3,300	$3,260	$6,283	$9,634
Private	Surface	3,300 to 10,000	$8,034	$16,923	$27,898
Private	Surface	10,000 to 50,000	$103,170	$131,580	$164,420
Private	Surface	50,000 to 100,000	$289,620	$398,790	$516,720
Private	Surface	100,000 to 1,000,000	$1,731,300	$2,038,300	$2,366,900
Public	Ground	Less than 100	$928	$1,332	$1,797
Public	Ground	100 to 500	$1,713	$2,387	$3,150
Public	Ground	500 to 1,000	$2,824	$4,052	$5,391
Public	Ground	1,000 to 3,300	$5,587	$7,873	$10,569
Public	Ground	3,300 to 10,000	$14,794	$21,231	$28,281
Public	Ground	10,000 to 50,000	$159,170	$175,200	$192,570
Public	Ground	50,000 to 100,000	$326,650	$408,980	$494,290
Public	Ground	100,000 to 1,000,000	$1,136,300	$1,466,200	$1,854,700
Public	Surface	Less than 100	$1,055	$1,665	$2,364

Table C-2: Mean Annualized Cost per CWSs, Option 1a (PFOA and PFOS MCLs of 4.0 ppt) (Commercial Cost of Capital, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile
Public	Surface	100 to 500	$1,821	$2,580	$3,461
Public	Surface	500 to 1,000	$2,785	$4,191	$5,823
Public	Surface	1,000 to 3,300	$5,432	$7,805	$10,483
Public	Surface	3,300 to 10,000	$14,773	$21,198	$28,582
Public	Surface	10,000 to 50,000	$135,360	$147,320	$160,520
Public	Surface	50,000 to 100,000	$277,130	$318,760	$362,860
Public	Surface	100,000 to 1,000,000	$779,220	$899,290	$1,031,900

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, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile
Private	Ground	Less than 100	$718	$967	$1,263
Private	Ground	100 to 500	$1,131	$1,554	$2,044
Private	Ground	500 to 1,000	$1,809	$2,737	$3,777
Private	Ground	1,000 to 3,300	$3,099	$4,810	$6,784
Private	Ground	3,300 to 10,000	$6,652	$12,398	$19,600
Private	Ground	10,000 to 50,000	$92,034	$117,230	$144,560
Private	Ground	50,000 to 100,000	$137,230	$283,530	$460,060
Private	Ground	100,000 to 1,000,000	$233,870	$460,410	$801,970
Private	Surface	Less than 100	$734	$1,157	$1,654
Private	Surface	100 to 500	$1,167	$1,714	$2,353
Private	Surface	500 to 1,000	$1,401	$2,759	$4,482
Private	Surface	1,000 to 3,300	$2,204	$4,595	$7,487
Private	Surface	3,300 to 10,000	$4,846	$12,161	$21,309
Private	Surface	10,000 to 50,000	$77,607	$100,900	$126,000
Private	Surface	50,000 to 100,000	$225,330	$321,250	$428,230
Private	Surface	100,000 to 1,000,000	$1,366,200	$1,648,800	$1,926,000
Public	Ground	Less than 100	$719	$1,013	$1,381
Public	Ground	100 to 500	$1,258	$1,786	$2,387
Public	Ground	500 to 1,000	$2,022	$2,978	$4,065
Public	Ground	1,000 to 3,300	$3,901	$5,734	$7,856
Public	Ground	3,300 to 10,000	$10,432	$15,276	$20,537
Public	Ground	10,000 to 50,000	$124,670	$138,230	$152,390
Public	Ground	50,000 to 100,000	$249,490	$318,880	$391,610
Public	Ground	100,000 to 1,000,000	$933,800	$1,203,700	$1,526,500

Table C-3: Mean Annualized Cost per CWSs, Option 1b (PFOA and PFOS MCLs of 5.0 ppt) (Commercial Cost of Capital, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile
Public	Surface	Less than 100	$794	$1,305	$1,869
Public	Surface	100 to 500	$1,339	$1,953	$2,637
Public	Surface	500 to 1,000	$2,039	$3,111	$4,422
Public	Surface	1,000 to 3,300	$3,702	$5,653	$7,798
Public	Surface	3,300 to 10,000	$10,766	$15,438	$21,019
Public	Surface	10,000 to 50,000	$103,590	$113,280	$123,480
Public	Surface	50,000 to 100,000	$202,770	$237,580	$272,480
Public	Surface	100,000 to 1,000,000	$580,900	$680,330	$788,060

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, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile
Private	Ground	Less than 100	$351	$443	$556
Private	Ground	100 to 500	$510	$673	$870
Private	Ground	500 to 1,000	$710	$1,069	$1,512
Private	Ground	1,000 to 3,300	$1,031	$1,748	$2,638
Private	Ground	3,300 to 10,000	$1,519	$4,104	$7,570
Private	Ground	10,000 to 50,000	$29,721	$42,855	$58,605
Private	Ground	50,000 to 100,000	$23,945	$80,063	$172,570
Private	Ground	100,000 to 1,000,000	$9,293	$78,509	$201,680
Private	Surface	Less than 100	$398	$579	$826
Private	Surface	100 to 500	$554	$800	$1,091
Private	Surface	500 to 1,000	$509	$1,153	$2,015
Private	Surface	1,000 to 3,300	$669	$1,697	$3,195
Private	Surface	3,300 to 10,000	$722	$3,874	$8,528
Private	Surface	10,000 to 50,000	$26,425	$38,368	$52,390
Private	Surface	50,000 to 100,000	$96,644	$154,310	$219,820
Private	Surface	100,000 to 1,000,000	$534,870	$702,270	$888,110
Public	Ground	Less than 100	$339	$463	$631
Public	Ground	100 to 500	$547	$736	$970
Public	Ground	500 to 1,000	$746	$1,106	$1,538
Public	Ground	1,000 to 3,300	$1,321	$1,981	$2,753
Public	Ground	3,300 to 10,000	$2,908	$4,826	$7,007
Public	Ground	10,000 to 50,000	$50,563	$57,131	$64,403

Table C-4: Mean Annualized Cost per CWSs, Option 1c (PFOA and PFOS MCLs of 10.0 ppt) (Commercial Cost of Capital, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile
Public	Ground	50,000 to 100,000	$97,827	$134,570	$174,320
Public	Ground	100,000 to 1,000,000	$430,830	$589,690	$757,930
Public	Surface	Less than 100	$408	$605	$906
Public	Surface	100 to 500	$593	$842	$1,148
Public	Surface	500 to 1,000	$743	$1,198	$1,739
Public	Surface	1,000 to 3,300	$1,151	$1,872	$2,741
Public	Surface	3,300 to 10,000	$3,140	$4,891	$7,248
Public	Surface	10,000 to 50,000	$38,452	$43,249	$48,396
Public	Surface	50,000 to 100,000	$63,513	$79,507	$96,985
Public	Surface	100,000 to 1,000,000	$211,710	$257,300	$310,390

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, Final Rule (PFOA and PFOS MCLs of 4.0 ppt each, PFHxS, PFNA, HFPO-DA MCLs of 10 ppt each and HI of 1) (Commercial Cost of Capital, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile
Private	Ground	Less than 100	$1,062	$1,425	$1,830
Private	Ground	100 to 500	$1,471	$2,053	$2,687
Private	Ground	500 to 1,000	$2,287	$3,463	$4,914
Private	Ground	1,000 to 3,300	$3,260	$5,798	$8,707
Private	Ground	3,300 to 10,000	$2,630	$14,634	$31,213
Private	Ground	10,000 to 50,000	$255	$83,271	$373,990
Private	Surface	Less than 100	$897	$1,574	$2,399
Private	Surface	100 to 500	$1,298	$2,464	$3,792
Private	Surface	500 to 1,000	$1,171	$4,275	$7,999
Private	Surface	1,000 to 3,300	$2,078	$6,699	$13,201
Private	Surface	3,300 to 10,000	$3,041	$21,674	$47,898
Private	Surface	10,000 to 50,000	$13,117	$105,950	$228,120
Private	Surface	100,000 to 1,000,000	$485	$406,490	$2,626,200
Public	Ground	Less than 100	$1,010	$1,463	$1,960
Public	Ground	100 to 500	$1,604	$2,277	$3,085
Public	Ground	500 to 1,000	$2,197	$3,504	$4,807
Public	Ground	1,000 to 3,300	$3,660	$6,348	$9,589

Table C-5: Mean Annualized Cost per NTNCWS, Final Rule (PFOA and PFOS MCLs of 4.0 ppt each, PFHxS, PFNA, HFPO-DA MCLs of 10 ppt each and HI of 1) (Commercial Cost of Capital, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile
Public	Ground	3,300 to 10,000	$520	$18,575	$43,571
Public	Ground	10,000 to 50,000	$76,609	$178,600	$318,660
Public	Surface	Less than 100	$649	$1,639	$2,937
Public	Surface	100 to 500	$1,123	$2,706	$4,634
Public	Surface	500 to 1,000	$460	$3,887	$9,499
Public	Surface	1,000 to 3,300	$1,880	$9,134	$19,778
Public	Surface	3,300 to 10,000	$673	$21,796	$53,103
Public	Surface	10,000 to 50,000	$1,058	$116,200	$287,200
Public	Surface	50,000 to 100,000	$320	$164,980	$813,410

Abbreviations: NTNCWS – non-transient, non-community water systems.

Table C-6: Mean Annualized Cost per NTNCWS, Option 1a (PFOA and PFOS MCLs of 4.0 ppt) (Commercial Cost of Capital, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile
Private	Ground	Less than 100	$1,060	$1,423	$1,842
Private	Ground	100 to 500	$1,470	$2,050	$2,685
Private	Ground	500 to 1,000	$2,258	$3,458	$4,910
Private	Ground	1,000 to 3,300	$3,257	$5,791	$8,707
Private	Ground	3,300 to 10,000	$2,629	$14,610	$31,213
Private	Ground	10,000 to 50,000	$255	$83,273	$374,330
Private	Surface	Less than 100	$897	$1,573	$2,377
Private	Surface	100 to 500	$1,298	$2,461	$3,874
Private	Surface	500 to 1,000	$1,347	$4,264	$7,990
Private	Surface	1,000 to 3,300	$2,078	$6,683	$13,196
Private	Surface	3,300 to 10,000	$3,022	$21,562	$47,812
Private	Surface	10,000 to 50,000	$11,769	$105,060	$228,110
Private	Surface	100,000 to 1,000,000	$485	$406,000	$2,626,200
Public	Ground	Less than 100	$1,039	$1,461	$1,950
Public	Ground	100 to 500	$1,604	$2,275	$3,037
Public	Ground	500 to 1,000	$2,273	$3,501	$4,961
Public	Ground	1,000 to 3,300	$3,658	$6,339	$9,547
Public	Ground	3,300 to 10,000	$574	$18,542	$43,571
Public	Ground	10,000 to 50,000	$72,552	$177,870	$310,330
Public	Surface	Less than 100	$622	$1,638	$2,937
Public	Surface	100 to 500	$1,121	$2,703	$4,626
Public	Surface	500 to 1,000	$461	$3,880	$9,499

Table C-6: Mean Annualized Cost per NTNCWS, Option 1a (PFOA and PFOS MCLs of 4.0 ppt) (Commercial Cost of Capital, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile
Public	Surface	1,000 to 3,300	$1,836	$9,111	$19,774
Public	Surface	3,300 to 10,000	$685	$21,710	$53,501
Public	Surface	10,000 to 50,000	$1,047	$115,670	$287,190
Public	Surface	50,000 to 100,000	$320	$164,520	$819,920

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, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile
Private	Ground	Less than 100	$819	$1,091	$1,430
Private	Ground	100 to 500	$1,095	$1,546	$2,055
Private	Ground	500 to 1,000	$1,588	$2,550	$3,610
Private	Ground	1,000 to 3,300	$2,258	$4,238	$6,734
Private	Ground	3,300 to 10,000	$466	$10,549	$24,325
Private	Ground	10,000 to 50,000	$255	$64,926	$373,930
Private	Surface	Less than 100	$665	$1,230	$1,940
Private	Surface	100 to 500	$940	$1,897	$3,071
Private	Surface	500 to 1,000	$738	$3,205	$6,722
Private	Surface	1,000 to 3,300	$1,304	$4,925	$10,264
Private	Surface	3,300 to 10,000	$1,025	$15,634	$38,552
Private	Surface	10,000 to 50,000	$5,939	$81,784	$192,730
Private	Surface	100,000 to 1,000,000	$485	$281,790	$2,611,200
Public	Ground	Less than 100	$772	$1,116	$1,507
Public	Ground	100 to 500	$1,179	$1,700	$2,332
Public	Ground	500 to 1,000	$1,525	$2,567	$3,719
Public	Ground	1,000 to 3,300	$2,423	$4,607	$7,302
Public	Ground	3,300 to 10,000	$451	$13,317	$35,147
Public	Ground	10,000 to 50,000	$56,010	$143,490	$253,510
Public	Surface	Less than 100	$423	$1,268	$2,433
Public	Surface	100 to 500	$756	$2,052	$3,752
Public	Surface	500 to 1,000	$434	$2,885	$7,980
Public	Surface	1,000 to 3,300	$719	$6,669	$15,289
Public	Surface	3,300 to 10,000	$616	$15,623	$44,557
Public	Surface	10,000 to 50,000	$900	$87,432	$254,310
Public	Surface	50,000 to 100,000	$320	$119,290	$792,860

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, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile
Private	Ground	Less than 100	$396	$503	$626
Private	Ground	100 to 500	$493	$655	$872
Private	Ground	500 to 1,000	$554	$944	$1,453
Private	Ground	1,000 to 3,300	$622	$1,526	$2,711
Private	Ground	3,300 to 10,000	$373	$3,354	$10,888
Private	Ground	10,000 to 50,000	$255	$25,077	$270,500
Private	Surface	Less than 100	$391	$621	$967
Private	Surface	100 to 500	$481	$881	$1,473
Private	Surface	500 to 1,000	$556	$1,357	$3,384
Private	Surface	1,000 to 3,300	$560	$1,776	$5,059
Private	Surface	3,300 to 10,000	$801	$5,493	$19,049
Private	Surface	10,000 to 50,000	$1,537	$33,245	$107,290
Private	Surface	100,000 to 1,000,000	$485	$70,346	$2,253
Public	Ground	Less than 100	$364	$514	$692
Public	Ground	100 to 500	$502	$703	$968
Public	Ground	500 to 1,000	$526	$938	$1,468
Public	Ground	1,000 to 3,300	$620	$1,569	$2,815
Public	Ground	3,300 to 10,000	$392	$4,109	$14,446
Public	Ground	10,000 to 50,000	$1,172	$60,734	$135,230
Public	Surface	Less than 100	$360	$605	$1,214
Public	Surface	100 to 500	$467	$921	$1,850
Public	Surface	500 to 1,000	$406	$1,151	$3,866
Public	Surface	1,000 to 3,300	$624	$2,378	$7,248
Public	Surface	3,300 to 10,000	$565	$5,137	$20,873
Public	Surface	10,000 to 50,000	$799	$31,077	$129,900
Public	Surface	50,000 to 100,000	$320	$28,907	$1,192

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, Final Rule (PFOA and PFOS MCLs of 4.0 ppt each, PFHxS, PFNA, HFPO-DA MCLs of 10 ppt each and HI of 1) (Commercial Cost of Capital, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile
Private	Ground	Less than 100	$17,069	$18,234	$20,341
Private	Ground	100 to 500	$26,064	$28,544	$32,445
Private	Ground	500 to 1,000	$42,741	$48,767	$55,660
Private	Ground	1,000 to 3,300	$70,091	$82,118	$94,266
Private	Ground	3,300 to 10,000	$154,050	$197,420	$245,690
Private	Ground	10,000 to 50,000	$406,670	$480,910	$558,610
Private	Ground	50,000 to 100,000	$821,410	$1,181,000	$1,638,200
Private	Ground	100,000 to 1,000,000	$832,170	$1,336,100	$2,082,500
Private	Surface	Less than 100	$16,415	$20,279	$24,844
Private	Surface	100 to 500	$26,031	$30,894	$36,481
Private	Surface	500 to 1,000	$38,491	$51,538	$66,115
Private	Surface	1,000 to 3,300	$65,675	$89,941	$119,330
Private	Surface	3,300 to 10,000	$138,490	$204,110	$282,990
Private	Surface	10,000 to 50,000	$462,160	$545,250	$646,910
Private	Surface	50,000 to 100,000	$955,880	$1,221,100	$1,520,900
Private	Surface	100,000 to 1,000,000	$3,434,000	$4,068,900	$4,778,600
Public	Ground	Less than 100	$17,122	$19,489	$22,283
Public	Ground	100 to 500	$30,915	$34,127	$38,672
Public	Ground	500 to 1,000	$50,185	$55,639	$62,416
Public	Ground	1,000 to 3,300	$92,430	$101,270	$111,700
Public	Ground	3,300 to 10,000	$204,820	$227,420	$250,830
Public	Ground	10,000 to 50,000	$536,600	$577,270	$624,280
Public	Ground	50,000 to 100,000	$1,059,500	$1,245,500	$1,432,900
Public	Ground	100,000 to 1,000,000	$3,193,800	$3,953,500	$4,810,300
Public	Surface	Less than 100	$17,258	$21,668	$26,782
Public	Surface	100 to 500	$32,031	$36,806	$42,508
Public	Surface	500 to 1,000	$51,310	$60,222	$69,960
Public	Surface	1,000 to 3,300	$101,320	$113,880	$127,150
Public	Surface	3,300 to 10,000	$245,060	$272,710	$300,950
Public	Surface	10,000 to 50,000	$559,260	$591,960	$627,160
Public	Surface	50,000 to 100,000	$1,045,200	$1,145,300	$1,250,900
Public	Surface	100,000 to 1,000,000	$2,444,300	$2,730,100	$3,038,100

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 4.0 ppt) (Commercial Cost of Capital, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile
Private	Ground	Less than 100	$17,045	$18,229	$20,315
Private	Ground	100 to 500	$26,062	$28,529	$32,248
Private	Ground	500 to 1,000	$42,668	$48,726	$55,660
Private	Ground	1,000 to 3,300	$70,579	$82,038	$94,258
Private	Ground	3,300 to 10,000	$154,500	$197,170	$245,670
Private	Ground	10,000 to 50,000	$402,560	$476,330	$559,570
Private	Ground	50,000 to 100,000	$753,860	$1,103,900	$1,554,600
Private	Ground	100,000 to 1,000,000	$831,540	$1,321,800	$2,082,000
Private	Surface	Less than 100	$16,329	$20,276	$24,844
Private	Surface	100 to 500	$26,031	$30,878	$36,318
Private	Surface	500 to 1,000	$38,391	$51,502	$66,090
Private	Surface	1,000 to 3,300	$65,916	$89,852	$119,330
Private	Surface	3,300 to 10,000	$138,690	$203,870	$284,260
Private	Surface	10,000 to 50,000	$453,760	$542,640	$644,220
Private	Surface	50,000 to 100,000	$956,050	$1,216,600	$1,515,400
Private	Surface	100,000 to 1,000,000	$3,350,100	$3,968,400	$4,676,400
Public	Ground	Less than 100	$17,105	$19,483	$22,254
Public	Ground	100 to 500	$30,913	$34,114	$38,744
Public	Ground	500 to 1,000	$50,275	$55,606	$62,017
Public	Ground	1,000 to 3,300	$92,102	$101,180	$111,050
Public	Ground	3,300 to 10,000	$203,340	$227,150	$251,310
Public	Ground	10,000 to 50,000	$532,140	$574,040	$621,150
Public	Ground	50,000 to 100,000	$1,054,300	$1,237,700	$1,424,300
Public	Ground	100,000 to 1,000,000	$3,106,900	$3,863,500	$4,706,400
Public	Surface	Less than 100	$17,121	$21,663	$26,702
Public	Surface	100 to 500	$32,031	$36,793	$42,498
Public	Surface	500 to 1,000	$51,387	$60,190	$69,800
Public	Surface	1,000 to 3,300	$101,440	$113,830	$126,210
Public	Surface	3,300 to 10,000	$245,950	$272,540	$300,750
Public	Surface	10,000 to 50,000	$556,580	$590,090	$625,700
Public	Surface	50,000 to 100,000	$1,044,100	$1,138,600	$1,243,900
Public	Surface	100,000 to 1,000,000	$2,437,300	$2,710,800	$3,009,900

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, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile
Private	Ground	Less than 100	$16,944	$18,186	$20,183
Private	Ground	100 to 500	$25,801	$28,381	$32,205
Private	Ground	500 to 1,000	$41,940	$48,235	$55,777
Private	Ground	1,000 to 3,300	$68,304	$80,715	$95,280
Private	Ground	3,300 to 10,000	$143,480	$192,440	$245,560
Private	Ground	10,000 to 50,000	$359,950	$438,390	$526,620
Private	Ground	50,000 to 100,000	$615,410	$948,460	$1,392,700
Private	Ground	100,000 to 1,000,000	$592,580	$1,050,700	$1,666,100
Private	Surface	Less than 100	$15,352	$20,226	$25,790
Private	Surface	100 to 500	$25,187	$30,707	$36,861
Private	Surface	500 to 1,000	$35,312	$50,902	$69,988
Private	Surface	1,000 to 3,300	$61,201	$88,843	$122,710
Private	Surface	3,300 to 10,000	$125,770	$199,450	$288,180
Private	Surface	10,000 to 50,000	$425,910	$517,180	$619,540
Private	Surface	50,000 to 100,000	$903,940	$1,187,900	$1,530,900
Private	Surface	100,000 to 1,000,000	$2,983,000	$3,596,100	$4,295,000
Public	Ground	Less than 100	$16,725	$19,436	$22,825
Public	Ground	100 to 500	$30,519	$33,905	$38,294
Public	Ground	500 to 1,000	$49,063	$55,040	$61,899
Public	Ground	1,000 to 3,300	$90,153	$99,584	$110,890
Public	Ground	3,300 to 10,000	$194,730	$219,840	$245,950
Public	Ground	10,000 to 50,000	$500,080	$541,560	$585,800
Public	Ground	50,000 to 100,000	$984,600	$1,176,400	$1,382,200
Public	Ground	100,000 to 1,000,000	$2,976,200	$3,699,500	$4,589,800
Public	Surface	Less than 100	$16,658	$21,625	$27,893
Public	Surface	100 to 500	$30,778	$36,528	$42,197
Public	Surface	500 to 1,000	$50,009	$59,678	$70,593
Public	Surface	1,000 to 3,300	$97,524	$112,380	$127,200
Public	Surface	3,300 to 10,000	$237,730	$268,390	$300,680
Public	Surface	10,000 to 50,000	$535,660	$569,340	$605,460
Public	Surface	50,000 to 100,000	$964,720	$1,070,500	$1,176,500
Public	Surface	100,000 to 1,000,000	$2,209,200	$2,490,600	$2,798,400

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, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile
Private	Ground	Less than 100	$16,187	$18,039	$20,295
Private	Ground	100 to 500	$24,624	$27,953	$32,203
Private	Ground	500 to 1,000	$36,548	$46,598	$57,978
Private	Ground	1,000 to 3,300	$56,592	$76,752	$99,883
Private	Ground	3,300 to 10,000	$98,819	$176,800	$276,220
Private	Ground	10,000 to 50,000	$239,310	$324,260	$419,790
Private	Ground	50,000 to 100,000	$174,140	$435,320	$800,260
Private	Ground	100,000 to 1,000,000	$0	$507,980	$1,175,000
Private	Surface	Less than 100	$14,097	$19,438	$31,100
Private	Surface	100 to 500	$21,045	$30,103	$41,645
Private	Surface	500 to 1,000	$0	$46,865	$82,138
Private	Surface	1,000 to 3,300	$38,218	$83,454	$147,830
Private	Surface	3,300 to 10,000	$33,649	$175,380	$342,640
Private	Surface	10,000 to 50,000	$313,190	$418,160	$549,020
Private	Surface	50,000 to 100,000	$739,270	$1,151,400	$1,661,200
Private	Surface	100,000 to 1,000,000	$1,983,800	$2,659,800	$3,430,300
Public	Ground	Less than 100	$15,074	$19,344	$25,334
Public	Ground	100 to 500	$28,359	$33,254	$38,562
Public	Ground	500 to 1,000	$44,109	$53,122	$62,386
Public	Ground	1,000 to 3,300	$81,392	$94,806	$110,780
Public	Ground	3,300 to 10,000	$162,180	$200,800	$243,170
Public	Ground	10,000 to 50,000	$403,050	$446,600	$493,580
Public	Ground	50,000 to 100,000	$800,390	$1,030,600	$1,305,800
Public	Ground	100,000 to 1,000,000	$2,533,900	$3,560,800	$4,827,400
Public	Surface	Less than 100	$13,493	$20,325	$33,607
Public	Surface	100 to 500	$27,077	$35,995	$46,563
Public	Surface	500 to 1,000	$41,856	$58,095	$76,850
Public	Surface	1,000 to 3,300	$82,653	$108,100	$135,510
Public	Surface	3,300 to 10,000	$211,580	$257,220	$310,940
Public	Surface	10,000 to 50,000	$479,020	$522,730	$567,080
Public	Surface	50,000 to 100,000	$710,630	$831,140	$960,360
Public	Surface	100,000 to 1,000,000	$1,681,100	$1,948,700	$2,250,100

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, Final Rule (PFOA and PFOS MCLs of 4.0 ppt each, PFHxS, PFNA, HFPO-DA MCLs of 10 ppt each and HI of 1) (Commercial Cost of Capital, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile
Private	Ground	Less than 100	$18,125	$19,394	$21,513
Private	Ground	100 to 500	$26,112	$28,871	$32,747
Private	Ground	500 to 1,000	$41,173	$48,876	$56,797
Private	Ground	1,000 to 3,300	$61,540	$79,960	$101,090
Private	Ground	3,300 to 10,000	$94,778	$198,840	$334,310
Private	Ground	10,000 to 50,000	$0	$153,320	$747,450
Private	Surface	Less than 100	$14,470	$19,966	$26,745
Private	Surface	100 to 500	$22,702	$31,823	$43,690
Private	Surface	500 to 1,000	$27,919	$52,731	$89,480
Private	Surface	1,000 to 3,300	$46,653	$90,370	$151,200
Private	Surface	3,300 to 10,000	$61,259	$201,560	$362,440
Private	Surface	10,000 to 50,000	$80,420	$344,440	$635,510
Private	Surface	100,000 to 1,000,000	$0	$405,770	$2,626,200
Public	Ground	Less than 100	$17,587	$20,244	$23,461
Public	Ground	100 to 500	$29,859	$33,627	$38,060
Public	Ground	500 to 1,000	$46,021	$54,139	$63,827
Public	Ground	1,000 to 3,300	$73,407	$93,702	$117,030
Public	Ground	3,300 to 10,000	$0	$226,260	$450,430
Public	Ground	10,000 to 50,000	$354,000	$583,990	$886,520
Public	Surface	Less than 100	$14,436	$21,607	$35,667
Public	Surface	100 to 500	$22,321	$35,767	$53,193
Public	Surface	500 to 1,000	$0	$48,161	$103,640
Public	Surface	1,000 to 3,300	$42,909	$109,430	$198,840
Public	Surface	3,300 to 10,000	$0	$218,700	$432,330
Public	Surface	10,000 to 50,000	$0	$496,320	$1,058,900
Public	Surface	50,000 to 100,000	$0	$164,480	$813,410

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 4.0 ppt) (Commercial Cost of Capital, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile
Private	Ground	Less than 100	$18,107	$19,382	$21,454
Private	Ground	100 to 500	$26,166	$28,855	$32,634
Private	Ground	500 to 1,000	$41,173	$48,850	$57,065
Private	Ground	1,000 to 3,300	$62,677	$79,915	$99,887
Private	Ground	3,300 to 10,000	$94,778	$198,790	$334,310
Private	Ground	10,000 to 50,000	$0	$153,370	$747,450
Private	Surface	Less than 100	$14,470	$19,961	$27,243
Private	Surface	100 to 500	$22,702	$31,808	$43,690
Private	Surface	500 to 1,000	$28,203	$52,680	$89,480
Private	Surface	1,000 to 3,300	$46,415	$90,272	$156,990
Private	Surface	3,300 to 10,000	$61,841	$201,080	$371,800
Private	Surface	10,000 to 50,000	$80,395	$341,770	$674,000
Private	Surface	100,000 to 1,000,000	$0	$405,290	$2,626,200
Public	Ground	Less than 100	$17,571	$20,235	$23,461
Public	Ground	100 to 500	$29,855	$33,613	$38,060
Public	Ground	500 to 1,000	$46,021	$54,116	$63,827
Public	Ground	1,000 to 3,300	$73,407	$93,646	$118,760
Public	Ground	3,300 to 10,000	$0	$226,060	$450,430
Public	Ground	10,000 to 50,000	$344,310	$581,700	$892,940
Public	Surface	Less than 100	$14,568	$21,588	$34,339
Public	Surface	100 to 500	$22,808	$35,742	$53,625
Public	Surface	500 to 1,000	$0	$48,080	$110,060
Public	Surface	1,000 to 3,300	$46,115	$109,240	$198,840
Public	Surface	3,300 to 10,000	$0	$218,000	$432,330
Public	Surface	10,000 to 50,000	$0	$494,380	$1,058,900
Public	Surface	50,000 to 100,000	$0	$164,030	$813,410

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, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile
Private	Ground	Less than 100	$17,868	$19,332	$21,416
Private	Ground	100 to 500	$25,641	$28,705	$32,721
Private	Ground	500 to 1,000	$39,619	$48,074	$58,246
Private	Ground	1,000 to 3,300	$59,279	$79,088	$103,620
Private	Ground	3,300 to 10,000	$0	$187,240	$353,360
Private	Ground	10,000 to 50,000	$0	$121,770	$747,450
Private	Surface	Less than 100	$14,121	$19,889	$28,660
Private	Surface	100 to 500	$21,471	$31,606	$45,109
Private	Surface	500 to 1,000	$0	$50,236	$96,546
Private	Surface	1,000 to 3,300	$39,623	$87,040	$160,550
Private	Surface	3,300 to 10,000	$0	$185,300	$395,900
Private	Surface	10,000 to 50,000	$49,308	$312,590	$645,540
Private	Surface	100,000 to 1,000,000	$0	$281,060	$2,611,200
Public	Ground	Less than 100	$17,264	$20,174	$23,615
Public	Ground	100 to 500	$29,340	$33,471	$38,413
Public	Ground	500 to 1,000	$44,370	$53,869	$63,845
Public	Ground	1,000 to 3,300	$69,070	$92,799	$121,850
Public	Ground	3,300 to 10,000	$0	$204,330	$450,430
Public	Ground	10,000 to 50,000	$320,530	$564,510	$934,820
Public	Surface	Less than 100	$0	$20,246	$38,340
Public	Surface	100 to 500	$20,146	$34,922	$55,444
Public	Surface	500 to 1,000	$0	$41,467	$112,980
Public	Surface	1,000 to 3,300	$0	$101,530	$204,050
Public	Surface	3,300 to 10,000	$0	$192,000	$449,400
Public	Surface	10,000 to 50,000	$0	$429,680	$1,045,500
Public	Surface	50,000 to 100,000	$0	$118,780	$792,860

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, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile
Private	Ground	Less than 100	$16,701	$19,048	$21,947
Private	Ground	100 to 500	$23,921	$28,137	$33,235
Private	Ground	500 to 1,000	$32,668	$46,118	$63,177
Private	Ground	1,000 to 3,300	$42,426	$74,725	$126,040
Private	Ground	3,300 to 10,000	$0	$111,920	$300,960
Private	Ground	10,000 to 50,000	$0	$48,529	$540,710
Private	Surface	Less than 100	$0	$16,884	$34,969
Private	Surface	100 to 500	$0	$26,855	$57,097
Private	Surface	500 to 1,000	$0	$30,398	$95,051
Private	Surface	1,000 to 3,300	$0	$53,774	$174,080
Private	Surface	3,300 to 10,000	$0	$109,750	$362,260
Private	Surface	10,000 to 50,000	$0	$197,870	$641,740
Private	Surface	100,000 to 1,000,000	$0	$69,622	$0
Public	Ground	Less than 100	$15,092	$19,867	$26,321
Public	Ground	100 to 500	$26,580	$32,932	$39,958
Public	Ground	500 to 1,000	$38,268	$52,281	$70,819
Public	Ground	1,000 to 3,300	$52,381	$89,382	$144,700
Public	Ground	3,300 to 10,000	$0	$105,680	$392,840
Public	Ground	10,000 to 50,000	$0	$475,260	$991,080
Public	Surface	Less than 100	$0	$10,828	$33,753
Public	Surface	100 to 500	$0	$23,143	$62,659
Public	Surface	500 to 1,000	$0	$17,870	$87,218
Public	Surface	1,000 to 3,300	$0	$55,142	$192,870
Public	Surface	3,300 to 10,000	$0	$88,754	$349,690
Public	Surface	10,000 to 50,000	$0	$210,300	$864,930
Public	Surface	50,000 to 100,000	$0	$28,417	$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, Final Rule (PFOA and PFOS MCLs of 4.0 ppt each, PFHxS, PFNA, HFPO-DA MCLs of 10 ppt each and HI of 1) (Commercial Cost of Capital, $2022)

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	$162	$162	$221	$285	$858
Private	Ground	100 to 500	$190	$190	$316	$441	$1,095
Private	Ground	500 to 1,000	$183	$184	$311	$606	$1,549
Private	Ground	1,000 to 3,300	$190	$207	$357	$776	$3,141
Private	Ground	3,300 to 10,000	$185	$281	$458	$964	$12,678
Private	Surface	Less than 100	$250	$250	$323	$429	$1,157
Private	Surface	100 to 500	$283	$283	$417	$534	$1,297
Private	Surface	500 to 1,000	$269	$269	$444	$689	$2,228
Private	Surface	1,000 to 3,300	$259	$259	$433	$751	$2,436
Private	Surface	3,300 to 10,000	$196	$228	$360	$839	$14,797
Public	Ground	Less than 100	$162	$162	$219	$285	$867
Public	Ground	100 to 500	$190	$190	$317	$427	$1,106
Public	Ground	500 to 1,000	$183	$184	$311	$545	$1,387
Public	Ground	1,000 to 3,300	$190	$207	$355	$733	$2,726
Public	Ground	3,300 to 10,000	$185	$289	$494	$980	$16,246
Public	Surface	Less than 100	$250	$250	$351	$449	$1,232
Public	Surface	100 to 500	$283	$283	$414	$519	$1,271
Public	Surface	500 to 1,000	$269	$269	$447	$685	$1,559
Public	Surface	1,000 to 3,300	$259	$259	$433	$727	$1,783
Public	Surface	3,300 to 10,000	$196	$198	$323	$666	$5,027

Abbreviations: CWS – community water system.

Table C-18: Distribution of Annualized Cost for Small CWSs, Option 1a (PFOA and PFOS MCLs of 4.0 ppt) (Commercial Cost of Capital, $2022)

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	$162	$162	$219	$285	$859
Private	Ground	100 to 500	$190	$190	$316	$438	$1,092
Private	Ground	500 to 1,000	$183	$184	$311	$603	$1,541
Private	Ground	1,000 to 3,300	$190	$206	$357	$771	$3,053
Private	Ground	3,300 to 10,000	$185	$281	$456	$959	$12,639
Private	Surface	Less than 100	$250	$250	$322	$429	$1,157
Private	Surface	100 to 500	$283	$283	$415	$534	$1,298
Private	Surface	500 to 1,000	$269	$269	$443	$685	$2,226
Private	Surface	1,000 to 3,300	$259	$259	$433	$747	$2,405
Private	Surface	3,300 to 10,000	$196	$227	$359	$833	$14,755
Public	Ground	Less than 100	$162	$162	$218	$284	$866
Public	Ground	100 to 500	$190	$190	$317	$425	$1,105
Public	Ground	500 to 1,000	$183	$184	$311	$542	$1,396
Public	Ground	1,000 to 3,300	$190	$206	$354	$728	$2,629
Public	Ground	3,300 to 10,000	$185	$289	$491	$974	$16,056
Public	Surface	Less than 100	$250	$250	$350	$449	$1,231
Public	Surface	100 to 500	$283	$283	$413	$518	$1,270
Public	Surface	500 to 1,000	$269	$269	$447	$682	$1,555
Public	Surface	1,000 to 3,300	$259	$259	$433	$723	$1,803
Public	Surface	3,300 to 10,000	$196	$198	$323	$662	$4,974

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, $2022)

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	$162	$162	$218	$281	$759
Private	Ground	100 to 500	$190	$190	$316	$379	$939
Private	Ground	500 to 1,000	$183	$184	$310	$554	$1,067
Private	Ground	1,000 to 3,300	$190	$206	$354	$678	$1,360
Private	Ground	3,300 to 10,000	$185	$281	$444	$880	$2,410
Private	Surface	Less than 100	$250	$250	$320	$420	$950
Private	Surface	100 to 500	$283	$283	$413	$484	$1,181
Private	Surface	500 to 1,000	$269	$269	$443	$595	$1,294
Private	Surface	1,000 to 3,300	$259	$259	$433	$676	$1,295
Private	Surface	3,300 to 10,000	$196	$227	$340	$724	$3,021
Public	Ground	Less than 100	$162	$162	$218	$281	$744
Public	Ground	100 to 500	$190	$190	$316	$371	$945
Public	Ground	500 to 1,000	$183	$184	$310	$502	$1,008
Public	Ground	1,000 to 3,300	$190	$206	$353	$649	$1,296
Public	Ground	3,300 to 10,000	$185	$288	$475	$895	$2,274
Public	Surface	Less than 100	$250	$250	$349	$425	$997
Public	Surface	100 to 500	$283	$283	$410	$480	$1,170
Public	Surface	500 to 1,000	$269	$269	$447	$590	$1,212
Public	Surface	1,000 to 3,300	$259	$259	$433	$656	$1,242
Public	Surface	3,300 to 10,000	$196	$198	$321	$564	$1,319

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, $2022)

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	$162	$162	$216	$281	$359
Private	Ground	100 to 500	$190	$190	$315	$352	$608
Private	Ground	500 to 1,000	$183	$184	$310	$487	$806
Private	Ground	1,000 to 3,300	$190	$206	$353	$609	$961
Private	Ground	3,300 to 10,000	$185	$281	$421	$744	$1,228
Private	Surface	Less than 100	$250	$250	$318	$420	$515
Private	Surface	100 to 500	$283	$283	$410	$472	$839
Private	Surface	500 to 1,000	$269	$269	$442	$498	$936
Private	Surface	1,000 to 3,300	$259	$259	$433	$540	$971
Private	Surface	3,300 to 10,000	$196	$227	$324	$582	$1,085
Public	Ground	Less than 100	$162	$162	$217	$281	$351
Public	Ground	100 to 500	$190	$190	$316	$352	$610
Public	Ground	500 to 1,000	$183	$184	$310	$456	$637
Public	Ground	1,000 to 3,300	$190	$206	$353	$604	$919
Public	Ground	3,300 to 10,000	$185	$288	$452	$755	$1,212
Public	Surface	Less than 100	$250	$250	$346	$420	$599
Public	Surface	100 to 500	$283	$283	$407	$472	$795
Public	Surface	500 to 1,000	$269	$269	$447	$497	$884
Public	Surface	1,000 to 3,300	$259	$259	$433	$503	$901
Public	Surface	3,300 to 10,000	$196	$198	$296	$518	$909

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, Final Rule (PFOA and PFOS MCLs of 4.0 ppt each, PFHxS, PFNA, HFPO-DA MCLs of 10 ppt each and HI of 1) (Commercial Cost of Capital, $2022)

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	$162	$162	$261	$341	$912
Private	Ground	100 to 500	$181	$190	$283	$412	$1,057
Private	Ground	500 to 1,000	$156	$183	$294	$480	$1,434
Private	Ground	1,000 to 3,300	$189	$190	$320	$657	$2,661
Private	Ground	3,300 to 10,000	$185	$186	$285	$656	$13,612
Private	Surface	Less than 100	$250	$250	$394	$498	$1,441
Private	Surface	100 to 500	$283	$283	$464	$688	$1,963
Private	Surface	500 to 1,000	$269	$278	$467	$893	$5,618
Private	Surface	1,000 to 3,300	$259	$259	$421	$958	$4,991
Private	Surface	3,300 to 10,000	$213	$321	$658	$1,852	$31,905
Public	Ground	Less than 100	$162	$162	$260	$337	$928
Public	Ground	100 to 500	$190	$190	$287	$373	$1,021
Public	Ground	500 to 1,000	$183	$183	$289	$389	$1,092
Public	Ground	1,000 to 3,300	$190	$190	$319	$560	$1,969
Public	Ground	3,300 to 10,000	$186	$248	$345	$684	$22,620
Public	Surface	Less than 100	$250	$250	$359	$472	$1,794
Public	Surface	100 to 500	$283	$283	$449	$698	$2,703
Public	Surface	500 to 1,000	$269	$270	$382	$577	$4,910
Public	Surface	1,000 to 3,300	$259	$279	$487	$1,066	$9,462
Public	Surface	3,300 to 10,000	$196	$214	$372	$1,197	$26,572

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, $2022)

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	$162	$162	$260	$339	$907
Private	Ground	100 to 500	$181	$190	$283	$410	$1,051
Private	Ground	500 to 1,000	$156	$183	$294	$478	$1,431
Private	Ground	1,000 to 3,300	$188	$190	$319	$654	$2,653
Private	Ground	3,300 to 10,000	$185	$186	$284	$652	$13,540
Private	Surface	Less than 100	$250	$250	$393	$498	$1,440
Private	Surface	100 to 500	$283	$283	$464	$684	$1,953
Private	Surface	500 to 1,000	$269	$278	$467	$890	$5,579
Private	Surface	1,000 to 3,300	$259	$259	$421	$955	$4,977
Private	Surface	3,300 to 10,000	$213	$320	$654	$1,836	$31,636
Public	Ground	Less than 100	$162	$162	$259	$336	$933
Public	Ground	100 to 500	$190	$190	$286	$372	$1,019
Public	Ground	500 to 1,000	$183	$183	$288	$387	$1,085
Public	Ground	1,000 to 3,300	$190	$190	$319	$557	$1,971
Public	Ground	3,300 to 10,000	$186	$247	$344	$680	$22,497
Public	Surface	Less than 100	$250	$250	$358	$471	$1,792
Public	Surface	100 to 500	$283	$283	$449	$694	$2,689
Public	Surface	500 to 1,000	$269	$270	$381	$576	$4,909
Public	Surface	1,000 to 3,300	$259	$279	$487	$1,061	$9,428
Public	Surface	3,300 to 10,000	$196	$214	$371	$1,191	$26,455

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, $2022)

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	$162	$162	$259	$302	$838
Private	Ground	100 to 500	$181	$190	$279	$359	$957
Private	Ground	500 to 1,000	$156	$183	$290	$416	$980
Private	Ground	1,000 to 3,300	$189	$190	$319	$574	$1,169
Private	Ground	3,300 to 10,000	$185	$186	$284	$548	$4,888
Private	Surface	Less than 100	$250	$250	$393	$466	$999
Private	Surface	100 to 500	$283	$283	$464	$607	$1,248
Private	Surface	500 to 1,000	$269	$278	$457	$804	$2,755
Private	Surface	1,000 to 3,300	$259	$259	$421	$838	$2,270
Private	Surface	3,300 to 10,000	$213	$315	$615	$1,509	$14,494
Public	Ground	Less than 100	$162	$162	$259	$301	$825
Public	Ground	100 to 500	$190	$190	$285	$338	$925
Public	Ground	500 to 1,000	$183	$183	$286	$344	$924
Public	Ground	1,000 to 3,300	$190	$190	$319	$495	$1,083
Public	Ground	3,300 to 10,000	$186	$247	$335	$594	$8,372
Public	Surface	Less than 100	$250	$250	$357	$437	$1,049
Public	Surface	100 to 500	$283	$283	$449	$612	$1,399
Public	Surface	500 to 1,000	$269	$270	$380	$515	$2,462
Public	Surface	1,000 to 3,300	$259	$278	$473	$953	$4,249
Public	Surface	3,300 to 10,000	$196	$214	$345	$960	$11,166

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, $2022)

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	$162	$162	$256	$281	$541
Private	Ground	100 to 500	$181	$190	$271	$320	$614
Private	Ground	500 to 1,000	$156	$183	$281	$344	$647
Private	Ground	1,000 to 3,300	$189	$190	$319	$486	$895
Private	Ground	3,300 to 10,000	$185	$186	$284	$428	$887
Private	Surface	Less than 100	$250	$250	$392	$423	$694
Private	Surface	100 to 500	$283	$283	$463	$525	$903
Private	Surface	500 to 1,000	$269	$277	$450	$717	$1,139
Private	Surface	1,000 to 3,300	$259	$259	$420	$625	$1,389
Private	Surface	3,300 to 10,000	$213	$304	$554	$1,234	$2,215
Public	Ground	Less than 100	$162	$162	$257	$281	$534
Public	Ground	100 to 500	$190	$190	$281	$320	$575
Public	Ground	500 to 1,000	$183	$183	$283	$311	$586
Public	Ground	1,000 to 3,300	$190	$190	$319	$388	$750
Public	Ground	3,300 to 10,000	$186	$247	$322	$516	$842
Public	Surface	Less than 100	$250	$250	$356	$420	$612
Public	Surface	100 to 500	$283	$283	$448	$511	$920
Public	Surface	500 to 1,000	$269	$270	$378	$455	$830
Public	Surface	1,000 to 3,300	$259	$277	$449	$795	$1,461
Public	Surface	3,300 to 10,000	$196	$214	$312	$732	$1,667

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, Final Rule (PFOA and PFOS MCLs of 4.0 ppt each, PFHxS, PFNA, HFPO-DA MCLs of 10 ppt each and HI of 1) (Commercial Cost of Capital, $2022)

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	$12,750	$13,445	$14,523	$16,725	$30,195
Private	Ground	100 to 500	$17,003	$18,703	$22,738	$31,722	$49,790
Private	Ground	500 to 1,000	$24,843	$31,251	$41,268	$54,307	$83,580
Private	Ground	1,000 to 3,300	$35,629	$47,594	$65,988	$95,435	$144,530
Private	Ground	3,300 to 10,000	$58,719	$90,639	$165,080	$241,650	$341,780
Private	Surface	Less than 100	$13,451	$14,569	$15,794	$19,020	$32,602
Private	Surface	100 to 500	$17,809	$19,671	$24,002	$33,208	$53,699
Private	Surface	500 to 1,000	$25,064	$30,530	$39,135	$55,808	$84,746
Private	Surface	1,000 to 3,300	$37,748	$49,678	$67,880	$97,672	$150,360
Private	Surface	3,300 to 10,000	$57,404	$89,217	$151,960	$238,820	$351,490
Public	Ground	Less than 100	$13,272	$14,190	$15,621	$18,367	$32,161
Public	Ground	100 to 500	$19,193	$22,308	$28,496	$38,173	$56,711
Public	Ground	500 to 1,000	$28,965	$36,305	$47,597	$61,034	$93,788
Public	Ground	1,000 to 3,300	$42,284	$56,853	$78,948	$121,920	$189,720
Public	Ground	3,300 to 10,000	$67,894	$100,630	$194,660	$287,850	$420,440
Public	Surface	Less than 100	$13,983	$15,193	$16,803	$21,445	$34,256
Public	Surface	100 to 500	$20,177	$23,419	$29,974	$40,734	$64,081
Public	Surface	500 to 1,000	$30,679	$38,278	$48,596	$66,562	$106,290
Public	Surface	1,000 to 3,300	$47,855	$62,781	$85,383	$140,850	$210,670
Public	Surface	3,300 to 10,000	$83,040	$153,700	$227,760	$330,790	$488,940

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, $2022)

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	$12,750	$13,444	$14,523	$16,721	$30,175
Private	Ground	100 to 500	$17,000	$18,699	$22,730	$31,709	$49,758
Private	Ground	500 to 1,000	$24,829	$31,232	$41,240	$54,258	$83,465
Private	Ground	1,000 to 3,300	$35,604	$47,550	$65,923	$95,320	$144,350
Private	Ground	3,300 to 10,000	$58,663	$90,506	$164,840	$241,320	$341,230
Private	Surface	Less than 100	$13,451	$14,569	$15,792	$19,010	$32,603
Private	Surface	100 to 500	$17,805	$19,666	$23,995	$33,190	$53,660
Private	Surface	500 to 1,000	$25,058	$30,516	$39,103	$55,752	$84,657
Private	Surface	1,000 to 3,300	$37,739	$49,639	$67,831	$97,568	$150,260
Private	Surface	3,300 to 10,000	$57,294	$89,035	$151,700	$238,440	$350,960
Public	Ground	Less than 100	$13,272	$14,189	$15,620	$18,361	$32,132
Public	Ground	100 to 500	$19,191	$22,302	$28,489	$38,159	$56,689
Public	Ground	500 to 1,000	$28,950	$36,289	$47,574	$60,996	$93,686
Public	Ground	1,000 to 3,300	$42,251	$56,809	$78,883	$121,730	$189,640
Public	Ground	3,300 to 10,000	$67,835	$100,470	$194,460	$287,420	$419,990
Public	Surface	Less than 100	$13,983	$15,192	$16,800	$21,423	$34,249
Public	Surface	100 to 500	$20,173	$23,414	$29,965	$40,710	$64,052
Public	Surface	500 to 1,000	$30,669	$38,270	$48,580	$66,520	$106,180
Public	Surface	1,000 to 3,300	$47,829	$62,751	$85,354	$140,740	$210,600
Public	Surface	3,300 to 10,000	$83,018	$153,580	$227,660	$330,500	$488,610

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, $2022)

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	$12,744	$13,435	$14,509	$16,689	$30,245
Private	Ground	100 to 500	$16,962	$18,644	$22,623	$31,536	$49,241
Private	Ground	500 to 1,000	$24,492	$30,654	$40,663	$53,661	$81,797
Private	Ground	1,000 to 3,300	$34,843	$46,451	$64,668	$93,525	$140,540
Private	Ground	3,300 to 10,000	$56,508	$86,484	$155,640	$234,470	$327,280
Private	Surface	Less than 100	$13,322	$14,486	$15,717	$19,194	$30,953
Private	Surface	100 to 500	$17,725	$19,601	$23,791	$32,883	$51,940
Private	Surface	500 to 1,000	$25,152	$29,874	$38,097	$54,332	$79,085
Private	Surface	1,000 to 3,300	$37,209	$48,299	$65,996	$95,109	$142,570
Private	Surface	3,300 to 10,000	$58,036	$83,906	$141,760	$227,440	$329,830
Public	Ground	Less than 100	$13,248	$14,160	$15,579	$18,349	$31,377
Public	Ground	100 to 500	$19,130	$22,195	$28,291	$37,922	$56,127
Public	Ground	500 to 1,000	$28,629	$35,770	$46,975	$60,482	$92,174
Public	Ground	1,000 to 3,300	$41,636	$55,600	$77,506	$119,090	$187,280
Public	Ground	3,300 to 10,000	$66,000	$94,623	$187,120	$277,530	$408,740
Public	Surface	Less than 100	$13,758	$15,033	$16,692	$21,288	$33,078
Public	Surface	100 to 500	$20,024	$23,218	$29,664	$40,359	$62,450
Public	Surface	500 to 1,000	$30,155	$37,760	$48,043	$65,797	$103,350
Public	Surface	1,000 to 3,300	$46,963	$61,882	$84,056	$138,370	$208,570
Public	Surface	3,300 to 10,000	$79,968	$147,850	$223,690	$326,190	$483,870

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, $2022)

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	$12,726	$13,423	$14,474	$16,567	$29,647
Private	Ground	100 to 500	$16,852	$18,475	$22,290	$30,930	$47,110
Private	Ground	500 to 1,000	$23,340	$28,728	$38,086	$51,291	$73,348
Private	Ground	1,000 to 3,300	$32,489	$42,724	$59,347	$85,865	$124,860
Private	Ground	3,300 to 10,000	$63,179	$74,975	$120,970	$195,620	$266,600
Private	Surface	Less than 100	$14,263	$14,428	$15,247	$17,908	$24,626
Private	Surface	100 to 500	$17,999	$19,247	$22,685	$30,699	$42,930
Private	Surface	500 to 1,000	$30,887	$31,200	$34,564	$43,639	$62,927
Private	Surface	1,000 to 3,300	$48,078	$49,267	$57,787	$78,196	$117,010
Private	Surface	3,300 to 10,000	$91,326	$93,156	$112,970	$162,800	$255,790
Public	Ground	Less than 100	$13,157	$14,009	$15,354	$18,431	$28,042
Public	Ground	100 to 500	$18,884	$21,800	$27,477	$36,972	$53,864
Public	Ground	500 to 1,000	$27,398	$33,878	$44,461	$58,528	$85,588
Public	Ground	1,000 to 3,300	$39,739	$52,128	$73,006	$111,030	$176,390
Public	Ground	3,300 to 10,000	$60,139	$82,868	$160,830	$253,570	$375,840
Public	Surface	Less than 100	$14,956	$15,059	$15,876	$18,713	$26,060
Public	Surface	100 to 500	$19,711	$22,613	$28,278	$38,733	$55,114
Public	Surface	500 to 1,000	$28,949	$35,217	$45,324	$62,094	$87,753
Public	Surface	1,000 to 3,300	$42,915	$57,728	$79,786	$126,990	$193,340
Public	Surface	3,300 to 10,000	$75,406	$128,950	$208,950	$307,780	$464,170

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, Final Rule (PFOA and PFOS MCLs of 4.0 ppt each, PFHxS, PFNA, HFPO-DA MCLs of 10 ppt each and HI of 1) (Commercial Cost of Capital, $2022)

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	$12,451	$13,181	$14,416	$17,845	$38,382
Private	Ground	100 to 500	$17,039	$18,775	$22,782	$31,590	$50,907
Private	Ground	500 to 1,000	$26,001	$32,521	$41,022	$52,515	$79,603
Private	Ground	1,000 to 3,300	$34,937	$47,451	$63,747	$87,675	$129,160
Private	Ground	3,300 to 10,000	$108,430	$113,140	$147,680	$194,980	$271,070
Private	Surface	Less than 100	$12,596	$13,501	$14,949	$19,443	$29,428
Private	Surface	100 to 500	$17,916	$19,541	$23,718	$33,776	$47,778
Private	Surface	500 to 1,000	$30,616	$31,305	$37,024	$50,835	$73,636
Private	Surface	1,000 to 3,300	$44,409	$47,126	$60,542	$87,911	$130,210
Private	Surface	3,300 to 10,000	$89,611	$91,902	$124,350	$196,240	$306,580
Public	Ground	Less than 100	$12,920	$13,794	$15,400	$19,662	$36,481
Public	Ground	100 to 500	$18,966	$22,126	$28,266	$37,222	$54,701
Public	Ground	500 to 1,000	$29,992	$37,182	$45,574	$56,605	$86,674
Public	Ground	1,000 to 3,300	$42,391	$56,862	$72,128	$98,453	$159,680
Public	Ground	3,300 to 10,000	$133,780	$135,070	$157,540	$208,870	$317,210
Public	Surface	Less than 100	$15,324	$15,423	$16,416	$20,009	$28,258
Public	Surface	100 to 500	$21,224	$22,143	$26,479	$36,213	$49,068
Public	Surface	500 to 1,000	$38,033	$38,046	$38,993	$43,067	$59,764
Public	Surface	1,000 to 3,300	$63,245	$64,197	$75,362	$103,100	$154,320
Public	Surface	3,300 to 10,000	$142,410	$142,740	$157,880	$197,200	$296,500

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, $2022)

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	$12,450	$13,180	$14,413	$17,834	$38,373
Private	Ground	100 to 500	$17,038	$18,770	$22,774	$31,567	$50,857
Private	Ground	500 to 1,000	$25,991	$32,511	$41,004	$52,461	$79,515
Private	Ground	1,000 to 3,300	$34,920	$47,438	$63,728	$87,595	$129,030
Private	Ground	3,300 to 10,000	$108,520	$113,230	$147,790	$195,000	$270,800
Private	Surface	Less than 100	$12,595	$13,499	$14,950	$19,420	$29,411
Private	Surface	100 to 500	$17,914	$19,540	$23,712	$33,744	$47,744
Private	Surface	500 to 1,000	$30,623	$31,300	$36,993	$50,766	$73,525
Private	Surface	1,000 to 3,300	$44,475	$47,171	$60,500	$87,701	$130,060
Private	Surface	3,300 to 10,000	$89,650	$91,923	$123,960	$195,490	$305,670
Public	Ground	Less than 100	$12,919	$13,792	$15,397	$19,644	$36,471
Public	Ground	100 to 500	$18,962	$22,120	$28,257	$37,209	$54,651
Public	Ground	500 to 1,000	$29,984	$37,183	$45,561	$56,590	$86,580
Public	Ground	1,000 to 3,300	$42,375	$56,843	$72,105	$98,325	$159,530
Public	Ground	3,300 to 10,000	$133,820	$135,110	$157,390	$208,740	$316,590
Public	Surface	Less than 100	$15,310	$15,409	$16,399	$19,981	$28,247
Public	Surface	100 to 500	$21,210	$22,132	$26,475	$36,185	$48,997
Public	Surface	500 to 1,000	$37,995	$38,008	$38,954	$42,993	$59,642
Public	Surface	1,000 to 3,300	$63,193	$64,144	$75,370	$102,930	$154,010
Public	Surface	3,300 to 10,000	$141,960	$142,290	$157,490	$196,700	$295,600

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, $2022)

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	$12,441	$13,173	$14,395	$17,866	$37,796
Private	Ground	100 to 500	$16,994	$18,713	$22,658	$31,418	$50,164
Private	Ground	500 to 1,000	$25,367	$31,510	$40,057	$51,693	$76,955
Private	Ground	1,000 to 3,300	$33,885	$46,020	$62,235	$85,860	$124,840
Private	Ground	3,300 to 10,000	$116,740	$118,180	$137,910	$174,780	$254,240
Private	Surface	Less than 100	$12,934	$13,521	$14,884	$19,077	$26,928
Private	Surface	100 to 500	$18,569	$19,587	$23,329	$32,422	$44,212
Private	Surface	500 to 1,000	$32,811	$33,031	$36,224	$45,969	$68,309
Private	Surface	1,000 to 3,300	$48,775	$49,690	$58,778	$80,200	$125,140
Private	Surface	3,300 to 10,000	$99,823	$100,360	$117,680	$166,250	$273,720
Public	Ground	Less than 100	$12,907	$13,759	$15,342	$19,667	$35,400
Public	Ground	100 to 500	$18,891	$22,001	$28,049	$37,008	$54,283
Public	Ground	500 to 1,000	$29,480	$36,685	$45,184	$56,346	$84,445
Public	Ground	1,000 to 3,300	$41,109	$55,446	$70,910	$97,287	$153,630
Public	Ground	3,300 to 10,000	$136,940	$137,190	$148,180	$182,210	$277,450
Public	Surface	Less than 100	$15,374	$15,401	$15,954	$18,270	$25,901
Public	Surface	100 to 500	$22,637	$22,967	$25,984	$33,572	$46,835
Public	Surface	500 to 1,000	$34,784	$34,784	$35,146	$37,399	$49,010
Public	Surface	1,000 to 3,300	$66,752	$67,005	$72,937	$90,648	$138,740
Public	Surface	3,300 to 10,000	$140,200	$140,280	$146,950	$169,230	$246,610

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, $2022)

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	$12,375	$13,131	$14,296	$17,751	$34,871
Private	Ground	100 to 500	$16,815	$18,491	$22,165	$30,419	$46,664
Private	Ground	500 to 1,000	$25,081	$28,923	$36,345	$47,778	$64,512
Private	Ground	1,000 to 3,300	$40,119	$42,603	$54,075	$73,768	$103,380
Private	Ground	3,300 to 10,000	$95,371	$95,371	$96,363	$100,690	$129,210
Private	Surface	Less than 100	$13,632	$13,637	$13,914	$15,226	$20,728
Private	Surface	100 to 500	$20,645	$20,662	$21,303	$24,048	$34,055
Private	Surface	500 to 1,000	$26,102	$26,105	$26,261	$27,217	$35,049
Private	Surface	1,000 to 3,300	$44,383	$44,383	$44,782	$47,239	$64,471
Private	Surface	3,300 to 10,000	$88,851	$88,851	$89,884	$95,680	$132,330
Public	Ground	Less than 100	$12,805	$13,612	$15,098	$19,358	$30,326
Public	Ground	100 to 500	$18,482	$21,440	$27,084	$35,855	$50,906
Public	Ground	500 to 1,000	$29,018	$34,032	$42,141	$53,541	$72,239
Public	Ground	1,000 to 3,300	$47,962	$51,574	$63,811	$86,975	$124,370
Public	Ground	3,300 to 10,000	$93,410	$93,410	$93,659	$96,190	$118,780
Public	Surface	Less than 100	$10,001	$10,001	$10,021	$10,173	$11,801
Public	Surface	100 to 500	$19,793	$19,794	$19,977	$20,935	$26,985
Public	Surface	500 to 1,000	$17,025	$17,025	$17,025	$17,117	$18,765
Public	Surface	1,000 to 3,300	$47,907	$47,907	$48,190	$49,706	$62,882
Public	Surface	3,300 to 10,000	$79,247	$79,247	$79,367	$81,463	$98,701

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 in CWSs, Final Rule (PFOA and PFOS MCLs of 4.0 ppt each, PFHxS, PFNA, HFPO-DA MCLs of 10 ppt each and HI of 1) (Commercial Cost of Capital, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile
Private	Ground	Less than 100	$42	$57	$74
Private	Ground	100 to 500	$24	$33	$43
Private	Ground	500 to 1,000	$9	$13	$18
Private	Ground	1,000 to 3,300	$6	$9	$13
Private	Ground	3,300 to 10,000	$4	$7	$11
Private	Ground	10,000 to 50,000	$14	$17	$21
Private	Ground	50,000 to 100,000	$9	$16	$23
Private	Ground	100,000 to 1,000,000	$5	$9	$14
Private	Surface	Less than 100	$36	$56	$80
Private	Surface	100 to 500	$18	$27	$37
Private	Surface	500 to 1,000	$6	$12	$18
Private	Surface	1,000 to 3,300	$4	$7	$11
Private	Surface	3,300 to 10,000	$3	$7	$11
Private	Surface	10,000 to 50,000	$9	$12	$15
Private	Surface	50,000 to 100,000	$11	$15	$19
Private	Surface	100,000 to 1,000,000	$13	$15	$18
Public	Ground	Less than 100	$49	$71	$95
Public	Ground	100 to 500	$22	$30	$40
Public	Ground	500 to 1,000	$7	$10	$14
Public	Ground	1,000 to 3,300	$5	$8	$10
Public	Ground	3,300 to 10,000	$13	$18	$24
Public	Ground	10,000 to 50,000	$15	$17	$18
Public	Ground	50,000 to 100,000	$11	$14	$17
Public	Ground	100,000 to 1,000,000	$12	$15	$19
Public	Surface	Less than 100	$53	$81	$115
Public	Surface	100 to 500	$19	$28	$37
Public	Surface	500 to 1,000	$7	$10	$13
Public	Surface	1,000 to 3,300	$5	$7	$9
Public	Surface	3,300 to 10,000	$12	$17	$23
Public	Surface	10,000 to 50,000	$13	$14	$16
Public	Surface	50,000 to 100,000	$11	$12	$14
Public	Surface	100,000 to 1,000,000	$11	$12	$14

Table C-33: Mean Annualized Cost per Household in CWSs, Final Rule (PFOA and PFOS MCLs of 4.0 ppt each, PFHxS, PFNA, HFPO-DA MCLs of 10 ppt each and HI of 1) (Commercial Cost of Capital, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile

Abbreviations: CWS – community water system.

Table C-34: Mean Annualized Cost per Household in CWSs, Option 1a (PFOA and PFOS MCLs of 4.0 ppt) (Commercial Cost of Capital, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile
Private	Ground	Less than 100	$42	$57	$74
Private	Ground	100 to 500	$24	$33	$43
Private	Ground	500 to 1,000	$9	$13	$18
Private	Ground	1,000 to 3,300	$6	$9	$13
Private	Ground	3,300 to 10,000	$4	$7	$11
Private	Ground	10,000 to 50,000	$14	$17	$21
Private	Ground	50,000 to 100,000	$9	$14	$22
Private	Ground	100,000 to 1,000,000	$5	$9	$14
Private	Surface	Less than 100	$36	$56	$80
Private	Surface	100 to 500	$18	$27	$37
Private	Surface	500 to 1,000	$6	$12	$18
Private	Surface	1,000 to 3,300	$4	$7	$11
Private	Surface	3,300 to 10,000	$3	$7	$11
Private	Surface	10,000 to 50,000	$9	$12	$15
Private	Surface	50,000 to 100,000	$10	$14	$19
Private	Surface	100,000 to 1,000,000	$12	$15	$17
Public	Ground	Less than 100	$49	$71	$96
Public	Ground	100 to 500	$22	$30	$41
Public	Ground	500 to 1,000	$7	$10	$14
Public	Ground	1,000 to 3,300	$5	$8	$10
Public	Ground	3,300 to 10,000	$13	$18	$24
Public	Ground	10,000 to 50,000	$15	$16	$18
Public	Ground	50,000 to 100,000	$11	$14	$17
Public	Ground	100,000 to 1,000,000	$12	$15	$18
Public	Surface	Less than 100	$53	$81	$115
Public	Surface	100 to 500	$19	$28	$38
Public	Surface	500 to 1,000	$7	$10	$13
Public	Surface	1,000 to 3,300	$5	$7	$9
Public	Surface	3,300 to 10,000	$12	$17	$24
Public	Surface	10,000 to 50,000	$13	$14	$16
Public	Surface	50,000 to 100,000	$11	$12	$14

Table C-34: Mean Annualized Cost per Household in CWSs, Option 1a (PFOA and PFOS MCLs of 4.0 ppt) (Commercial Cost of Capital, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile
Public	Surface	100,000 to 1,000,000	$11	$12	$14

Abbreviations: CWS – community water system.

Table C-35: Mean Annualized Cost per Household in CWSs, Option 1b (PFOA and PFOS MCLs of 5.0 ppt) (Commercial Cost of Capital, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile
Private	Ground	Less than 100	$32	$43	$57
Private	Ground	100 to 500	$18	$25	$33
Private	Ground	500 to 1,000	$6	$10	$14
Private	Ground	1,000 to 3,300	$4	$7	$10
Private	Ground	3,300 to 10,000	$3	$5	$8
Private	Ground	10,000 to 50,000	$10	$13	$16
Private	Ground	50,000 to 100,000	$6	$11	$17
Private	Ground	100,000 to 1,000,000	$3	$6	$11
Private	Surface	Less than 100	$27	$44	$64
Private	Surface	100 to 500	$14	$21	$29
Private	Surface	500 to 1,000	$4	$9	$14
Private	Surface	1,000 to 3,300	$3	$5	$8
Private	Surface	3,300 to 10,000	$2	$5	$8
Private	Surface	10,000 to 50,000	$7	$9	$12
Private	Surface	50,000 to 100,000	$8	$12	$16
Private	Surface	100,000 to 1,000,000	$10	$12	$14
Public	Ground	Less than 100	$38	$54	$73
Public	Ground	100 to 500	$16	$23	$31
Public	Ground	500 to 1,000	$5	$8	$11
Public	Ground	1,000 to 3,300	$4	$6	$8
Public	Ground	3,300 to 10,000	$9	$13	$18
Public	Ground	10,000 to 50,000	$12	$13	$14
Public	Ground	50,000 to 100,000	$8	$11	$13
Public	Ground	100,000 to 1,000,000	$9	$12	$15
Public	Surface	Less than 100	$40	$64	$93
Public	Surface	100 to 500	$15	$21	$29
Public	Surface	500 to 1,000	$5	$7	$10
Public	Surface	1,000 to 3,300	$3	$5	$7
Public	Surface	3,300 to 10,000	$9	$13	$17
Public	Surface	10,000 to 50,000	$10	$11	$12

Table C-35: Mean Annualized Cost per Household in CWSs, Option 1b (PFOA and PFOS MCLs of 5.0 ppt) (Commercial Cost of Capital, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile
Public	Surface	50,000 to 100,000	$8	$9	$11
Public	Surface	100,000 to 1,000,000	$8	$9	$11

Abbreviations: CWS – community water system.

Table C-36: Mean Annualized Cost per Household in CWSs, Option 1c (PFOA and PFOS MCLs of 10.0 ppt) (Commercial Cost of Capital, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile
Private	Ground	Less than 100	$16	$20	$25
Private	Ground	100 to 500	$8	$11	$14
Private	Ground	500 to 1,000	$3	$4	$6
Private	Ground	1,000 to 3,300	$1	$2	$4
Private	Ground	3,300 to 10,000	$1	$2	$3
Private	Ground	10,000 to 50,000	$3	$5	$6
Private	Ground	50,000 to 100,000	$1	$3	$6
Private	Ground	100,000 to 1,000,000	$0	$1	$3
Private	Surface	Less than 100	$15	$22	$32
Private	Surface	100 to 500	$7	$10	$14
Private	Surface	500 to 1,000	$2	$4	$6
Private	Surface	1,000 to 3,300	$1	$2	$4
Private	Surface	3,300 to 10,000	$0	$2	$3
Private	Surface	10,000 to 50,000	$2	$3	$5
Private	Surface	50,000 to 100,000	$3	$5	$8
Private	Surface	100,000 to 1,000,000	$4	$5	$7
Public	Ground	Less than 100	$18	$25	$33
Public	Ground	100 to 500	$7	$10	$13
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	$3	$4	$6
Public	Ground	10,000 to 50,000	$5	$5	$6
Public	Ground	50,000 to 100,000	$3	$4	$6
Public	Ground	100,000 to 1,000,000	$4	$6	$7
Public	Surface	Less than 100	$19	$30	$45
Public	Surface	100 to 500	$7	$9	$13
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	$4	$6
Public	Surface	10,000 to 50,000	$4	$4	$5
Public	Surface	50,000 to 100,000	$2	$3	$4
Public	Surface	100,000 to 1,000,000	$3	$4	$4

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, Final Rule (PFOA and PFOS MCLs of 4.0 ppt each, PFHxS, PFNA, HFPO-DA MCLs of 10 ppt each and HI of 1) (Commercial Cost of Capital, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile
Private	Ground	Less than 100	$755	$809	$899
Private	Ground	100 to 500	$413	$452	$513
Private	Ground	500 to 1,000	$151	$173	$198
Private	Ground	1,000 to 3,300	$99	$114	$130
Private	Ground	3,300 to 10,000	$67	$85	$104
Private	Ground	10,000 to 50,000	$45	$53	$62
Private	Ground	50,000 to 100,000	$32	$45	$62
Private	Ground	100,000 to 1,000,000	$12	$18	$27
Private	Surface	Less than 100	$567	$764	$1,004
Private	Surface	100 to 500	$310	$370	$444
Private	Surface	500 to 1,000	$120	$161	$206
Private	Surface	1,000 to 3,300	$76	$103	$132
Private	Surface	3,300 to 10,000	$56	$79	$106
Private	Surface	10,000 to 50,000	$40	$48	$57
Private	Surface	50,000 to 100,000	$35	$44	$55
Private	Surface	100,000 to 1,000,000	$26	$30	$34
Public	Ground	Less than 100	$884	$1,031	$1,190
Public	Ground	100 to 500	$388	$429	$486
Public	Ground	500 to 1,000	$129	$144	$161
Public	Ground	1,000 to 3,300	$89	$98	$108
Public	Ground	3,300 to 10,000	$176	$194	$215
Public	Ground	10,000 to 50,000	$51	$54	$59
Public	Ground	50,000 to 100,000	$36	$42	$48
Public	Ground	100,000 to 1,000,000	$33	$40	$47
Public	Surface	Less than 100	$803	$1,057	$1,373
Public	Surface	100 to 500	$344	$398	$461
Public	Surface	500 to 1,000	$121	$140	$162
Public	Surface	1,000 to 3,300	$90	$100	$110
Public	Surface	3,300 to 10,000	$199	$221	$245
Public	Surface	10,000 to 50,000	$54	$57	$61
Public	Surface	50,000 to 100,000	$41	$45	$49
Public	Surface	100,000 to 1,000,000	$34	$37	$40

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, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile
Private	Ground	Less than 100	$755	$809	$899
Private	Ground	100 to 500	$411	$451	$511
Private	Ground	500 to 1,000	$152	$173	$198
Private	Ground	1,000 to 3,300	$99	$114	$130
Private	Ground	3,300 to 10,000	$67	$85	$104
Private	Ground	10,000 to 50,000	$44	$53	$61
Private	Ground	50,000 to 100,000	$29	$42	$57
Private	Ground	100,000 to 1,000,000	$12	$18	$26
Private	Surface	Less than 100	$568	$764	$1,004
Private	Surface	100 to 500	$305	$370	$442
Private	Surface	500 to 1,000	$118	$161	$206
Private	Surface	1,000 to 3,300	$76	$102	$132
Private	Surface	3,300 to 10,000	$55	$79	$106
Private	Surface	10,000 to 50,000	$40	$48	$57
Private	Surface	50,000 to 100,000	$34	$44	$55
Private	Surface	100,000 to 1,000,000	$25	$28	$32
Public	Ground	Less than 100	$884	$1,031	$1,199
Public	Ground	100 to 500	$388	$429	$486
Public	Ground	500 to 1,000	$129	$144	$161
Public	Ground	1,000 to 3,300	$89	$98	$108
Public	Ground	3,300 to 10,000	$176	$194	$215
Public	Ground	10,000 to 50,000	$50	$54	$58
Public	Ground	50,000 to 100,000	$35	$42	$48
Public	Ground	100,000 to 1,000,000	$33	$39	$47
Public	Surface	Less than 100	$803	$1,057	$1,392
Public	Surface	100 to 500	$344	$398	$461
Public	Surface	500 to 1,000	$120	$140	$164
Public	Surface	1,000 to 3,300	$89	$100	$110
Public	Surface	3,300 to 10,000	$199	$221	$243
Public	Surface	10,000 to 50,000	$54	$57	$60
Public	Surface	50,000 to 100,000	$40	$44	$48
Public	Surface	100,000 to 1,000,000	$34	$37	$40

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, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile
Private	Ground	Less than 100	$743	$807	$895
Private	Ground	100 to 500	$408	$449	$511
Private	Ground	500 to 1,000	$148	$171	$197
Private	Ground	1,000 to 3,300	$95	$112	$131
Private	Ground	3,300 to 10,000	$64	$82	$106
Private	Ground	10,000 to 50,000	$40	$48	$57
Private	Ground	50,000 to 100,000	$25	$36	$51
Private	Ground	100,000 to 1,000,000	$9	$14	$23
Private	Surface	Less than 100	$527	$763	$1,044
Private	Surface	100 to 500	$296	$367	$450
Private	Surface	500 to 1,000	$111	$159	$216
Private	Surface	1,000 to 3,300	$72	$101	$135
Private	Surface	3,300 to 10,000	$50	$77	$109
Private	Surface	10,000 to 50,000	$37	$46	$56
Private	Surface	50,000 to 100,000	$33	$43	$55
Private	Surface	100,000 to 1,000,000	$22	$25	$29
Public	Ground	Less than 100	$864	$1,030	$1,234
Public	Ground	100 to 500	$383	$426	$485
Public	Ground	500 to 1,000	$127	$142	$160
Public	Ground	1,000 to 3,300	$88	$96	$107
Public	Ground	3,300 to 10,000	$168	$188	$210
Public	Ground	10,000 to 50,000	$47	$51	$55
Public	Ground	50,000 to 100,000	$33	$39	$46
Public	Ground	100,000 to 1,000,000	$31	$37	$45
Public	Surface	Less than 100	$775	$1,070	$1,474
Public	Surface	100 to 500	$333	$395	$465
Public	Surface	500 to 1,000	$117	$139	$164
Public	Surface	1,000 to 3,300	$87	$98	$110
Public	Surface	3,300 to 10,000	$192	$217	$242
Public	Surface	10,000 to 50,000	$51	$55	$59
Public	Surface	50,000 to 100,000	$38	$42	$46
Public	Surface	100,000 to 1,000,000	$31	$34	$38

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, $2022)

Ownership	Source Water	Population Served Size Category	5th Percentile	Mean	95th Percentile
Private	Ground	Less than 100	$702	$795	$909
Private	Ground	100 to 500	$386	$441	$513
Private	Ground	500 to 1,000	$129	$165	$205
Private	Ground	1,000 to 3,300	$79	$106	$137
Private	Ground	3,300 to 10,000	$42	$76	$117
Private	Ground	10,000 to 50,000	$25	$34	$44
Private	Ground	50,000 to 100,000	$7	$17	$30
Private	Ground	100,000 to 1,000,000	$0	$8	$18
Private	Surface	Less than 100	$365	$732	$1,387
Private	Surface	100 to 500	$248	$363	$512
Private	Surface	500 to 1,000	$0	$148	$276
Private	Surface	1,000 to 3,300	$45	$96	$173
Private	Surface	3,300 to 10,000	$12	$68	$129
Private	Surface	10,000 to 50,000	$27	$36	$48
Private	Surface	50,000 to 100,000	$26	$41	$59
Private	Surface	100,000 to 1,000,000	$16	$20	$25
Public	Ground	Less than 100	$747	$1,020	$1,373
Public	Ground	100 to 500	$353	$418	$490
Public	Ground	500 to 1,000	$115	$137	$161
Public	Ground	1,000 to 3,300	$79	$92	$105
Public	Ground	3,300 to 10,000	$140	$172	$205
Public	Ground	10,000 to 50,000	$37	$41	$46
Public	Ground	50,000 to 100,000	$26	$34	$43
Public	Ground	100,000 to 1,000,000	$25	$35	$46
Public	Surface	Less than 100	$430	$997	$1,815
Public	Surface	100 to 500	$284	$389	$522
Public	Surface	500 to 1,000	$97	$135	$179
Public	Surface	1,000 to 3,300	$75	$95	$117
Public	Surface	3,300 to 10,000	$170	$207	$248
Public	Surface	10,000 to 50,000	$45	$49	$54
Public	Surface	50,000 to 100,000	$28	$33	$38
Public	Surface	100,000 to 1,000,000	$24	$28	$32

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 PFAS based on available studies. The EPA used these relationships to estimate incremental changes in birth weight associated with reduced exposure to PFAS, namely PFOA and PFOS.

D.1 Weight of Evidence of Birth Weight Effects

In the *Health Effects Support Document* (HESD) for PFOA (U.S. EPA, 2016b), the 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, the EPA's *Final Human Health Toxicity Assessments for PFOA and PFOS,* found clear evidence of an association between PFOA and PFOS and birth weight in both toxicological and epidemiological studies (U.S. EPA, 2024b; U.S. EPA, 2024c). Based on these findings, the EPA's Office of Ground Water and Drinking Water (OGWDW) derived exposure-response estimates for both compounds.

D.2 Review of Available Meta-Analyses

The 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, & Longnecker, 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 the 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, the 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 the U.S. Environmental Protection Agency Office of Science and Technology (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 the 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, and Longnecker (2020) of -3.2 g per ng/mL.

The 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, & Longnecker, 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, & Longnecker, 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.
- 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.

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

(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, and Longnecker (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, and Longnecker (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
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; the EPA/OST– U.S. Environmental Protection Agency Office of Science and Technology; PFOA – perfluorooctanoic acid; PFOS – perfluorooctane sulfonic acid.

Notes:

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

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

[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).

between PFOA/PFOS and birth weight remained negative for all sample collection times, except for the initial sampling time (at conception).

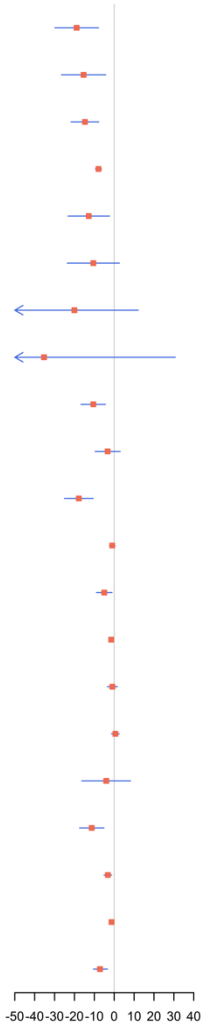
Negri et al. (2017) reported a pooled beta across eight included studies of -0.92 g (95% CI: -3.4, 1.6) for PFOS and twelve included studies of -12.8 g (95% CI: -23.2, -2.4) for PFOA each per each 1 ng/mL. Negri et al. (2017) conducted random effects meta-analyses based on 14 studies. In addition to 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, and Longnecker (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 (I^2 = 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).

Figure D-1: Results and Confidence Limits from PFOA, PFOS Meta-Analyses:

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



D.3 Exposure-Response Functions Based on Epidemiological Studies

The 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], the 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).

The EPA selected the exposure-response result for PFOS from the most recent meta-analysis of 32 observations from 29 publications reported by Dzierlenga, Crawford, and Longnecker (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, and Longnecker (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, and Longnecker (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.

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[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, and Longnecker (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, and Longnecker (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.

The EPA reanalyzed the pooled estimate from this study after determining that the original Dzierlenga, Crawford, and Longnecker (2020) pooled estimate included a duplicated estimate from Chen et al. (2017). The 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 the 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. The EPA developed a cross-sectional model to quantify this relationship based on recent 2016/17 and 2017/18 Centers for Disease Control and Prevention (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 & Stella, 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). The 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 and Finch (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 & Finch, 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 and Finch (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 & Finch, 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 and Finch (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, the 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, the EPA estimated separate relationships for non-Hispanic Black, non-Hispanic White, and Hispanic subpopulations.

In developing the singleton models, the EPA used similar variables and partitioning techniques as detailed in Ma et al. (2010). Specifically, the 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 & Finch, 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 & Hogan, 2012; Collins Jr & David, 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. The 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

[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] The 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.

pregnancy have decreased since 1989. While mean and median birth weight has decreased 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 & Stella, 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%)

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)
Mother's demographic characteristics		
Fraction Black	0.195	0.193 (-1%)
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, the 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

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

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 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

The 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, the 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. The 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 & Driscoll, 2020).

E.3.3 Identification of Infant Mortality Risk Factors

To identify infant mortality risk factors for inclusion in the regression analyses, the 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 the 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 & Driscoll, 2020). The majority of infant deaths in 2018 occurred among infants born preterm (gestational age < 37 weeks; Ely & Driscoll, 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 & Finch, 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 & Finch, 2010). Birth defects, such as the presence of congenital anomalies, also contribute to infant mortality (Ely & Driscoll, 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 & Finch, 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 & Driscoll, 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 & Driscoll, 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. The 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 the EPA's analysis is the relationship between birth weight and infant mortality. However, Ma and Finch (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 and Finch (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 & Finch, 2010), the 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. The 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, the 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] The EPA included categorized Apgar score variables based on analysis from Ma and Finch (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 and Finch (2010) also found that the inclusion Apgar scores in models predicting infant mortality significantly improved goodness of fit. The 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 and Finch (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] The 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; GA – gestational age; 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 & Driscoll, 2020). Infant mortality rates increased among infants born to older mothers, especially those over age 40 (Ely & Driscoll, 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). The 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

The 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 & David, 2009; Rice et al., 2017; Rowley & Hogan, 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, the 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, the EPA used actual observed values for the covariates rather than using covariate means.[23] For non-birth weight-gestational age variables, the EPA estimated marginal effects based on covariate values from all observations included in the models. For birth weight-gestational age variables, the 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 the EPA's preferred models. These models had the best fit and offered most intuitive results, in terms of variable sign and significance. The 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. The 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 the 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] The 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] The EPA calculated marginal effects using the "margins, dydx(*)" command in Stata (StataCorp, 2013b). The EPA used the default as observed option.

[24] The 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.[25] 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 R2 values are approximately 40%, which is in line with previous literature.[26] The agency notes that the estimated models are potentially subject to omitted variable bias from other sources, such as income level, but the 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.[27] 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

[25] The EPA reports the results of regression modeling using both odds ratios and marginal effects, which are more informative than reporting estimated coefficients. Because estimated coefficients are in log-odds units, they are difficult to interpret and are therefore often converted into odds ratios in epidemiological literature by taking the exponent of each regression coefficient. The EPA reported odds ratios via the "logit" command in Stata (StataCorp, 2013a).

[26] Ma and Finch (2010) reported a Pseudo R2 value of approximately 27%.

[27] 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%.

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.

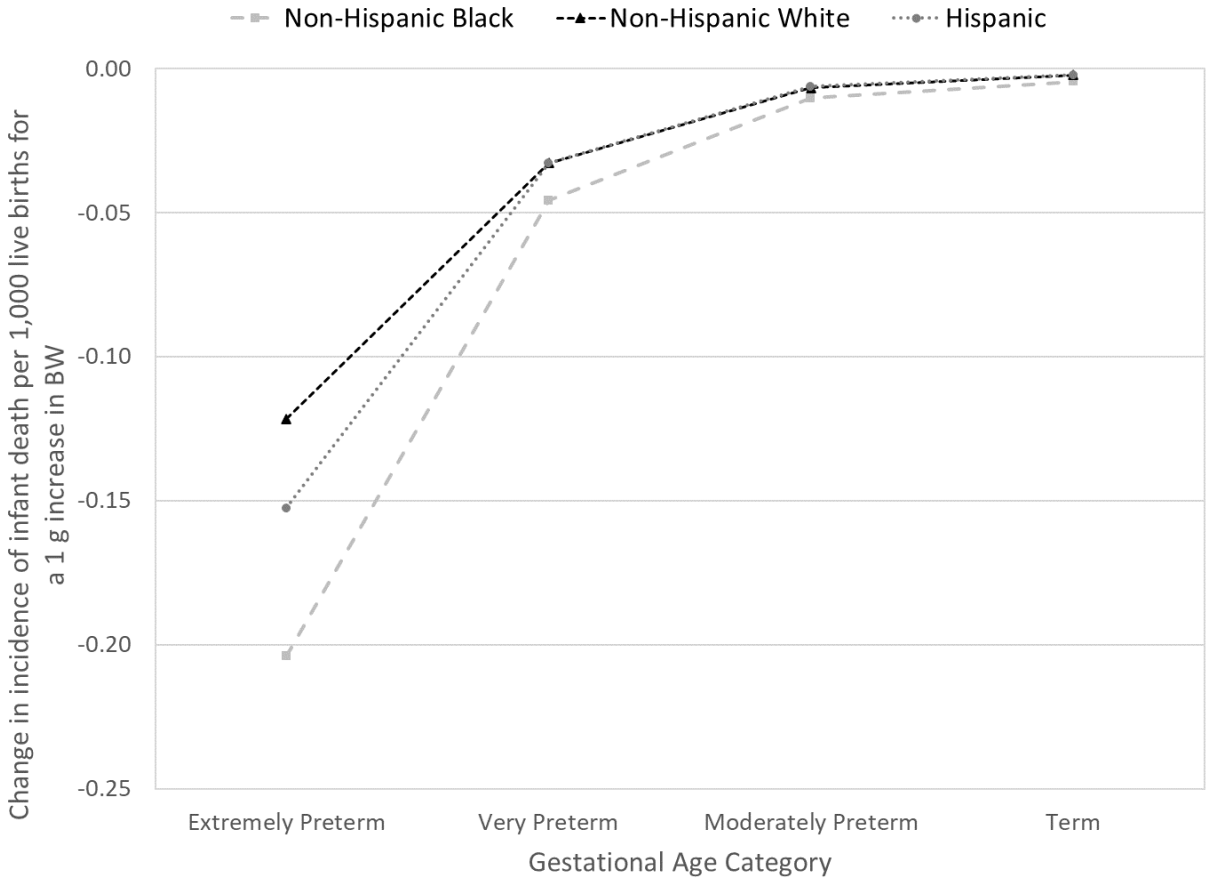


Figure E-1: Comparison of Change in Incidence of Infant Death per 1 g Increase in Birth Weight by Gestational Age Category and Race/Ethnicity (Deaths per 1,000 Births)

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_BOC at1 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.[28] 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 the 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 & Driscoll, 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

[28] 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%.

years, infants born to mothers younger than 20 years' experience 0.79, 0.61, and 0.68 additional infant deaths per 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)

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_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)
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			

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

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, the EPA estimated marginal effects based on covariate values from all observations in the models. For BW-GA variables, the 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

The 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, the 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, the 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]The 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 & Finch, 2010; Ely & Driscoll, 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). The 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), the 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 are likely not adequate to represent the relationship between birth weight and mortality.
The 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 the EPA's literature review to identify studies to estimate relationships between cholesterol levels and serum PFAS for inclusion in a meta-analysis of these relationships. This approach has been peer reviewed by the EPA's Science Advisory Board (SAB); 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. The 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

The 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 the EPA included literature from 2013 to 2020 (U.S. EPA, 2024b; U.S. EPA, 2024c). The relationships between exposure to PFAS and serum total cholesterol (TC) and high-density lipoprotein cholesterol (HDLC) identified based on these literature reviews allowed the EPA to generate inputs for the Pooled Cohort Atherosclerotic Cardiovascular Disease (ASCVD) risk model (Goff et al., 2014).[29,30]

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. The 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 evaluating the

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

[30] Note that the EPA evaluated HDLC effects as part of a sensitivity analysis (see Appendix K). The 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, 2024b; U.S. EPA, 2024c).

exposures of PFOA and PFOS. Because the EPA evaluates CVD risk among a general population of adults aged 40 to 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: The 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[31] were further evaluated for inclusion in the meta-analysis.

Research methods and study details: The 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]). The EPA retained studies with missing measures of effect estimate variance but with reported p-values for differences. For such studies, the 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.

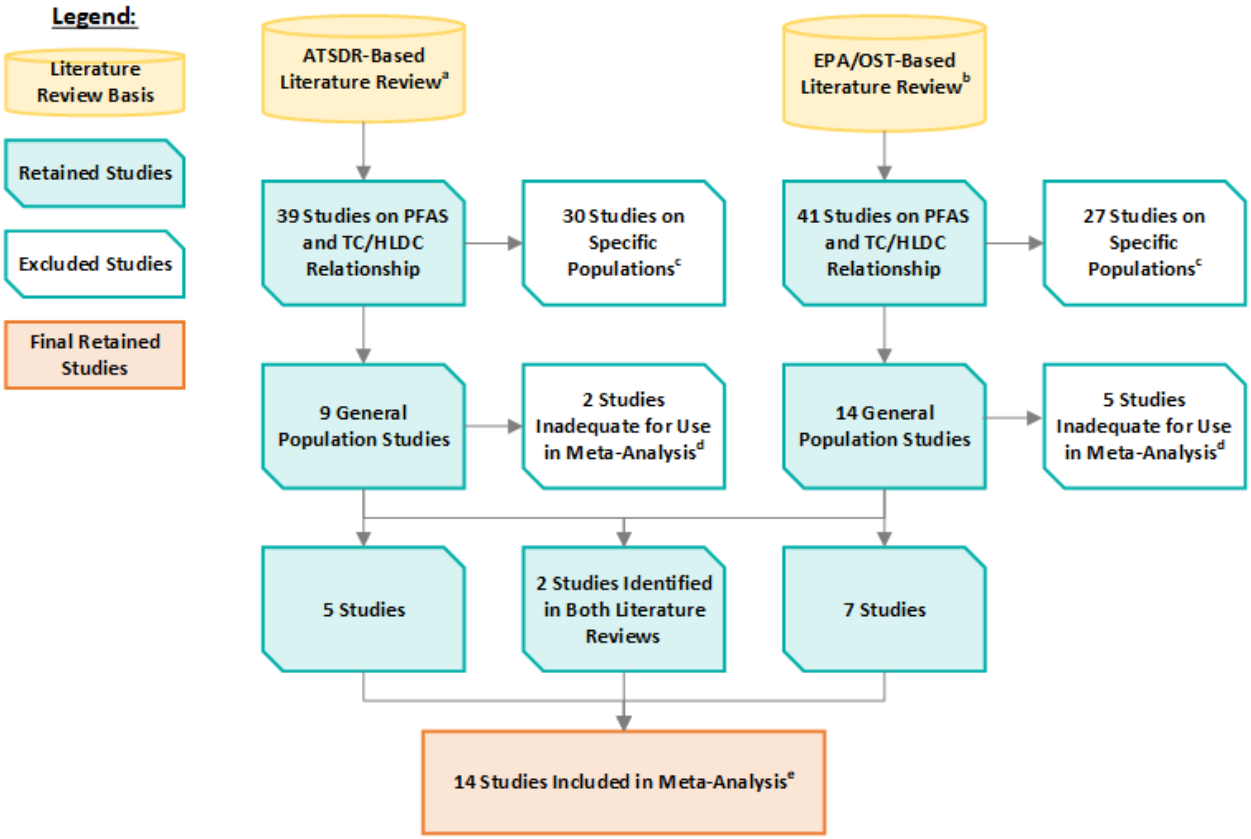
Additional exclusion criteria: The EPA also excluded studies that reported data only for pregnant women, infants, or children. Although there is some evidence that PFAS exposure is associated with cardiometabolic impairment in children and younger adults (Rappazzo et al., 2017), the EPA did not extract 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 the 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, the 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 & Ducatman, 2019; Y. Li et al., 2020; C. Y. Lin et al., 2020; P.-I.

[31] 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.

D. Lin 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 the EPA literature review that the EPA used to derive slope estimates for PFOA and PFOS associations with serum TC and HDLC levels.[32] Six of the studies that the 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 & Ducatman, 2019; Liu et al., 2018; Nelson et al., 2010); there were also general population studies from Canada (Fisher et al., 2013), Sweden (Y. Li et al., 2020),

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

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. The 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).

The 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, the 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.[33] Similarly, the 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). The 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.

[33] 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 & Ducatman, 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., 2020[b]	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 the 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, the 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). The 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 the EPA's *Final Human Health Toxicity Assessments for PFOA and PFOS* (U.S. EPA, 2024b; U.S. EPA, 2024c). 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), the 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, the 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), the EPA approximated the results for an untransformed analysis using the approach outlined by Rodríguez-Barranco et al. (2017) and Dzierlenga, Crawford, and Longnecker (2020). When not reported, the EPA assumed that the natural logarithm was the basis of the

transformation. An independent reviewer of the EPA 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[34] PFOA or PFOS in ng/mL. The EPA conducted random-effects meta-analyses using the DerSimonian and Laird (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), the 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.

The EPA assessed between-study heterogeneity using Cochran's Q test (Cochran, 1954) and the I^2 statistic (Higgins et al., 2003). The EPA developed forest plots to display the results. The EPA developed funnel plots and performed an Egger regression on the estimates of effect size to assess potential publication bias (Begg & Mazumdar, 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, the 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, the EPA conduced sensitivity analyses using trim-and-fill methods (Duval & Tweedie, 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, the EPA conducted several sensitivity analyses:

The EPA evaluated the impact of using other estimation methods for the between-study variance (tau2) besides the DerSimonian and Laird (1986) approach, such as restricted maximum likelihood (Raudenbush, 2009) or Sidik and Jonkman (2005).

- To assess potential impact of a single study on the overall effect estimate, the EPA conducted leave-one-out meta-analyses.
- To assess potential impact of study quality on the overall effect estimate, the 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), the 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 & Ducatman, 2019). The EPA also conducted a sensitivity analysis using a single pooled estimate from the four study-specific estimates.
- The 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

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

population study (Château-Degat et al., 2010), and the U.S. high-exposure community study (Steenland et al., 2009).

Six studies that the 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 2003–2014, while He et al. (2018) used 2003–2012 data; Jain and Ducatman (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, the 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).

The 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 & Sterne, 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 and Ducatman (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 and Ducatman (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 and Ducatman (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	1b	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. Tau2 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.

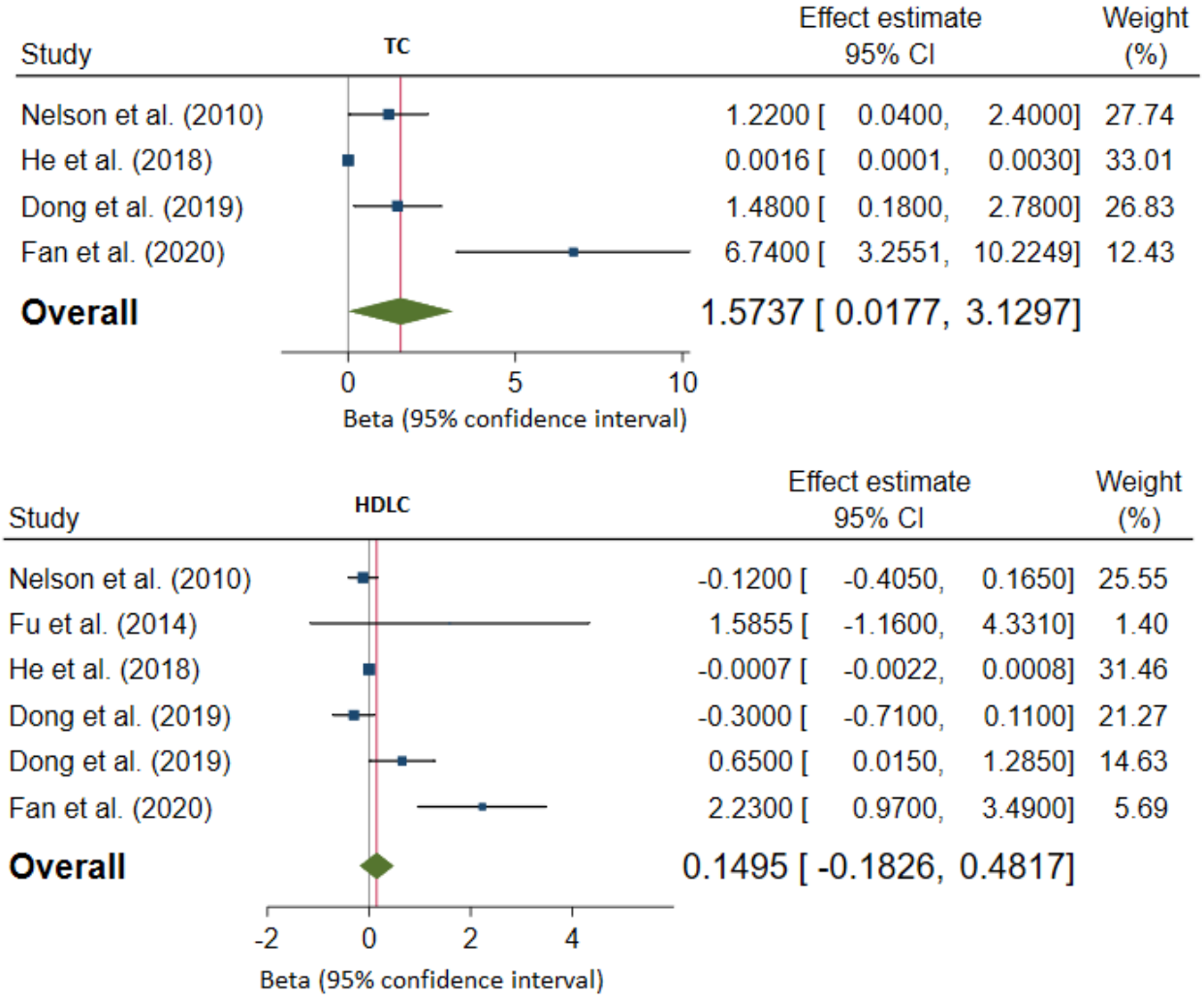


Figure F-2: Forest Plots Showing the Beta Coefficients Relating PFOA Concentrations to TC and HDLC in Each Study Reporting Linear Associations, and Pooled Estimates After Random-Effects Meta-Analysis.

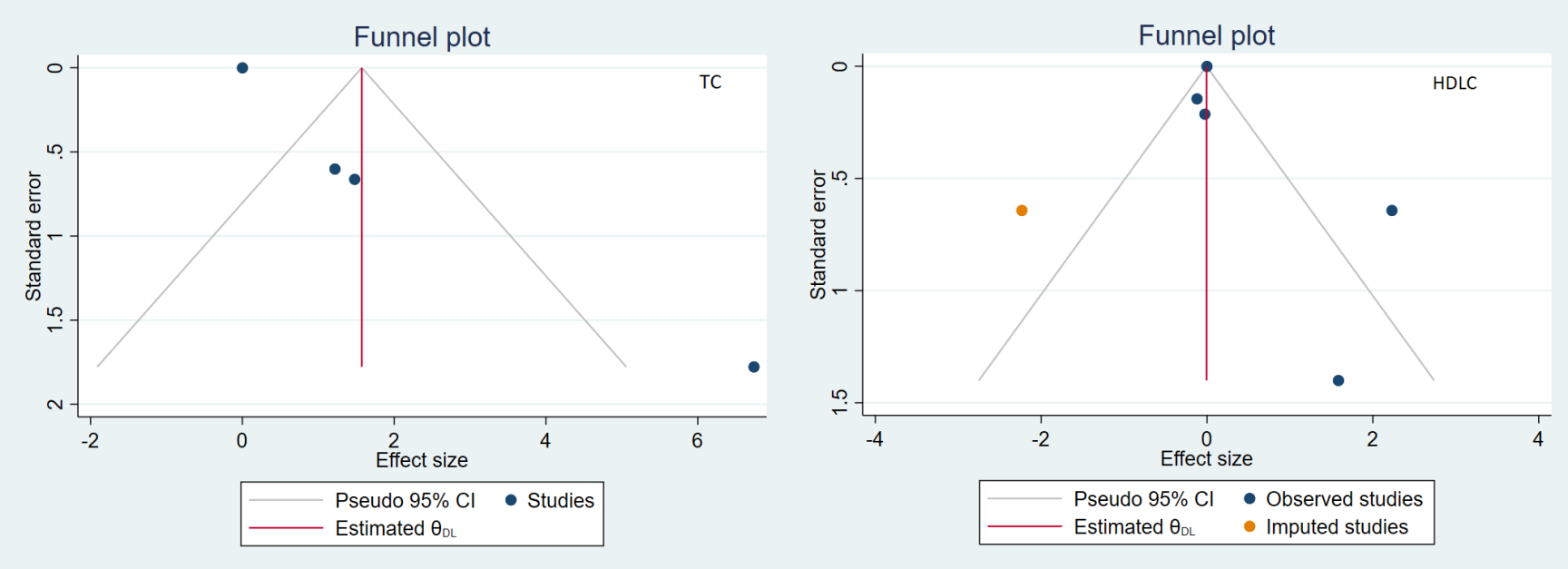


Figure F-3: Filled-in Funnel Plots to Evaluate Publication Bias of the PFOA and TC (Left) or HDLC (Right) Association in Studies Reporting Linear Associations.

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).

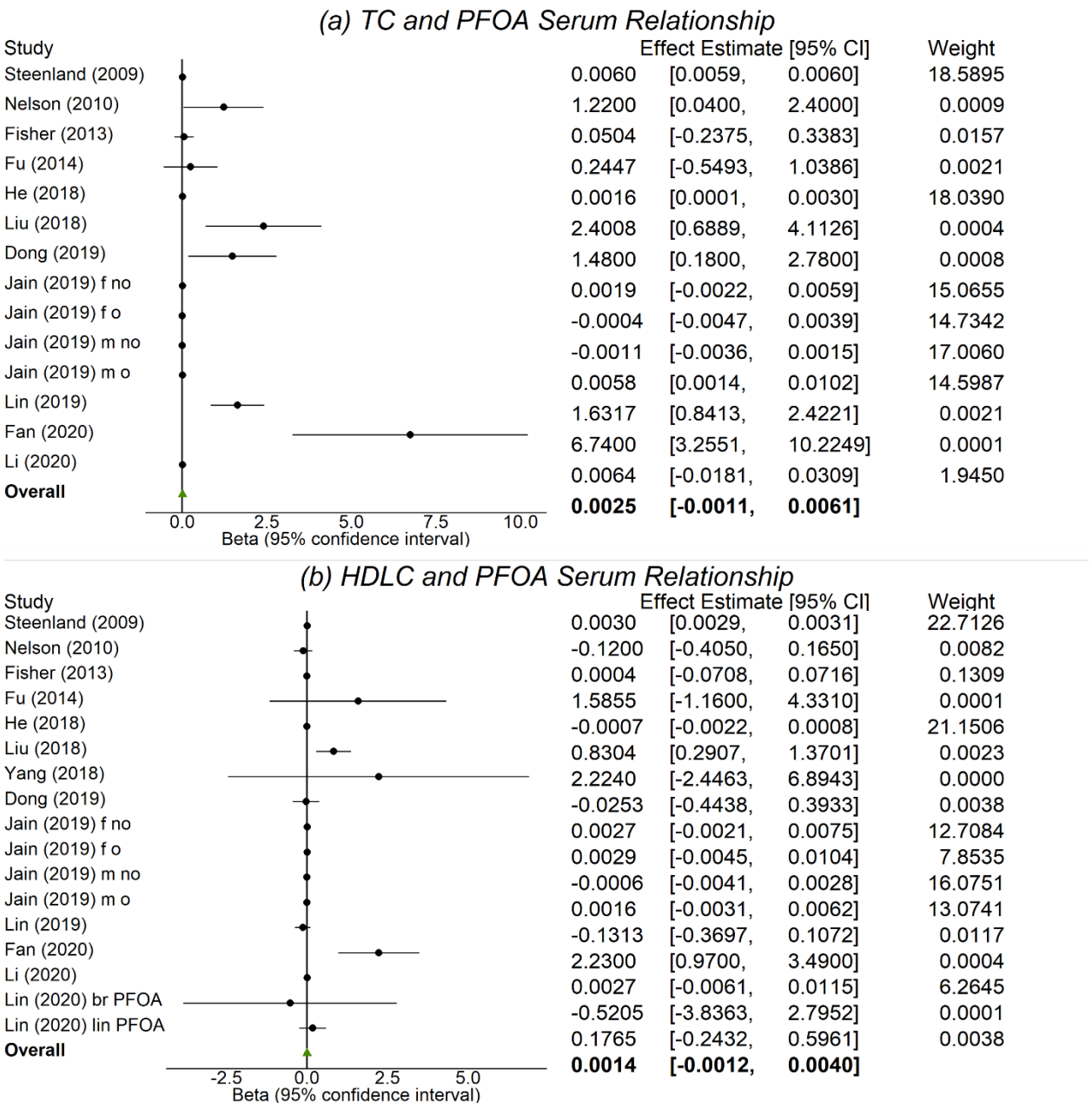


Figure F-4: Forest Plots Showing the Beta Coefficients Relating TC and HDLC to PFOA Concentrations in Each Study, and Pooled Estimates After Random-Effects Meta-Analysis.

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

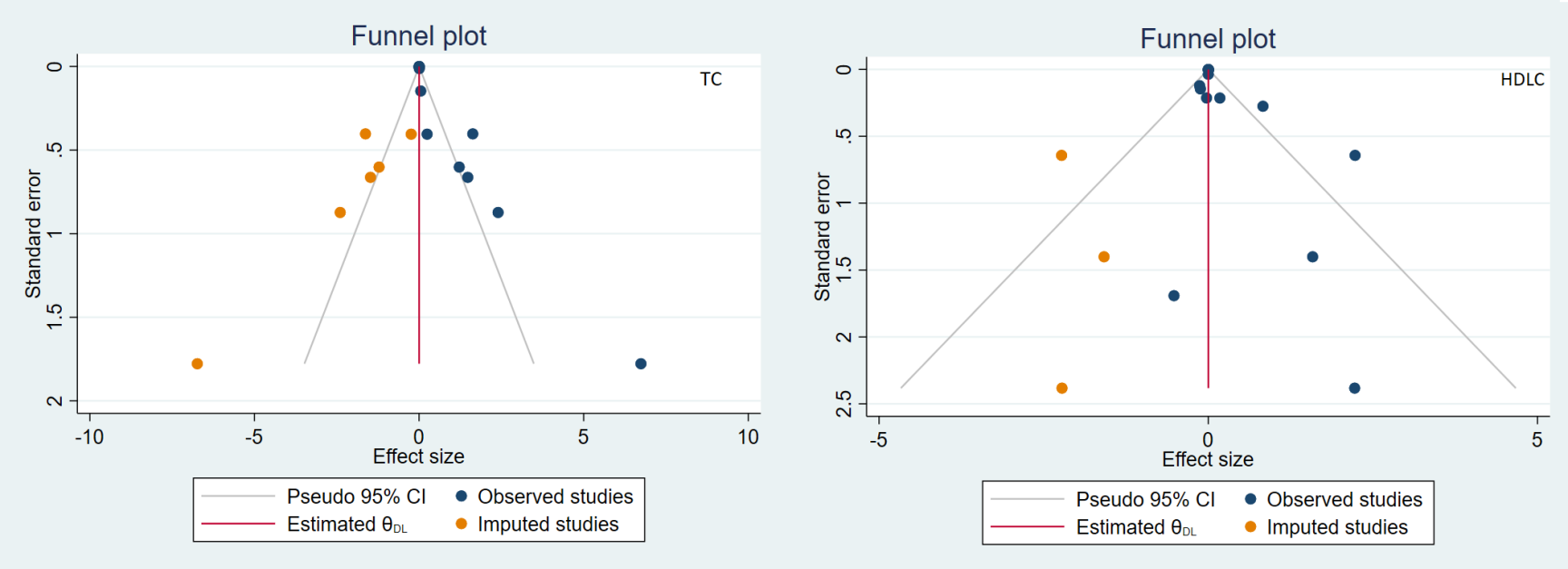


Figure F-5: Filled-in Funnel Plots to Evaluate Publication Bias of the PF OA and TC (Left) or HDLC (Right) Association.

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, I^2 = 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), the 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). The EPA observed similar results in leave-one-out analyses, sensitivity analyses restricted to U.S. or Canadian general population studies, and analyses excluding Jain and Ducatman (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: the 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), the 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.[35]

[35] The EPA characterizes uncertainty surrounding this estimate as described in Appendix L.

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	Tau2
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 and Ducatman (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 and Ducatman (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	2b	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: CI – confidence interval; HDLC– high-density lipoprotein cholesterol; TC– total cholesterol; NHANES – National Health and Nutrition Examination; PFOS– perfluorooctanesulfonic acid.

Notes:

[a]Q statistics for heterogeneity. Tau2 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) and Château-Degat et al. (2010).

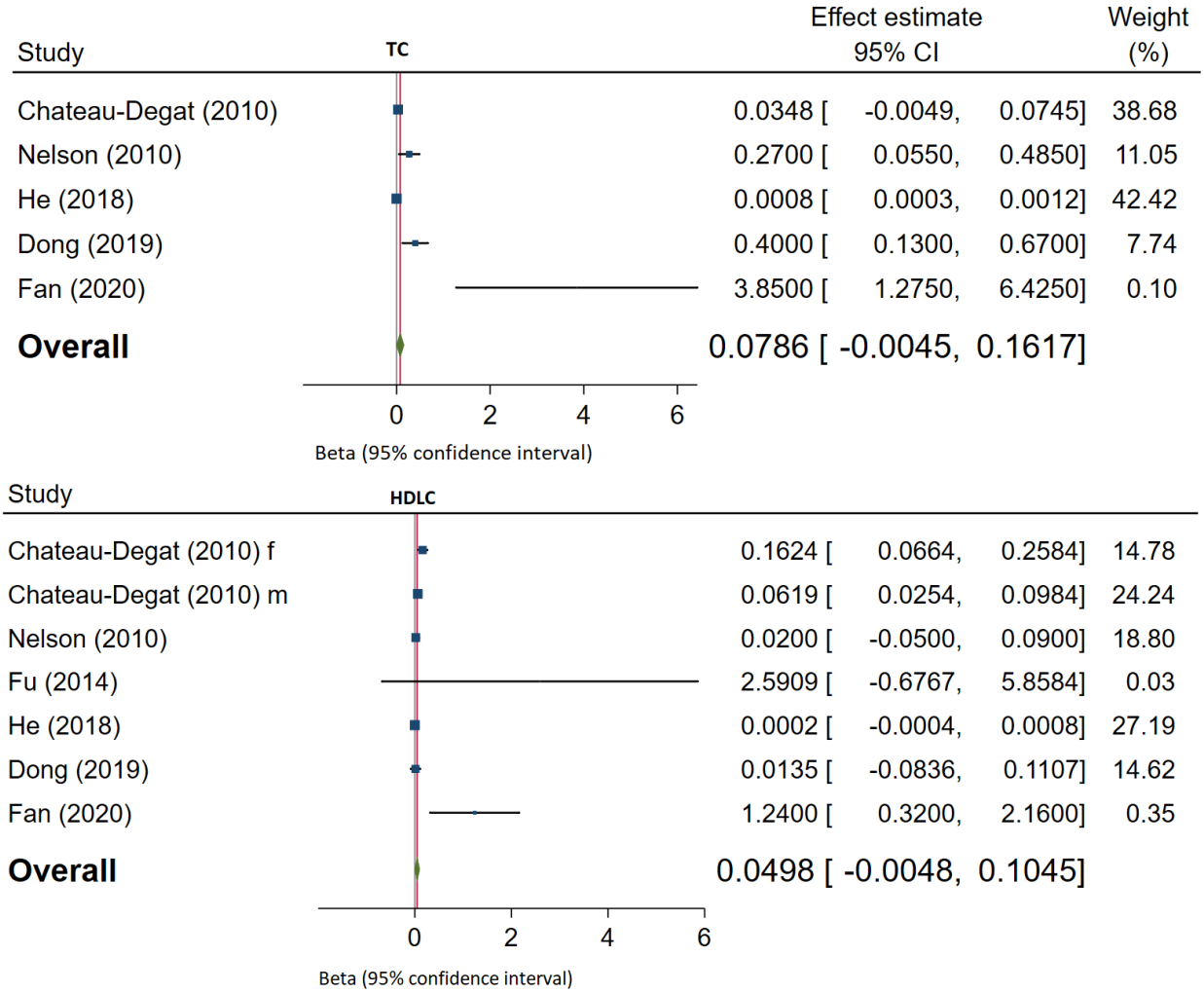


Figure F-6: Forest Plots Showing the Beta Coefficients Relating TC and HDLC to PFOS Concentrations in Each Study Reporting Linear Associations, and Pooled Estimates After Random-Effects Meta-Analysis.

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

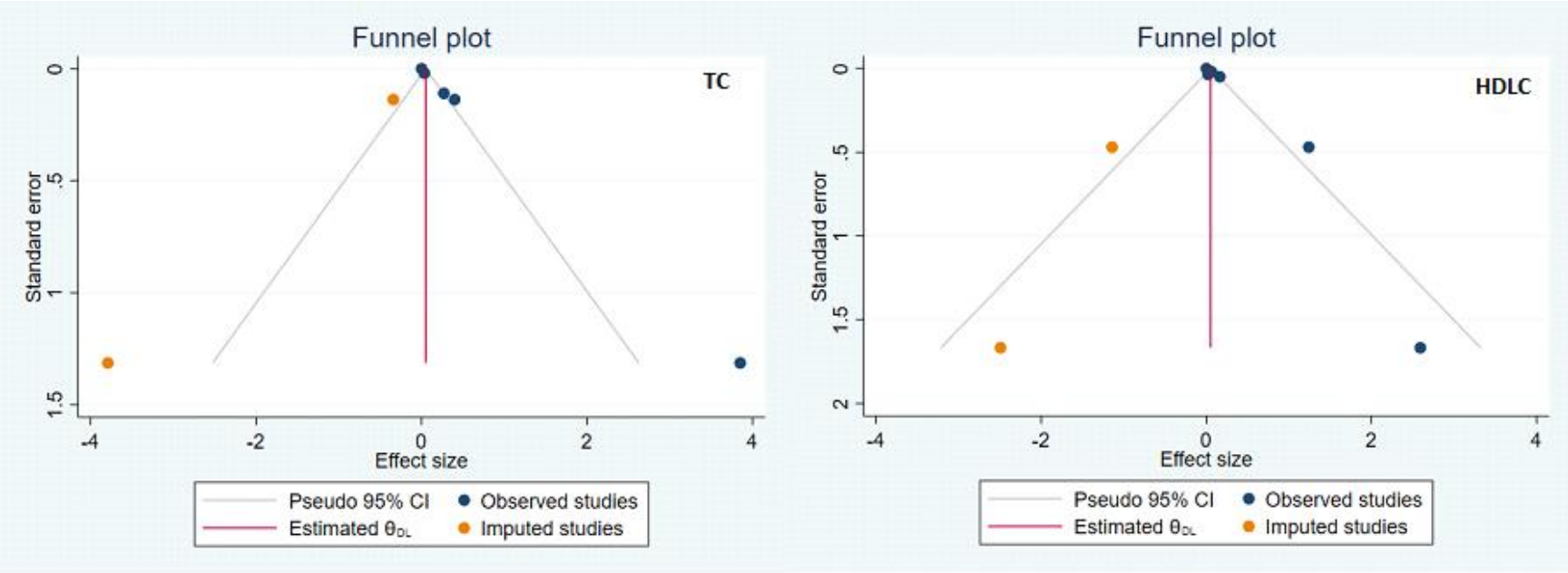


Figure F-7: Filled-in Funnel Plots to Evaluate Publication Bias of the PFOS and TC (Left) or HDLC (Right) Association in Studies Reporting Linear Associations.

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).

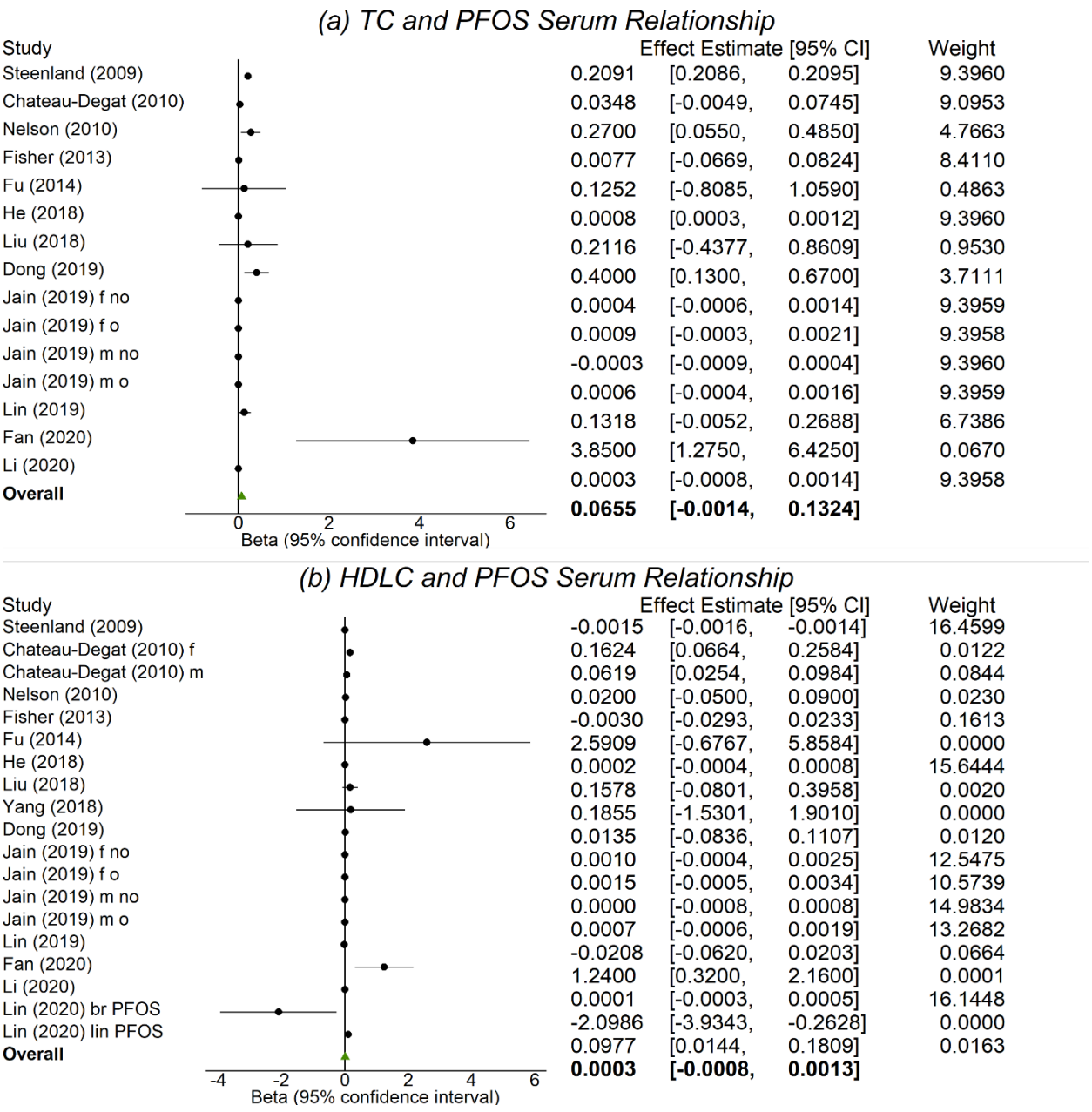


Figure F-8: Forest Plots Showing the Beta Coefficients Relating PFOS Concentrations to TC and HDLC in Each Study, and Pooled Estimates After Random-Effects Meta-Analysis.

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

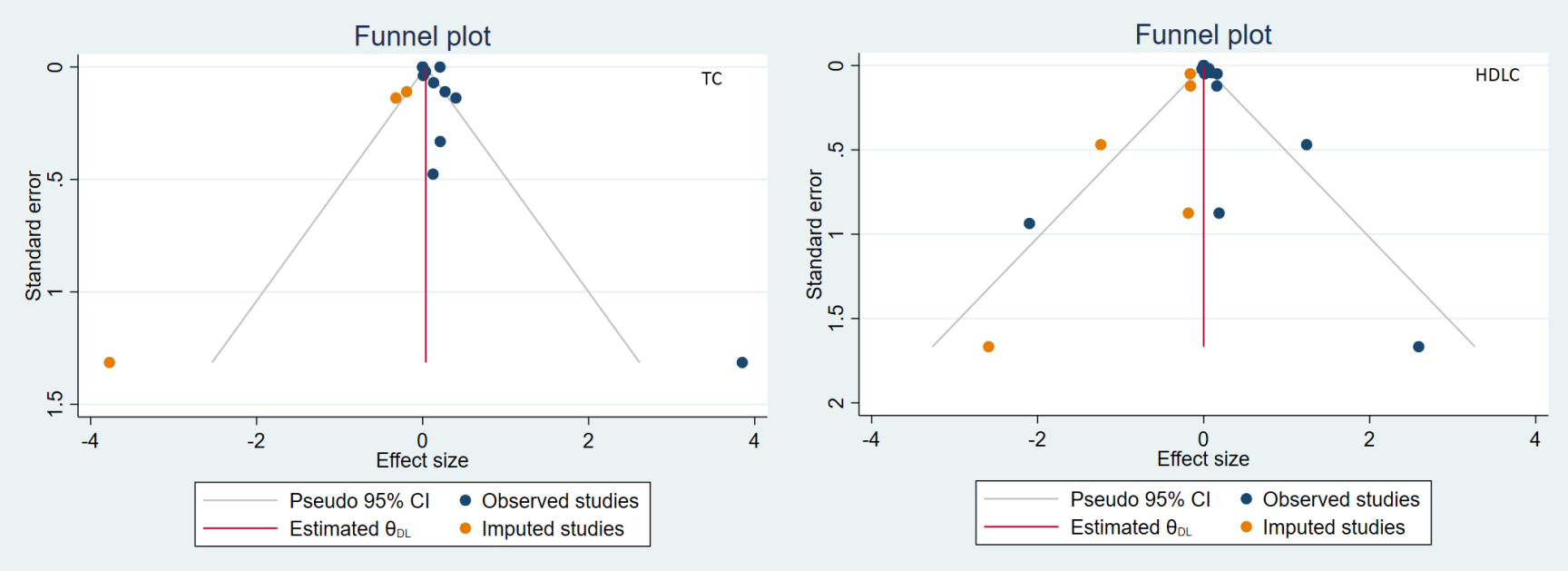


Figure F-9: Filled-in Funnel Plots to Evaluate Publication Bias of the PFOS and TC (Left) or HDLC (Right) Association.

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

The 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 the EPA's *Final Human Health Toxicity Assessments for PFOA and PFOS*, the EPA considered this medium quality study for estimating point of departure for potential use in toxicity value derivation (U.S. EPA, 2024b; U.S. EPA, 2024c).

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 and Ducatman (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.	The 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 & Mazumdar, 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 & Chu, 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 (BP) 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 the EPA's SAB; 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, 2024b; U.S. EPA, 2024c); therefore, the 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 (EA). First hard CVD events included in the model include 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. The 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, the 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, the 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.[36] The CVD model calculations are identical across the race/ethnicity and sex demographic subgroups but use subgroup-specific coefficients.[37] 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.[38] 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.

[36] 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.

[37] 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.

[38] 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. The EPA also relied on serum PFOA/PFOS values at age 85 for the 85+ cohort.

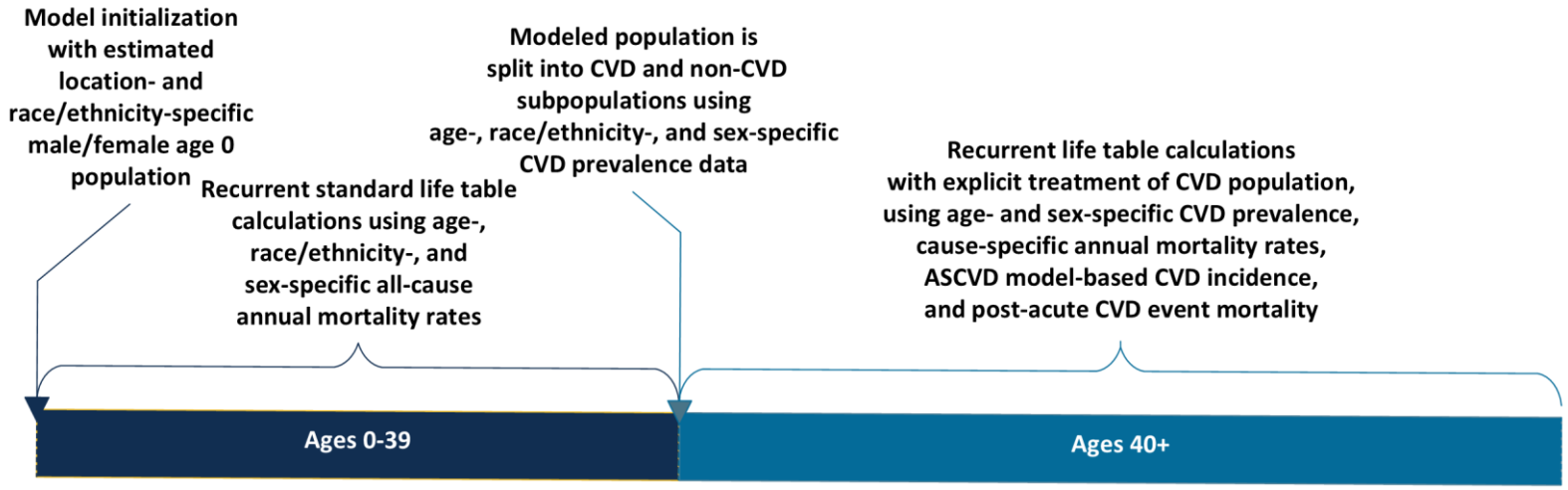


Figure G-1: Overview of Life Table Calculations in the CVD Model.

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[39] (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).

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

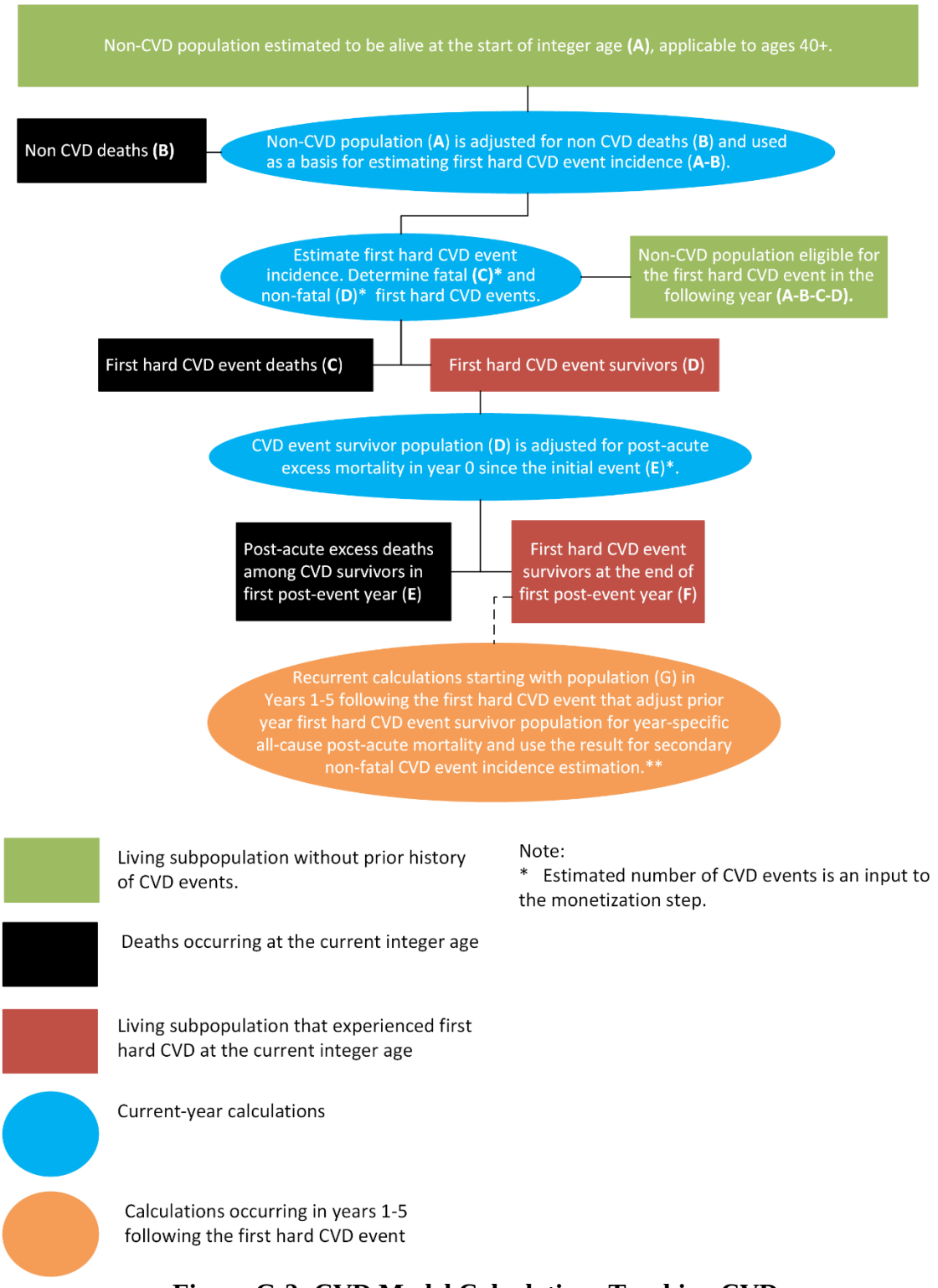


Figure G-2: CVD Model Calculations Tracking CVD and Non-CVD Subpopulations for a Specific Current Age of Cohort.

Table G-1 summarizes the data elements and notation of the CVD model.[40] 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.[41] 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, $A = \{0,1,2,\dots,99\}$. 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, $B = \{-T,\dots,0,1,\dots,T-40\}$
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 , 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., the EPA assumes that people who have just been born do not have CVD history by definition.

[40] 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.

[41] 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
ΔM_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, the 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. The 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, the 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, the 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. The 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: The 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, the 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). The 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. The 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)
			52	40	135	212
Males	18–44	Hispanic	(6–99)	(-4–83)	(55–214)	(111–313)
	45–64	Hispanic	276	421	735	1,142

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
			(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, the 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)

The 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). The 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.[42] 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, the 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). The 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. The 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.

[42] 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

The 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 the 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.[43]

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. The EPA derived these probabilities by adjusting all-cause post-acute mortality probabilities reported in Table G-7 for the ages 45–64 group[44] 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 & Xu, 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. The EPA used post-acute mortality data for non-Hispanic Whites to estimate mortality effects for the other race/ethnicity groups.

[43] 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%.

[44] The 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, the 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 & Xu, 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+

The 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 the EPA made to incorporate CVD mortality information in the model. First, the 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). The EPA derived the sex- and age-specific non-CVD mortality rates from U.S. Life Tables, 2017 (Arias & Xu, 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). The 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, the EPA calculated CVD mortality probability as the difference between the all-cause death probability and the non-CVD death probability. Third, the EPA calculated CVD mortality rate multipliers as a ratio of CVD mortality probability to the non-CVD death probability. The 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 Multiplierd	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 & Xu, 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 & Xu, 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:

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

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, the 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, the EPA uses age 85 as the input to ASCVD model at the start of the evaluation period. Finally, the 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:

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

The 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, the 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:

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

The 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, the 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 the 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, the 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 :

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

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, $q_{a,s,r,\text{OTH}}$, 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:

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

These estimates are used in combination with the baseline calibration factor, $\chi_{b,a,s,r,t}$, and the 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, $\chi_{b,a,s,r,t}$, the 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.

The 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:

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

The 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:

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

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.

The 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). The 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 & Xu, 2019); and CVD death rates, 1999–2019 (Centers for Disease Control and Prevention, 2020c).

For each race/ethnicity, sex, and age combination, the EPA first computed the ratio of CVD incidence based on reported data and incidence based on the ASCVD model. The 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) Sex: males, females 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 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) Sex: males, females 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+ Sex: males, females Race/Ethnicity: non-Hispanic White, non-Hispanic Black, non-Hispanic other, Hispanic 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) Sex: males, females 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) Sex: males, females 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) Sex: males, females 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) Sex: males, females 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 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 Age: integer ages 0 … 100 Race/Ethnicity: all, non-Hispanic White, non-Hispanic Black, Hispanic	U.S. Life Tables, 2017 (Arias & Xu, 2019)	The quantity used in modeling is qx (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 Age: integer ages 90 … 100 Race/Ethnicity: all, non-Hispanic White, non-Hispanic Black, Hispanic	U.S. Life Tables, 2017 (Arias & Xu, 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 qx from the 2017 U.S. life tables by the sex-specific ratio of non-CVD qx to all-cause qx 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 qx to all-cause qx 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 Age: integer ages 40 … 89 Race/Ethnicity: non-Hispanic White, non-Hispanic Black, non-Hispanic other, Hispanic	U.S. Life Tables 2017 (Arias & Xu, 2019); CVD death rates, 1999–2019 (Centers for Disease Control and Prevention, 2020c)	Annual non-CVD death probability is estimated by multiplying qx from 2017 U.S. life tables by the ratio of non-CVD qx to all-cause qx. The non-CVD qx estimate was obtained for each integer age by sex combination as the difference between all-cause qx from U.S. 2017 life tables and CVD qx 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 Age: age groups 18–44, 45–64, 65+ Race/Ethnicity: non-Hispanic White, non-Hispanic Black, non-Hispanic other, Hispanic 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 Age: age groups 18–44, 45–64, 65+ Race/Ethnicity: non-Hispanic White, non-Hispanic Black, non-Hispanic other, Hispanic 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 Age: age groups 18–44, 45–64, 65–84, 85+ 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. The 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 Race: all Age: age groups 40–65 Condition: MI	Thom et al. (2001); MI incidence based on the MEPS 2010–2017 analysis, U.S. Life Tables, 2017 (Arias & Xu, 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, the 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, the EPA further assumed that the annual probability of death between 1-year follow-up and 5-year follow-up was constant. Finally, the 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 Race: all Age: age group 65+ 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 Race: non-Hispanic White, non-Hispanic Black, Age: age groups 40–65 Condition: MI	Thom et al. (2001); MI incidence based on the MEPS 2010–2017 analysis, U.S. Life Tables, 2017 (Arias & Xu, 2019); CVD death rates 1999–2019 (Centers for Disease Control and Prevention, 2020c)	The 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). The 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, the 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, the 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 Race: all Age: ages 66 … 89 Condition: MI, IS	S. Li et al. (2019); U.S. Life Tables, 2017 (Arias & Xu, 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)	The 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, bladder, and liver 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 R. N. Anderson (1999). The 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 PM2.5-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 the 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.43F[45] 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. The 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 2029 to comply with the final regulation. To capture these effects while being consistent with the remainder of the benefit

[45] When referring to the "cancer-free" population, the 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.

framework, the EPA modeled changes in health outcomes resulting from changes in exposure over an evaluation period that starts in 2024 and ends in 2105.[46]

The model tracks all-cause mortality and cancer experience for a set of model populations defined by sex, location (if modeled), birth year $B = 1938, \ldots, 2024, 2025, \ldots, 2105$, and age attained by 2024 (for those alive in 2024), which is denoted by $A = 0,1,2,3, \ldots 85+$.[47] Each model population is followed from age 0 in year B to age $\min(100, 2105 - B)$ in year $\min(B + 100, 2105)$, 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 2024, 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, the 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.[48] The EPA omits sex and location-specific indices because calculation steps do not differ across sexes and locations. The EPA then describes the process for quantifying the evolution of the population under regulatory alternative exposures. Finally, the EPA describes the process for estimating the total calendar year y-specific health benefits. The EPA aggregates benefits estimates over all model populations ($(B, A) = \{(1938,85+), \ldots, (2024,0), (2025,0), \ldots, (2105,0)\}$).

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 2024 (years) for those alive in 2024, 0 for those born after 2024
P	Number of affected persons of age A in 2024 or persons aged 0 born after 2024
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

[46] Although benefits of lagged changes in lifetime cancer risk after 2105 may be attributed to changes in contaminant exposure during the analysis period, the EPA did not model effects beyond this period.

[47] Note that those born after the start of the evaluation period in 2023 (i.e., during 2024-2105) 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.

[48] 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
τ_a	Share of cancer deaths among all-cause deaths at age a
γ_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, the 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[49] $q_a(1-\tau_a)$ and new cancer diagnoses that occur with probability γ_a, which is approximated by age-specific annual cancer incidence rate IR_a. In the model, the EPA assumes that the new cancer diagnoses occur after general population non-cancer deaths and use the following recurrent equations for ages $a >$ 0:48F[50]

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 2024, the 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 2024, 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 $P \equiv l_{C=0,A,2024}(z_{A,2024})$. To initiate each set of recurrent equations for those born after 2024, the 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.

[49] 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.

[50] The 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), the 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, the 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 $\delta_{S=s,a}$, the 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, the EPA separately tracks $\min(85{,}2105 - B) - A + 1$ new stage-specific cancer populations from age-at-onset a to age $\min(85{,}2105 - B)$.49F[51] Next, a set of cancer duration k-dependent annual death probabilities is derived for each population from available data on relative survival rates50F[52] $r_{S=s,a,k}$ and general population annual death probabilities q_{a+k} as follows:

Equation H-5:

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

The 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., $k > 0$), the 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:

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

[51] In total, there are $4 \cdot (\min(85{,}2105 - B) - A + 1)$ new cancer populations being tracked for each model population.

[52] 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, the 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 2029), the EPA approximates the annual cancer probability γ_a by age-specific annual cancer incidence rate IR_a. The 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, the 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, the 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, the 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:

$$NC_{B,A,y,s} = [0 \le y - \max(2024, B) + A \le \min(85, 2105 - B)\,] \cdot \left(\tilde{l}_{S=s,y-\max(2024,B)+A,y,0}\left(z_{y-\max(2024,B)+A,y}\right) - \tilde{l}_{S=s,y-\max(2024,B)+A,0}\left(x_{y-\max(2024,B)+A,y}\right)\right)$$

Equation H-14:

$$LC_{B,A,y,s} = \sum_{k=1}^{100} [0 \le y - \max(2024, B) + A + k \le \min(85, 2105 - B)\,] \cdot \left(\tilde{l}_{S=s,y-\max(2024,B)+A-k,y,k}\left(z_{y-\max(2024,B)+A-k,y-k}\right) - \tilde{l}_{S=s,y-\max(2024,B)+A-k,y,k}\left(x_{y-\max(2024,B)+A-k,y-k}\right)\right)$$

Equation H-15:

$$ED_{B,A,y} = \sum_{k=0}^{100} [0 \le y - \max(2024, B) + A + k \le \min(85, 2105 - B)\,] \sum_{s \in S} \left(\tilde{e}_{S=s,y-\max(2024,B)+A-k,y,k}\left(z_{y-\max(2024,B)+A-k,y-k}\right) - \tilde{e}_{S=s,y-\max(2024,B)+A-k,y,k}\left(x_{y-\max(2024,B)+A-k,y-k}\right)\right)$$

These calculations are carried out to 2105.

H.2 Cancer Life Table Model Input Data

As noted in Section 6.6.2 of the economic analysis, the EPA relied on data sources including SDWIS/Fed, 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 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) Sex: males, females Cancer type: Kidney Cancer; Urinary Bladder (Invasive & In Situ) Cancer Race/ethnicity: All, non-Hispanic White, non-Hispanic Black, Hispanic, non-Hispanic Other	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+. The EPA assumed that the same IR applies to all ages within each age group. The EPA assumed that non-Hispanic Black iRs can be approximated by Black iRs. The EPA assumed

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

Data Element	Modeled Variability	Data Source	Notes
			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) Sex: males, females Race/ethnicity: All, non-Hispanic White, non-Hispanic Black, Hispanic, non-Hispanic Other	CDC/National Center for Health Statistics (NCHS) United States Life Tables, 2017 (Arias & Xu, 2019)	The EPA used race/ethnicity-, age- and sex-specific probabilities of dying within the integer age intervals. The 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) Sex: males, females Cancer type: Kidney Cancer; Urinary Bladder (Invasive & In Situ) Cancer 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)	The 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) Sex: males, females Cancer stage: localized, regional, distant, unstaged 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+. The 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) Sex: males, females Cancer stage: localized, regional, distant, unstaged Cancer type: Kidney Cancer 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+. The EPA assumed that the same cancer incidence shares by stage apply to all ages within each age group. The EPA assumed that non-Hispanic Black data can be approximated by Black data. The 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) Sex: males, females Duration: 1-year groups (durations 0 to 100 years) Cancer stage: localized, regional, distant, unstaged Cancer type: Urinary Bladder (Invasive & In Situ) Cancer	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+. The 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 10 years. For disease durations

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

Data Element	Modeled Variability	Data Source	Notes
			longer than 10 years the EPA applied 10-year relative survival rates.
Relative kidney cancer survival by cancer stage	Age at diagnosis: 1-year groups (ages 0 to 100) Sex: males, females Duration: 1-year groups (durations 0 to 100 years) Cancer stage: localized, regional, distant, unstaged Cancer type: Kidney Cancer 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+. The EPA assumed that the same cancer relative survival patterns apply to all ages within each age group. The EPA assumed that non-Hispanic Black data can be approximated by Black data. The 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 the 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[53] 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.

[53] 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	-
	Ages 15-39	2 years	98	77	20	-	96	76	20	-	95	70	15	-	92	67	15	-

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	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
	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

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	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
	Ages 65-74	10 years	80	47	5.6	27	54	32	3.8	18	85	48	2	28	47	27	1.1	16

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+	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	-
	Ages <15	9 years	97	94	72	-	96	93	71	-	93	95	58	-	92	94	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	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
	Ages 40-64	3 years	97	82	21	70	93	78	20	67	95	82	24	60	88	76	22	56

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	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
	Ages 65-74	7 years	89	69	10	44	76	59	8.2	38	87	59	10	26	68	46	7.8	20

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	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	-
	Ages <15	5 years	97	93	80	92	96	93	79	92	97	94	73	-	96	93	72	-

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	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
	Ages 15-39	10 years	95	69	13	77	93	68	12	76	94	65	7.7	66	90	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 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
	Ages 65-74	4 years	94	73	14	49	82	64	12	43	94	74	15	48	77	60	13	39

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	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
	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

Age	Females			Males		
	Rate per 100K		Percent Kidney Cancer	Rate per 100K		Percent Kidney Cancer
	All-Cause	Kidney Cancer		All-Cause	Kidney Cancer	
<1	537	0.04	0.007	646	0.045	0.007
1-4	22	0.070	0.31	28	0.079	0.28
5-9	11	0.084	0.80	13	0.065	0.50
10-14	12	0.043	0.36	17	0.036	0.21
15-19	29	0.042	0.15	68	0.042	0.062
20-24	46	0.063	0.14	129	0.099	0.077
25-29	61	0.075	0.12	150	0.14	0.093
30-34	82	0.13	0.16	169	0.20	0.12
35-39	111	0.23	0.21	199	0.49	0.25
40-44	159	0.40	0.25	259	1.1	0.43
45-49	246	0.91	0.37	390	2.5	0.65
50-54	376	1.8	0.47	609	4.9	0.80
55-59	545	3.1	0.57	916	8.5	0.92
60-64	785	4.7	0.60	1304	13	0.98
65-69	1166	7.1	0.61	1829	18	1.00
70-74	1844	10	0.56	2720	24	0.89
75-79	3027	14	0.47	4280	32	0.74
80-84	5193	19	0.37	7039	41	0.58
85+	-	-	0.21	-	-	0.37

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	0.0091	0.0020	554	0.043	0.0078
	1-4	20	0.060	0.73	26	0.080	0.30
	5-9	10	0.072	3.3	12	0.069	0.57
	10-14	12	0.044	2.7	16	0.025	0.15
	15-19	30	0.039	1.1	63	0.019	0.031
	20-24	48	0.043	0.53	124	0.040	0.032
	25-29	66	0.055	0.48	153	0.093	0.061
	30-34	89	0.098	0.60	177	0.15	0.087
	35-39	120	0.21	0.99	209	0.45	0.22
	40-44	168	0.38	1.3	269	1.1	0.42
	45-49	254	0.93	2.3	401	2.7	0.66
	50-54	380	1.9	3.0	616	5.1	0.84
	55-59	544	3.2	3.4	909	8.8	0.97
	60-64	779	4.9	3.6	1282	13	1.0
	65-69	1172	7.4	3.5	1810	19	1.0
	70-74	1881	11	3.0	2732	25	0.92
	75-79	3108	15	2.6	4347	33	0.76
	80-84	5351	20	2.1	7225	42	0.59
	85+	-	-	2.6	-	-	0.36
Non-Hispanic Black	<1	1042	0.031	0.0029	1249	0.029	0.0024
	1-4	36	0.11	0.77	45	0.10	0.23
	5-9	16	0.15	4.3	20	0.076	0.37

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	
	10-14	17	0.053	1.8	25	0.098	0.39
	15-19	34	0.095	2.1	111	0.14	0.12
	20-24	63	0.18	1.7	202	0.38	0.19
	25-29	86	0.21	1.4	232	0.40	0.17
	30-34	121	0.31	1.5	262	0.55	0.21
	35-39	173	0.39	1.3	312	0.96	0.31
	40-44	249	0.44	1.0	397	1.5	0.38
	45-49	377	1.1	1.8	572	2.9	0.51
	50-54	579	1.8	1.9	892	5.0	0.56
	55-59	844	3.2	2.1	1398	8.6	0.61
	60-64	1193	4.7	2.1	2052	14	0.66
	65-69	1656	7.3	2.2	2791	19	0.68
	70-74	2399	9.5	2.0	3820	24	0.63
	75-79	3616	13	1.9	5464	31	0.57
	80-84	5700	18	1.6	8058	37	0.45
	85+	-	-	2.4	-	-	0.36
Hispanic	<1	435	0.055	0.013	513	0.070	0.014
	1-4	19	0.063	0.82	23	0.056	0.25
	5-9	9	0.080	3.6	11	0.053	0.49
	10-14	11	0.042	2.3	14	0.018	0.13
	15-19	23	0.016	0.49	58	0.034	0.058
	20-24	34	0.041	0.66	106	0.082	0.078
	25-29	39	0.038	0.50	111	0.11	0.10

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	
	30-34	50	0.092	0.98	117	0.15	0.13
	35-39	65	0.23	2.0	137	0.40	0.29
	40-44	95	0.47	2.8	180	0.97	0.54
	45-49	149	0.80	3.0	275	2.3	0.84
	50-54	232	1.6	3.8	438	4.2	0.95
	55-59	355	3.1	4.7	665	7.4	1.1
	60-64	550	4.8	4.7	982	12	1.2
	65-69	840	6.9	4.3	1402	17	1.2
	70-74	1328	10	4.1	2113	23	1.1
	75-79	2251	14	3.3	3343	30	0.90
	80-84	3960	19	2.6	5411	34	0.63
	85+	-	-	2.7	-	-	0.44
Other	<1	409	0.22	0.053	498	0.000	0.000
	1-4	19	0.070	0.97	24	0.10	0.43
	5-9	10	0.041	1.7	12	0.053	0.46
	10-14	11	0.014	0.79	13	0.054	0.40
	15-19	23	0.027	0.90	48	0.052	0.11
	20-24	33	0.024	0.43	80	0.034	0.043
	25-29	37	0.051	0.74	85	0.095	0.11
	30-34	47	0.13	1.4	93	0.076	0.082
	35-39	62	0.15	1.4	113	0.26	0.23
	40-44	88	0.30	2.0	154	0.63	0.41
	45-49	139	0.55	2.3	234	1.4	0.61

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	
	50-54	210	0.96	2.6	354	2.9	0.82
	55-59	298	1.7	3.2	527	5.1	0.97
	60-64	438	2.2	2.7	754	8.1	1.1
	65-69	661	3.6	2.9	1081	9.6	0.89
	70-74	1066	6.2	3.0	1623	13	0.83
	75-79	1849	8.0	2.3	2661	17	0.64
	80-84	3363	12	1.9	4522	23	0.51
	85+	-	-	2.1	-	-	0.35

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[54] 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.

[54] 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

Age	Females			Males		
	Rate per 100K		Percent Bladder Cancer	Rate per 100K		Percent Bladder Cancer
	All-Cause	Bladder Cancer		All-Cause	Bladder Cancer	
<1	537	0	0	646	0.0090	0.0014
1-4	22	0.002	0.010	28	0.0011	0.0040
5-9	11	0.002	0.017	13	0.0009	0.0068
10-14	12	0.004	0.030	17	0.0034	0.0202
15-19	29	0.002	0.006	68	0.0033	0.0049
20-24	46	0.008	0.016	129	0.016	0.012
25-29	61	0.035	0.057	150	0.029	0.019
30-34	82	0.067	0.082	169	0.10	0.060
35-39	111	0.22	0.19	199	0.28	0.14
40-44	159	0.47	0.30	259	0.77	0.30
45-49	246	0.92	0.37	390	2.0	0.52
50-54	376	1.6	0.43	609	4.4	0.72
55-59	545	2.8	0.51	916	8.8	0.96
60-64	785	4.7	0.60	1304	16	1.2
65-69	1166	8.0	0.69	1829	27	1.5
70-74	1844	15	0.82	2720	49	1.8
75-79	3027	27	0.88	4280	88	2.1
80-84	5193	43	0.83	7039	146	2.1
85+	-	-	0.54	-	-	1.6

H.5 Baseline Liver Cancer Statistics

Table H-12 provides baseline liver cancer incidence data used in the life table model. Liver cancer incidence rates per 100,000 range from 0.089 to 32 for females and from 0.10 to 72 for males. Liver cancer incidence rates are highest for men in their 60s, 70s, and 80s, ranging from 58 per 100,000 to 72 per 100,000. Localized liver cancers comprise 35%-44% of all liver cancer incidence, whereas regional liver cancers comprise 20%-28%, distant liver cancers comprise 17%-29%, and unstaged liver cancers comprise 4.1%-26% of all liver cancer incidence.

Table H-12: Summary of Baseline Liver 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	1.3	50	24	18	7.1	1.8	46	28	22	4.1
1-4	0.52	50	24	18	7.1	0.77	46	28	22	4.1
5-9	0.12	50	24	18	7.1	0.13	46	28	22	4.1
10-14	0.089	50	24	18	7.1	0.10	46	28	22	4.1
15-19	0.16	39	23	29	8.8	0.16	35	27	28	10
20-24	0.19	39	23	29	8.8	0.19	35	27	28	10
25-29	0.27	39	23	29	8.8	0.41	35	27	28	10
30-34	0.44	39	23	29	8.8	0.74	35	27	28	10
35-39	0.80	39	23	29	8.8	1.3	35	27	28	10
40-44	1.4	43	24	21	12	2.4	41	27	18	14
45-49	2.2	43	24	21	12	5.9	41	27	18	14
50-54	4.6	43	24	21	12	16	41	27	18	14
55-59	9.5	43	24	21	12	36	41	27	18	14
60-64	16	43	24	21	12	58	41	27	18	14
65-69	23	44	23	21	13	72	41	27	18	14
70-74	24	44	23	21	13	64	41	27	18	14
75-79	30	36	20	18	26	63	38	24	17	21
80-84	32	36	20	18	26	66	38	24	17	21
85+	29	36	20	18	26	56	38	24	17	21

Table H-13: Summary of Race/Ethnicity-Specific Baseline Liver 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	1.3	52	23	18	7	1.7	45	28	21	6
	1-4	0.4	52	23	18	7	0.7	45	28	21	6
	5-9	0	52	23	18	7	0.2	45	28	21	6
	10-14	0	52	23	18	7	0	45	28	21	6
	15-19	0.2	39	26	28	8	0.2	37	24	30	10
	20-24	0.2	39	26	28	8	0.2	37	24	30	10
	25-29	0.3	39	26	28	8	0.3	37	24	30	10
	30-34	0.4	39	26	28	8	0.6	37	24	30	10
	35-39	0.7	39	26	28	8	0.8	37	24	30	10
	40-44	1.3	41	25	22	12	1.6	41	27	18	14
	45-49	1.8	41	25	22	12	3.8	41	27	18	14
	50-54	3.8	41	25	22	12	10.6	41	27	18	14
	55-59	7.7	41	25	22	12	27.5	41	27	18	14
	60-64	12.2	41	25	22	12	46	41	27	18	14
	65-69	16.8	40	24	23	12	56.8	40	27	18	14
	70-74	18.4	40	24	23	12	52.2	40	27	18	14
	75-79	23.4	33	20	19	27	53.6	38	24	18	20
	80-84	25.1	33	20	19	27	56.6	38	24	18	20
	85+	23.3	33	20	19	27	47.8	38	24	18	20
Non-Hispanic Black	<1	0	38	31	25	6	0	47	27	24	1
	1-4	0	38	31	25	6	0.6	47	27	24	1
	5-9	0	38	31	25	6	0	47	27	24	1
	10-14	0	38	31	25	6	0	47	27	24	1
	15-19	0	42	21	27	10	0	27	30	32	11
	20-24	0	42	21	27	10	0	27	30	32	11
	25-29	0	42	21	27	10	0.6	27	30	32	11
	30-34	0.7	42	21	27	10	1.2	27	30	32	11
	35-39	0.9	42	21	27	10	1.9	27	30	32	11
	40-44	1.1	41	26	19	13	2.3	38	29	19	14
	45-49	2.5	41	26	19	13	5	38	29	19	14
	50-54	4.9	41	26	19	13	12.8	38	29	19	14
	55-59	11.6	41	26	19	13	41.8	38	29	19	14
	60-64	23.8	41	26	19	13	86.8	38	29	19	14
	65-69	30.3	42	24	21	12	118	40	28	18	14
	70-74	22.9	42	24	21	12	85.6	40	28	18	14
	75-79	22	32	23	21	24	57.6	35	22	20	24
	80-84	25.9	32	23	21	24	48	35	22	20	24
	85+	25.7	32	23	21	24	38.7	35	22	20	24

Table H-13: Summary of Race/Ethnicity-Specific Baseline Liver 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	1.3	50	24	18	8	1.5	46	30	21	3
	1-4	0.7	50	24	18	8	1	46	30	21	3
	5-9	0	50	24	18	8	0	46	30	21	3
	10-14	0	50	24	18	8	0	46	30	21	3
	15-19	0	37	20	33	10	0	37	24	26	13
	20-24	0	37	20	33	10	0.2	37	24	26	13
	25-29	0.2	37	20	33	10	0.4	37	24	26	13
	30-34	0.3	37	20	33	10	0.6	37	24	26	13
	35-39	0.7	37	20	33	10	1.1	37	24	26	13
	40-44	1.2	46	21	19	14	2.5	43	25	16	15
	45-49	2.5	46	21	19	14	8.7	43	25	16	15
	50-54	6.4	46	21	19	14	26.9	43	25	16	15
	55-59	14.1	46	21	19	14	54.7	43	25	16	15
	60-64	25.1	46	21	19	14	81.4	43	25	16	15
	65-69	40.2	48	22	16	14	105	42	26	16	16
	70-74	46.2	48	22	16	14	102	42	26	16	16
	75-79	59.4	40	19	15	26	105.7	38	23	16	23
	80-84	64.4	40	19	15	26	106	38	23	16	23
	85+	58.1	40	19	15	26	97.7	38	23	16	23
Other	<1	1.3	50	24	18	7	1.8	46	28	22	4
	1-4	0.5	50	24	18	7	0.8	46	28	22	4
	5-9	0.1	50	24	18	7	0.1	46	28	22	4
	10-14	0.1	50	24	18	7	0.1	46	28	22	4
	15-19	0.2	39	23	29	9	0.2	35	27	28	10
	20-24	0.2	39	23	29	9	0.2	35	27	28	10
	25-29	0.3	39	23	29	9	0.4	35	27	28	10
	30-34	0.4	39	23	29	9	0.7	35	27	28	10
	35-39	0.8	39	23	29	9	1.3	35	27	28	10
	40-44	1.4	43	24	21	12	2.4	41	27	18	14
	45-49	2.2	43	24	21	12	5.9	41	27	18	14
	50-54	4.6	43	24	21	12	15.6	41	27	18	14
	55-59	9.5	43	24	21	12	35.6	41	27	18	14
	60-64	16.1	43	24	21	12	57.8	41	27	18	14
	65-69	22.5	44	23	21	13	71.7	41	27	18	14
	70-74	23.9	44	23	21	13	63.8	41	27	18	14
	75-79	29.6	36	20	18	26	63.2	38	24	17	21
	80-84	32.3	36	20	18	26	66	38	24	17	21
	85+	29.3	36	20	18	26	56.3	38	24	17	21

Table H-14 shows relative liver cancer survival rates[55] by sex, age group at diagnosis, cancer stage, and the number of years post diagnosis. The relative liver cancer survival ranges from 0% to 94%, 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 liver 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 liver cancer populations for the baseline scenario and the regulatory alternative. Finally, Table H-16 shows all-cause and liver cancer mortality rates used in the life table model. Liver cancer deaths <1% of all-cause mortality among females and among males.

Table H-14: Summary of Relative Liver Cancer Survival Used in the Model

Age at Diagnosis	Follow-Up Time	Females				Males			
		Relative Survival by Stage (Percent)				Relative Survival by Stage (Percent)			
		Localized	Regional	Distant	Unstaged	Localized	Regional	Distant	Unstaged
Ages <15	1 year	92	88	71	83	94	89	77	74
Ages <15	2 years	89	85	60	76	91	85	63	64
Ages <15	3 years	88	84	54	68	89	81	59	64
Ages <15	4 years	87	83	48	68	87	79	57	64
Ages <15	5 years	86	81	48	63	87	78	56	64
Ages <15	6 years	86	80	48	63	86	78	55	64
Ages <15	7 years	86	79	48	63	86	78	53	60
Ages <15	8 years	85	76	48	63	86	78	53	60
Ages <15	9 years	84	75	48	63	86	78	52	60
Ages <15	10 years	84	75	48	63	86	78	52	60
Ages 15-39	1 year	87	64	44	71	78	46	32	55
Ages 15-39	2 years	77	50	23	65	69	32	19	45
Ages 15-39	3 years	72	42	15	63	61	28	13	39
Ages 15-39	4 years	67	37	13	57	59	23	10	37
Ages 15-39	5 years	65	34	11	54	55	22	9	34
Ages 15-39	6 years	63	31	11	51	54	19	8	33
Ages 15-39	7 years	60	29	11	48	51	18	7	33

[55] Relative liver 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-14: Summary of Relative Liver Cancer Survival Used in the Model

Age at Diagnosis	Follow-Up Time	Females				Males			
		Relative Survival by Stage (Percent)				Relative Survival by Stage (Percent)			
		Localized	Regional	Distant	Unstaged	Localized	Regional	Distant	Unstaged
Ages 15-39	8 years	58	28	11	48	50	17	6	32
Ages 15-39	9 years	57	28	11	48	49	17	6	32
Ages 15-39	10 years	57	27	11	48	46	17	5	31
Ages 40-64	1 year	75	49	25	44	70	40	16	35
Ages 40-64	2 years	61	31	12	33	55	25	7	23
Ages 40-64	3 years	52	23	8	28	46	18	4	17
Ages 40-64	4 years	47	20	6	23	40	15	3	14
Ages 40-64	5 years	43	17	5	21	36	13	2	11
Ages 40-64	6 years	40	16	4	19	33	11	2	10
Ages 40-64	7 years	38	15	4	18	31	10	2	9
Ages 40-64	8 years	36	14	3	17	29	10	2	8
Ages 40-64	9 years	35	13	3	16	28	9	2	8
Ages 40-64	10 years	34	13	3	15	27	9	1	7
Ages 65-74	1 year	70	43	21	35	69	41	17	32
Ages 65-74	2 years	54	25	9	23	54	26	7	20
Ages 65-74	3 years	45	18	6	17	45	18	4	14
Ages 65-74	4 years	39	14	4	14	38	14	3	11
Ages 65-74	5 years	34	12	3	12	33	11	2	9
Ages 65-74	6 years	30	10	3	10	29	10	2	7
Ages 65-74	7 years	28	10	2	8	26	8	2	6
Ages 65-74	8 years	25	9	2	7	24	8	1	6
Ages 65-74	9 years	23	8	2	7	23	7	1	5

Table H-14: Summary of Relative Liver Cancer Survival Used in the Model

Age at Diagnosis	Follow-Up Time	Females				Males			
		Relative Survival by Stage (Percent)				Relative Survival by Stage (Percent)			
		Localized	Regional	Distant	Unstaged	Localized	Regional	Distant	Unstaged
Ages 65-74	10 years	22	7	2	6	21	6	1	5
Ages 75+	1 year	52	28	14	22	55	30	12	22
Ages 75+	2 years	37	15	6	12	40	17	5	13
Ages 75+	3 years	28	10	3	8	29	11	3	8
Ages 75+	4 years	23	7	2	5	23	8	2	5
Ages 75+	5 years	19	6	2	4	19	6	1	4
Ages 75+	6 years	16	4	1	3	15	5	1	3
Ages 75+	7 years	14	4	1	2	13	3	1	2
Ages 75+	8 years	12	3	1	2	11	3	1	2
Ages 75+	9 years	11	2	1	2	9	2	1	2
Ages 75+	10 years	10	2	1	2	8	2	0	2

Table H-15: Summary of Race/Ethnicity-Specific Relative Liver Cancer Survival Used in the Model

Race/Ethnicity	Age at Diagnosis	Follow-Up Time	Females				Males			
			Relative Survival by Stage (Percent)				Relative Survival by Stage (Percent)			
			Localized	Regional	Distant	Unstaged	Localized	Regional	Distant	Unstaged
Non-Hispanic White	Ages <15	1 year	91	85	69	100	94	90	75	100
	Ages <15	2 years	85	84	61	100	89	87	59	100
	Ages <15	3 years	85	84	59	100	89	83	53	100
	Ages <15	4 years	85	84	54	100	88	82	49	100
	Ages <15	5 years	84	79	54	100	87	82	49	100
	Ages <15	6 years	84	79	54	100	87	80	49	100
	Ages <15	7 years	84	77	54	100	87	80	49	100
	Ages <15	8 years	84	77	54	100	87	80	49	100
	Ages <15	9 years	82	73	54	100	87	80	49	100
	Ages <15	10 years	82	73	54	100	87	80	49	100
	Ages 15-39	1 year	89	71	47	67	80	68	44	67
	Ages 15-39	2 years	80	58	23	60	71	46	24	52
	Ages 15-39	3 years	76	49	19	60	66	41	18	48
	Ages 15-39	4 years	70	42	15	56	63	33	13	44
	Ages 15-39	5 years	67	38	14	53	63	31	12	42
	Ages 15-39	6 years	63	32	14	51	61	27	11	42
	Ages 15-39	7 years	62	32	12	48	60	26	10	42
	Ages 15-39	8 years	61	32	12	48	60	26	7	39
	Ages 15-39	9 years	58	32	12	48	59	26	7	39
	Ages 15-39	10 years	58	30	12	48	55	26	7	36
	Ages 40-64	1 year	73	51	26	45	69	41	17	34

Table H-15: Summary of Race/Ethnicity-Specific Relative Liver Cancer Survival Used in the Model

Race/Ethnicity	Age at Diagnosis	Follow-Up Time	Females				Males			
			Relative Survival by Stage (Percent)				Relative Survival by Stage (Percent)			
			Localized	Regional	Distant	Unstaged	Localized	Regional	Distant	Unstaged
	Ages 40-64	2 years	59	33	13	33	55	25	7	23
	Ages 40-64	3 years	51	24	8	27	46	18	4	17
	Ages 40-64	4 years	46	21	6	23	40	15	3	14
	Ages 40-64	5 years	42	19	5	20	36	13	2	12
	Ages 40-64	6 years	40	17	4	19	33	12	2	11
	Ages 40-64	7 years	37	15	4	18	31	11	1	10
	Ages 40-64	8 years	36	14	3	17	29	10	1	9
	Ages 40-64	9 years	34	14	3	16	28	9	1	8
	Ages 40-64	10 years	33	14	2	15	27	9	1	7
	Ages 65-74	1 year	68	41	23	30	68	41	18	31
	Ages 65-74	2 years	54	24	10	21	53	25	7	19
	Ages 65-74	3 years	44	18	5	15	43	18	4	13
	Ages 65-74	4 years	39	14	3	12	37	13	3	10
	Ages 65-74	5 years	35	12	2	11	32	10	2	8
	Ages 65-74	6 years	31	10	1	10	28	9	2	7
	Ages 65-74	7 years	30	10	1	9	25	8	2	6
	Ages 65-74	8 years	28	9	1	8	23	7	1	5
	Ages 65-74	9 years	26	9	1	7	21	7	1	5
	Ages 65-74	10 years	24	8	1	6	20	6	1	5
	Ages 75+	1 year	48	27	13	18	54	29	13	19
	Ages 75+	2 years	35	14	6	9	38	16	5	11

Table H-15: Summary of Race/Ethnicity-Specific Relative Liver Cancer Survival Used in the Model

Race/Ethnicity	Age at Diagnosis	Follow-Up Time	Females				Males			
			Relative Survival by Stage (Percent)				Relative Survival by Stage (Percent)			
			Localized	Regional	Distant	Unstaged	Localized	Regional	Distant	Unstaged
	Ages 75+	3 years	25	9	3	6	28	10	3	7
	Ages 75+	4 years	21	6	2	4	22	7	2	4
	Ages 75+	5 years	18	5	2	2	18	4	1	3
	Ages 75+	6 years	16	4	1	2	15	3	1	3
	Ages 75+	7 years	14	3	1	1	12	3	1	2
	Ages 75+	8 years	12	2	1	1	11	3	1	2
	Ages 75+	9 years	10	2	1	1	8	2	1	2
	Ages 75+	10 years	9	2	1	1	6	1	0	2
Non-Hispanic Black	Ages <15	1 year	96	100	100	100	88	85	100	100
	Ages <15	2 years	96	100	100	100	88	81	100	100
	Ages <15	3 years	96	100	100	100	88	73	100	100
	Ages <15	4 years	91	100	100	100	79	73	100	100
	Ages <15	5 years	91	100	100	100	79	73	100	100
	Ages <15	6 years	91	100	100	100	79	73	100	100
	Ages <15	7 years	91	100	100	100	79	73	100	100
	Ages <15	8 years	84	100	100	100	79	73	100	100
	Ages <15	9 years	84	100	100	100	79	73	100	100
	Ages <15	10 years	84	100	100	100	79	73	100	100
	Ages 15-39	1 year	76	57	43	100	73	29	19	45
	Ages 15-39	2 years	68	40	29	100	64	24	12	42
	Ages 15-39	3 years	60	38	14	100	54	18	8	33

Table H-15: Summary of Race/Ethnicity-Specific Relative Liver Cancer Survival Used in the Model

Race/Ethnicity	Age at Diagnosis	Follow-Up Time	Females				Males			
			Relative Survival by Stage (Percent)				Relative Survival by Stage (Percent)			
			Localized	Regional	Distant	Unstaged	Localized	Regional	Distant	Unstaged
	Ages 15-39	4 years	57	35	14	100	50	13	5	33
	Ages 15-39	5 years	54	31	14	100	45	11	5	33
	Ages 15-39	6 years	54	31	14	100	44	7	5	33
	Ages 15-39	7 years	52	27	14	100	40	6	5	33
	Ages 15-39	8 years	50	27	14	100	38	6	5	33
	Ages 15-39	9 years	50	27	14	100	38	6	5	33
	Ages 15-39	10 years	50	27	14	100	36	6	100	33
	Ages 40-64	1 year	72	43	20	43	65	33	15	31
	Ages 40-64	2 years	58	27	11	29	50	19	7	19
	Ages 40-64	3 years	49	20	7	23	39	13	3	13
	Ages 40-64	4 years	43	16	4	20	33	11	2	10
	Ages 40-64	5 years	38	14	3	19	28	9	2	9
	Ages 40-64	6 years	35	13	2	17	26	8	2	7
	Ages 40-64	7 years	34	12	2	15	23	7	2	6
	Ages 40-64	8 years	32	11	2	15	22	6	2	5
	Ages 40-64	9 years	31	10	2	15	19	5	2	4
	Ages 40-64	10 years	30	10	2	15	18	5	2	4
	Ages 65-74	1 year	71	39	18	36	67	36	14	29
	Ages 65-74	2 years	57	24	7	25	52	24	7	18
	Ages 65-74	3 years	51	18	4	18	42	16	4	12
	Ages 65-74	4 years	42	13	4	16	36	14	2	9

Table H-15: Summary of Race/Ethnicity-Specific Relative Liver Cancer Survival Used in the Model

Race/Ethnicity	Age at Diagnosis	Follow-Up Time	Females				Males			
			Relative Survival by Stage (Percent)				Relative Survival by Stage (Percent)			
			Localized	Regional	Distant	Unstaged	Localized	Regional	Distant	Unstaged
	Ages 65-74	5 years	36	11	4	14	32	11	1	7
	Ages 65-74	6 years	31	10	3	10	28	10	1	7
	Ages 65-74	7 years	26	10	3	7	24	8	1	4
	Ages 65-74	8 years	21	7	3	7	22	6	1	4
	Ages 65-74	9 years	19	7	3	5	21	6	0	4
	Ages 65-74	10 years	19	4	3	5	18	5	0	4
	Ages 75+	1 year	50	19	15	22	51	21	9	24
	Ages 75+	2 years	34	10	7	16	36	11	4	12
	Ages 75+	3 years	25	9	4	10	27	8	4	9
	Ages 75+	4 years	25	6	1	5	19	7	3	6
	Ages 75+	5 years	19	4	0	5	14	7	2	3
	Ages 75+	6 years	16	4	0	3	13	7	2	2
	Ages 75+	7 years	14	2	0	3	11	5	100	0
	Ages 75+	8 years	14	1	0	3	10	5	100	0
	Ages 75+	9 years	14	100	0	3	8	100	100	0
	Ages 75+	10 years	13	100	0	3	8	100	100	0
Hispanic	Ages <15	1 year	93	93	70	100	93	87	82	100
	Ages <15	2 years	92	86	60	100	92	83	68	100
	Ages <15	3 years	88	86	52	100	89	78	66	100
	Ages <15	4 years	88	84	49	100	87	75	63	100
	Ages <15	5 years	87	82	49	100	87	74	61	100

Table H-15: Summary of Race/Ethnicity-Specific Relative Liver Cancer Survival Used in the Model

Race/Ethnicity	Age at Diagnosis	Follow-Up Time	Females				Males			
			Relative Survival by Stage (Percent)				Relative Survival by Stage (Percent)			
			Localized	Regional	Distant	Unstaged	Localized	Regional	Distant	Unstaged
	Ages <15	6 years	87	82	49	100	86	74	61	100
	Ages <15	7 years	85	82	49	100	86	74	59	100
	Ages <15	8 years	85	75	49	100	86	74	59	100
	Ages <15	9 years	85	75	49	100	86	74	56	100
	Ages <15	10 years	85	75	49	100	86	74	56	100
	Ages 15-39	1 year	88	64	38	80	79	49	43	55
	Ages 15-39	2 years	74	49	20	72	71	37	29	42
	Ages 15-39	3 years	69	41	13	62	63	29	18	36
	Ages 15-39	4 years	62	37	11	57	59	28	15	33
	Ages 15-39	5 years	60	34	9	57	53	26	13	28
	Ages 15-39	6 years	60	32	9	57	53	24	11	28
	Ages 15-39	7 years	50	32	9	57	51	24	11	28
	Ages 15-39	8 years	50	25	9	57	49	24	11	28
	Ages 15-39	9 years	50	25	9	57	48	24	11	28
	Ages 15-39	10 years	50	25	9	57	46	24	6	28
	Ages 40-64	1 year	75	48	25	42	68	43	16	36
	Ages 40-64	2 years	59	30	13	33	53	26	7	23
	Ages 40-64	3 years	51	22	8	27	43	18	4	16
	Ages 40-64	4 years	45	19	6	22	37	14	3	12
	Ages 40-64	5 years	41	16	5	19	32	12	3	10
	Ages 40-64	6 years	37	15	5	18	29	11	3	9

Table H-15: Summary of Race/Ethnicity-Specific Relative Liver Cancer Survival Used in the Model

Race/Ethnicity	Age at Diagnosis	Follow-Up Time	Females				Males			
			Relative Survival by Stage (Percent)				Relative Survival by Stage (Percent)			
			Localized	Regional	Distant	Unstaged	Localized	Regional	Distant	Unstaged
	Ages 40-64	7 years	35	15	4	18	27	10	2	8
	Ages 40-64	8 years	33	13	4	17	26	9	2	8
	Ages 40-64	9 years	32	13	4	15	24	9	2	7
	Ages 40-64	10 years	31	13	4	13	23	8	2	7
	Ages 65-74	1 year	67	43	20	39	66	41	17	32
	Ages 65-74	2 years	49	24	11	22	49	25	8	20
	Ages 65-74	3 years	38	16	8	17	39	17	5	14
	Ages 65-74	4 years	31	12	6	14	32	11	3	11
	Ages 65-74	5 years	26	10	5	11	27	10	2	9
	Ages 65-74	6 years	23	8	5	7	23	9	1	6
	Ages 65-74	7 years	21	7	5	6	21	8	1	5
	Ages 65-74	8 years	19	6	5	6	18	7	1	4
	Ages 65-74	9 years	17	6	2	6	17	7	1	4
	Ages 65-74	10 years	16	6	2	6	14	6	100	4
	Ages 75+	1 year	52	28	14	27	51	30	11	24
	Ages 75+	2 years	36	15	5	15	34	16	4	14
	Ages 75+	3 years	27	9	3	10	24	10	3	9
	Ages 75+	4 years	20	6	2	7	16	8	2	6
	Ages 75+	5 years	15	4	2	5	13	6	1	4
	Ages 75+	6 years	13	3	1	3	11	4	1	3
	Ages 75+	7 years	11	1	1	3	9	2	1	3

Table H-15: Summary of Race/Ethnicity-Specific Relative Liver Cancer Survival Used in the Model

Race/Ethnicity	Age at Diagnosis	Follow-Up Time	Females				Males			
			Relative Survival by Stage (Percent)				Relative Survival by Stage (Percent)			
			Localized	Regional	Distant	Unstaged	Localized	Regional	Distant	Unstaged
	Ages 75+	8 years	9	100	100	3	8	2	1	3
	Ages 75+	9 years	8	100	100	3	6	2	0	3
	Ages 75+	10 years	7	100	100	3	4	2	0	3
Other	Ages <15	1 year	88	71	83	88	94	89	77	74
	Ages <15	2 years	85	60	76	85	91	85	63	64
	Ages <15	3 years	84	54	68	84	89	81	59	64
	Ages <15	4 years	83	48	68	83	87	79	57	64
	Ages <15	5 years	81	48	63	81	87	78	56	64
	Ages <15	6 years	80	48	63	80	86	78	55	64
	Ages <15	7 years	79	48	63	79	86	78	53	60
	Ages <15	8 years	76	48	63	76	86	78	53	60
	Ages <15	9 years	75	48	63	75	86	78	52	60
	Ages <15	10 years	75	48	63	75	86	78	52	60
	Ages 15-39	1 year	64	44	71	64	78	46	32	55
	Ages 15-39	2 years	50	23	65	50	69	32	19	45
	Ages 15-39	3 years	42	15	63	42	61	28	13	39
	Ages 15-39	4 years	37	13	57	37	59	23	10	37
	Ages 15-39	5 years	34	11	54	34	55	22	9	34
	Ages 15-39	6 years	31	11	51	31	54	19	8	33
	Ages 15-39	7 years	29	11	48	29	51	18	7	33
	Ages 15-39	8 years	28	11	48	28	50	17	6	32

Table H-15: Summary of Race/Ethnicity-Specific Relative Liver Cancer Survival Used in the Model

Race/Ethnicity	Age at Diagnosis	Follow-Up Time	Females				Males			
			Relative Survival by Stage (Percent)				Relative Survival by Stage (Percent)			
			Localized	Regional	Distant	Unstaged	Localized	Regional	Distant	Unstaged
	Ages 15-39	9 years	28	11	48	28	49	17	6	32
	Ages 15-39	10 years	27	11	48	27	46	17	5	31
	Ages 40-64	1 year	49	25	44	49	70	40	16	35
	Ages 40-64	2 years	31	12	33	31	55	25	7	23
	Ages 40-64	3 years	23	8	28	23	46	18	4	17
	Ages 40-64	4 years	20	6	23	20	40	15	3	14
	Ages 40-64	5 years	17	5	21	17	36	13	2	11
	Ages 40-64	6 years	16	4	19	16	33	11	2	10
	Ages 40-64	7 years	15	4	18	15	31	10	2	9
	Ages 40-64	8 years	14	3	17	14	29	10	2	8
	Ages 40-64	9 years	13	3	16	13	28	9	2	8
	Ages 40-64	10 years	13	3	15	13	27	9	1	7
	Ages 65-74	1 year	43	21	35	43	69	41	17	32
	Ages 65-74	2 years	25	9	23	25	54	26	7	20
	Ages 65-74	3 years	18	6	17	18	45	18	4	14
	Ages 65-74	4 years	14	4	14	14	38	14	3	11
	Ages 65-74	5 years	12	3	12	12	33	11	2	9
	Ages 65-74	6 years	10	3	10	10	29	10	2	7
	Ages 65-74	7 years	10	2	8	10	26	8	2	6
	Ages 65-74	8 years	9	2	7	9	24	8	1	6
	Ages 65-74	9 years	8	2	7	8	23	7	1	5

Table H-15: Summary of Race/Ethnicity-Specific Relative Liver Cancer Survival Used in the Model

Race/Ethnicity	Age at Diagnosis	Follow-Up Time	Females				Males			
			Relative Survival by Stage (Percent)				Relative Survival by Stage (Percent)			
			Localized	Regional	Distant	Unstaged	Localized	Regional	Distant	Unstaged
	Ages 65-74	10 years	7	2	6	7	21	6	1	5
	Ages 75+	1 year	28	14	22	28	55	30	12	22
	Ages 75+	2 years	15	6	12	15	40	17	5	13
	Ages 75+	3 years	10	3	8	10	29	11	3	8
	Ages 75+	4 years	7	2	5	7	23	8	2	5
	Ages 75+	5 years	6	2	4	6	19	6	1	4
	Ages 75+	6 years	4	1	3	4	15	5	1	3
	Ages 75+	7 years	4	1	2	4	13	3	1	2
	Ages 75+	8 years	3	1	2	3	11	3	1	2
	Ages 75+	9 years	2	1	2	2	9	2	1	2
	Ages 75+	10 years	2	1	2	2	8	2	0	2

Table H-16: Summary of All-Cause and Liver Cancer Mortality Data Used in the Model

Age	Females			Males		
	Rate per 100K		Percent Liver Cancer	Rate per 100K		Percent Liver Cancer
	All-Cause	Liver Cancer		All-Cause	Liver Cancer	
<1	579	0.071	0.012	702	0.06	0.009
1-4	25	0.066	0.270	31	0.12	0.39
5-9	12	0.000	0.000	14	0.027	0.19
10-14	13	0.005	0.040	19	0.010	0.05
15-19	33	0.025	0.08	78	0.038	0.049
20-24	47	0.053	0.11	136	0.08	0.06
25-29	60	0.10	0.17	148	0.18	0.12
30-34	80	0.19	0.24	165	0.35	0.21
35-39	113	0.34	0.30	204	0.70	0.34
40-44	168	0.72	0.43	281	1.6	0.56
45-49	253	1.5	0.59	419	4.6	1.1
50-54	378	3.1	0.81	631	11	1.7
55-59	558	5.5	1.0	933	20	2.2
60-64	833	8.6	1.0	1361	29	2.1
65-69	1256	12	1.0	1963	33	1.7
70-74	1996	17	0.83	2977	38	1.3
75-79	3270	23	0.70	4704	45	1.0
80-84	5550	28	0.50	7623	52	0.69
85+	-	-	0.24	-	-	0.35

Table H-17: Summary of Race/Ethnicity-Specific All-Cause and Liver Cancer Mortality Data Used in the Model

Race/Ethnicity	Age	Females			Males		
		Rate per 100K		Percent Liver Cancer	Rate per 100K		Percent Liver Cancer
		All-Cause	Liver Cancer		All-Cause	Liver Cancer	
Non-Hispanic White	<1	486	0.083	0.017	600	0.12	0.019
	1-4	22	0.088	0.40	28	0.15	0.51
	5-9	11	0	0	13	0.038	0.29
	10-14	13	0.009	0.074	19	0.018	0.096
	15-19	35	0.042	0.12	73	0.065	0.090
	20-24	48	0.090	0.19	127	0.089	0.070
	25-29	61	0.11	0.18	144	0.15	0.10
	30-34	82	0.18	0.22	164	0.23	0.14
	35-39	114	0.32	0.28	203	0.48	0.24
	40-44	166	0.62	0.38	279	1.2	0.41
	45-49	249	1.3	0.51	412	3.7	0.89
	50-54	369	2.7	0.73	615	9.2	1.5
	55-59	547	4.7	0.86	907	17	1.9
	60-64	820	7.4	0.90	1326	24	1.8
	65-69	1251	10	0.82	1932	28	1.4
	70-74	2015	15	0.72	2972	33	1.1
	75-79	3322	20	0.60	4747	41	0.87
	80-84	5670	25	0.44	7774	48	0.62
	85+	-	-	0.21	-	-	0.32
Non-Hispanic Black	<1	1148	0.17	0.015	1386	0	0
	1-4	39	0	0	49	0	0
	5-9	17	0	0	22	0	0

Table H-17: Summary of Race/Ethnicity-Specific All-Cause and Liver Cancer Mortality Data Used in the Model

Race/Ethnicity	Age	Females			Males		
		Rate per 100K		Percent Liver Cancer	Rate per 100K		Percent Liver Cancer
		All-Cause	Liver Cancer		All-Cause	Liver Cancer	
	10-14	18	0	0	28	0	0
	15-19	38	0	0	121	0	0
	20-24	67	0	0	221	0.13	0.059
	25-29	93	0.16	0.18	250	0.38	0.15
	30-34	131	0.32	0.25	278	0.78	0.28
	35-39	192	0.49	0.25	339	1.3	0.39
	40-44	288	1.0	0.36	455	2.6	0.57
	45-49	427	2.3	0.54	673	6.9	1.0
	50-54	625	4.8	0.77	1015	17	1.7
	55-59	894	8.8	0.98	1513	35	2.3
	60-64	1280	13	1.0	2185	53	2.4
	65-69	1815	16	0.89	3012	58	1.9
	70-74	2650	19	0.72	4212	52	1.2
	75-79	4007	24	0.60	6073	48	0.79
	80-84	6198	29	0.47	8873	54	0.61
	85+	-	-	0.27	-	-	0.35
Hispanic	<1	469	0	0	556	0	0
	1-4	21	0.076	0.36	26	0.16	0.62
	5-9	10	0	0	12	0.024	0.20
	10-14	12	0	0	16	0	0
	15-19	26	0	0	70	0	0
	20-24	35	0	0	117	0.024	0.021
	25-29	40	0.028	0.070	116	0.080	0.068

Table H-17: Summary of Race/Ethnicity-Specific All-Cause and Liver Cancer Mortality Data Used in the Model

Race/Ethnicity	Age	Females			Males		
		Rate per 100K		Percent Liver Cancer	Rate per 100K		Percent Liver Cancer
		All-Cause	Liver Cancer		All-Cause	Liver Cancer	
	30-34	50	0.13	0.26	123	0.22	0.18
	35-39	70	0.29	0.42	151	0.46	0.30
	40-44	103	0.68	0.66	207	1.6	0.77
	45-49	160	1.7	1.0	311	5.4	1.7
	50-54	247	3.3	1.3	476	14	2.9
	55-59	380	7.0	1.8	713	27	3.8
	60-64	595	12	2.0	1059	39	3.7
	65-69	922	19	2.1	1546	49	3.2
	70-74	1468	28	1.9	2356	57	2.4
	75-79	2463	41	1.7	3702	71	1.9
	80-84	4241	48	1.1	5873	79	1.3
	85+	-	-	0.55	-	-	0.74
Other	<1	419	0	0	510	0	0
	1-4	21	0	0	26	0	0
	5-9	11	0	0	12	0	0
	10-14	12	0	0	15	0	0
	15-19	27	0	0	55	0	0
	20-24	33	0	0	83	0	0
	25-29	36	0.056	0.15	83	0.39	0.47
	30-34	47	0.21	0.44	92	0.95	1.0
	35-39	64	0.39	0.61	118	2.2	1.9
	40-44	93	1.0	1.1	164	4.1	2.5
	45-49	145	2.0	1.4	246	8.9	3.6

Table H-17: Summary of Race/Ethnicity-Specific All-Cause and Liver Cancer Mortality Data Used in the Model

Race/Ethnicity	Age	Females			Males		
		Rate per 100K		Percent Liver Cancer	Rate per 100K		Percent Liver Cancer
		All-Cause	Liver Cancer		All-Cause	Liver Cancer	
	50-54	216	3.3	1.5	366	16	4.4
	55-59	314	6.9	2.2	545	27	5.0
	60-64	474	12	2.5	797	37	4.7
	65-69	727	18	2.5	1169	47	4.0
	70-74	1178	28	2.3	1785	61	3.4
	75-79	1999	42	2.1	2933	75	2.6
	80-84	3573	57	1.6	4885	95	1.9
	85+	-	-	0.71	-	-	0.93

H.6 RCC Valuation Data

The EPA identified the study selected for use in evaluating potential medical costs avoided as a result of the final PFAS rule and 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 literature published in English language peer reviewed sources during 2010-2021.[56] The searches were executed in the Google Scholar article database. The EPA reviewed 153 references retrieved by the willingness to pay-oriented searches and the top 348 references retrieved by the COI-oriented searches.[57]

The search did not identify any suitable kidney cancer willingness to pay 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 the 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 the EPA are provided in Table H-12.

[56] The query terms used for willingness to pay-oriented and COI-oriented searches are available upon request.

[57] The 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 willingness to pay-oriented search result set and 1,342 references in the COI-oriented search result set. The EPA reviewed all 153 references in the willingness to pay-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-18: 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 and Tsiatis (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-18: 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 NCCN Evidence Blocks as of December 31, 2018; costs based on Medicare prices from the January 2019 Medicare ASP file	2018	Calculated Medicare costs for all first-line and maintenance treatments for 30 cancers with the highest incidence in the US that had published 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 of treatment. No

Table H-18: 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
								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-18: 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 Incremental Cost-Effectiveness Ratio /QALY; cost effectiveness analysis of two different treatments for RCC	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.

Table H-18: 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
								In the analysis, 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 RCC; 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

Table H-18: 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 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 RCC	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

Table H-18: 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 with AEs, 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-18: 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 RCC	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-18: 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 event; CPI – consumer price index; HMO – Health Maintenance Organization; MEPS – Medical Expenditure Panel Survey; mRCC metastatic renal cell carcinoma; KC – kidney cancer; NCCN – National Comprehensive Cancer Network; NCI– 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

The 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, the EPA extracted 182 datasets from the ICR TSD database, which included some quarterly RSSCTs and some long-term pilots. The 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 all regulatory scenarios. Note that the same approaches described in this appendix were used to estimate TOC removal. The 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 were not available for 20-min EBCT effluent concentrations, then only 10-min EBCT data were included in the analysis. For all datasets and EBCTs, the EPA used a logistic function to estimate the expected breakthrough curve over time (effluent concentrations vs. time). Since the logistic function is non-linear, the EPA used the Python function scipy.optimize.curve_fit to estimate equation parameters.

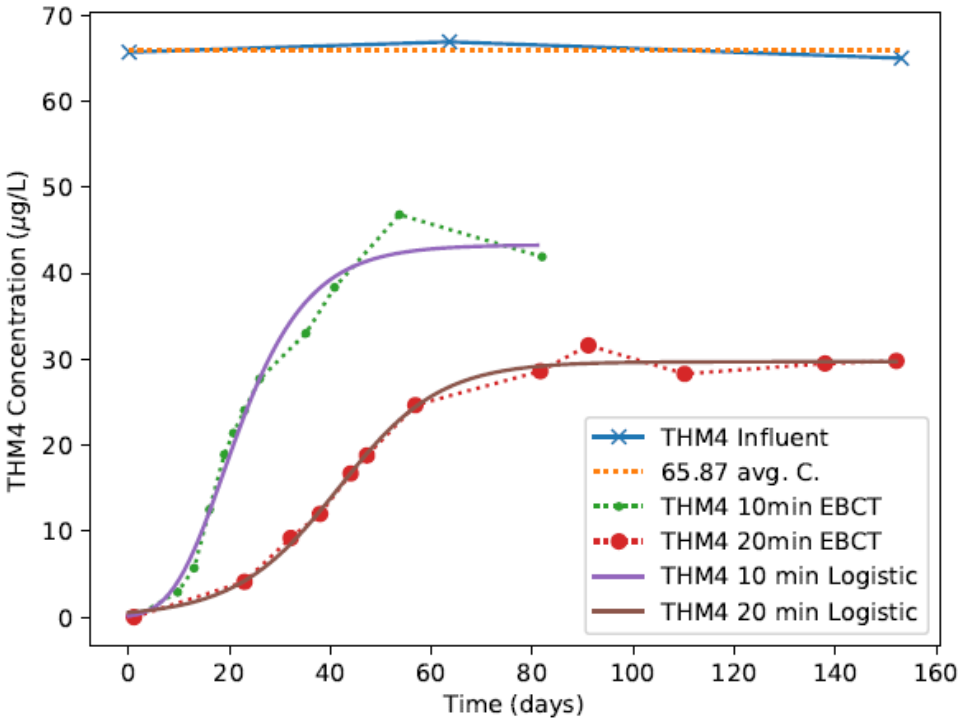


Figure I-1: Example Breakthrough Curve for THM4 from the ICR Dataset with Logistic Fit Functions Shown

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). The 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.

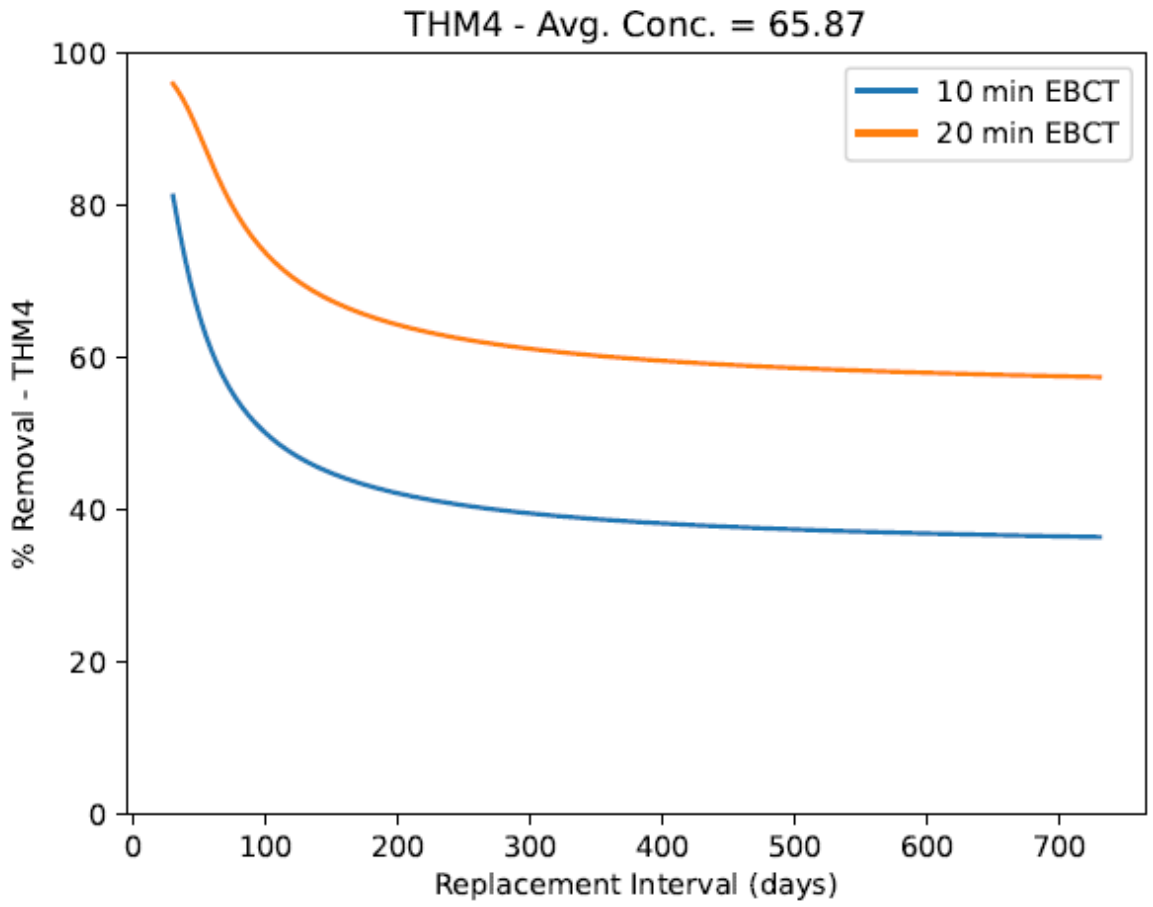


Figure I-2: Example Percent Removal Results vs. Time based on Logistic Plots Shown in Figure I-1

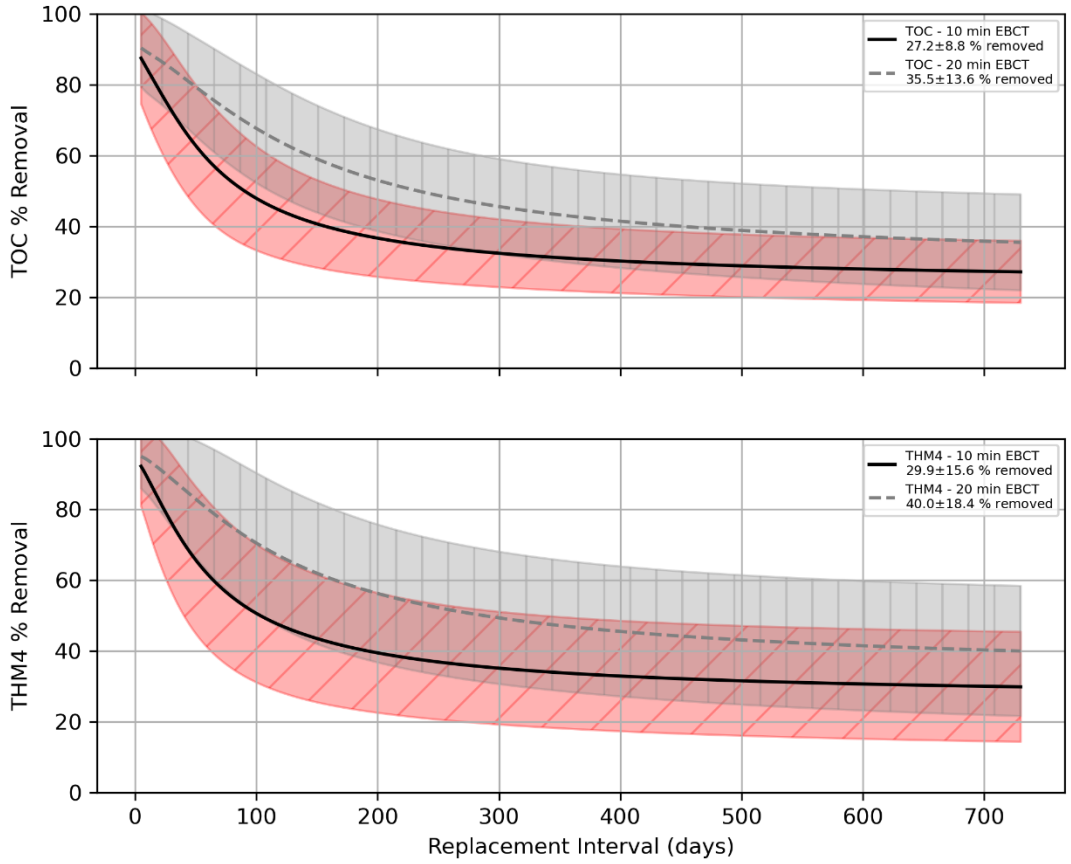


Figure I-3: Mean Percentage Removal (Shaded Area ± 1 Standard Deviation)

The percent removal formula provides a conservative estimate for removal over each EBCT. The 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.

The 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, ground water 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.

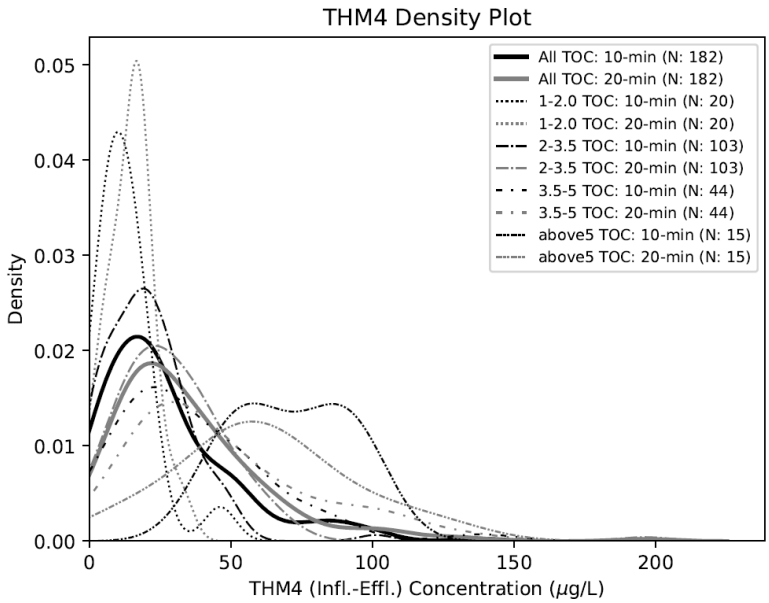


Figure I-4: Probability Density Function of Concentration Difference at 2 Years of Carbon Life (Subdivided by TOC level)

I.2 Discussion of Other Models

The EPA explored another existing model to determine THM4 removal (ΔTHM4) resulting from granular activated carbon (GAC) treatment. The Water Treatment Plant (WTP) 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 WTP 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 WTP model include types of chemicals used, dosing concentrations, contact times, and full process train information, which the 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, the EPA fit the THM4 results reported in the ICR dataset directly. In contrast, the WTP model would need to have simulated all various treatment trains, including GAC, to calculate TOC levels followed by a conversion with then another model equation to predict the ΔTHM4. Both the simulation of treatment trains to calculate TOC levels and conversion to predict the ΔTHM4 would add uncertainty to this approach. 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 (DS) varied based on the typical disinfectant used in the PWS. Table I-1 shows the 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 – ground water; 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; GW – ground water; ICR TSD – Information Collection Rule Treatment Study Database; SW – surface water; 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; GW – ground water; ICR TSD – Information Collection Rule Treatment Study Database; SW – surface water; 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; GW – ground water; ICR TSD – Information Collection Rule Treatment Study Database; SW – surface water; 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; GW – ground water; ICR TSD – Information Collection Rule Treatment Study Database; SW – surface water; 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) THM4 data, the 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, the 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, the 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

The EPA follows U.S. EPA (2010) to estimate the economic value of avoiding premature mortality. To obtain a Value of Statistical Life (VSL) suitable for valuation of mortality risk reductions during 2024-2105, the EPA relies on the base value estimate of $4.8 million ($1990, 1990 income year), which is the central tendency of the Value of Statistical Life distribution recommended for use in the EPA's regulatory impact analyses (U.S. EPA, 2010). The EPA adjusted the base Value of Statistical Life estimate for inflation and income growth as follows:

Equation J-1:

$$V_{t,2022} = V_{1990,1990} \cdot \frac{P_{2022}}{P_{1990}} \cdot \left(\frac{Y_t}{Y_{1990}}\right)^{\epsilon}$$

Where:

$V_{t,2022}$	VSL value ($2022) updated for use in evaluation year t, $t = 2024 \ldots 2050$;
$V_{1990,1990}$	Base VSL value of $4,800,000 ($1990, 1990 income year);
P_{2022}	Gross Domestic Product (GDP) price deflator index value in 2022;
P_{1990}	GDP price deflator index value in 1990;
Y_t	Projected income per capita ($2012) in evaluation year t, $t = 2024 \ldots 2050$;
Y_{1990}	Historical income per capita ($2012) in 1990;
ϵ	VSL income elasticity of 0.4 as recommended by U.S. EPA (U.S. EPA, 2010).

The EPA used disposable personal annual income to represent U.S. income per capita. Because the PFAS analysis spans a future time period from 2024 to 2105, the 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.

The EPA's SafeWater model requires a single income growth factor to project the 2024 Value of Statistical Life (in $2022) to future years (2025 through 2105). Based on the Value of Statistical Life estimates calculated using Equation J-1, the EPA calculated the compound annual growth rate, $CAGR$, of Value of Statistical Life values from 2024 to 2050 as follows:

Equation J-2:

$$CAGR = \left(\frac{V_{2050,2022}}{V_{2024,2022}}\right)^{\left(\frac{1}{2050-2024}\right)} - 1$$

The EPA used the calculated CAGR value to approximate Value of Statistical Life growth during the analysis period (2024 to 2105) based on the 2022 Value of Statistical Life value estimated using Equation J-1.

Equation J-3:

$$V_{t,2022} = V_{2024,2022} \cdot (1 + CAGR)^{t-2024}$$

Table J-1 summarizes the projected Value of Statistical Life estimates through 2050 and the approximated Value of Statistical Life estimates through 2105.

Table J-1: Estimated Value of Statistical Life 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 Value of Statistical Life ($2022)	Approximated Value of Statistical Life ($2022)
1990	30,327	-	1	9,597,133	-
2024	-	47,987	1.201330302	11,529,327	11,529,327
2025	-	48,917	1.210595048	11,618,242	11,601,616
2026	-	49,760	1.218899284	11,697,939	11,674,358
2027	-	50,616	1.2272399	11,777,985	11,747,556
2028	-	51,496	1.235732098	11,859,486	11,821,214
2029	-	52,407	1.244430191	11,942,963	11,895,333
2030	-	53,393	1.253742955	12,032,338	11,969,916
2031	-	54,326	1.262455217	12,115,951	12,044,968
2032	-	55,258	1.271073774	12,198,665	12,120,490
2033	-	56,207	1.279765868	12,282,084	12,196,485
2034	-	57,145	1.288265959	12,363,660	12,272,957
2035	-	58,072	1.296586905	12,443,518	12,349,909
2036	-	58,985	1.304696423	12,521,346	12,427,343
2037	-	59,874	1.312534459	12,596,568	12,505,262
2038	-	60,753	1.320206338	12,670,196	12,583,670
2039	-	61,643	1.327910067	12,744,130	12,662,570
2040	-	62,513	1.335367798	12,815,703	12,741,964
2041	-	63,408	1.342991031	12,888,864	12,821,856
2042	-	64,346	1.350901532	12,964,782	12,902,249
2043	-	65,282	1.358723314	13,039,849	12,983,146
2044	-	66,210	1.366414095	13,113,658	13,064,550
2045	-	67,148	1.374127034	13,187,681	13,146,465
2046	-	68,095	1.381844195	13,261,743	13,228,894
2047	-	69,069	1.389721143	13,337,339	13,311,839
2048	-	70,076	1.397792319	13,414,799	13,395,304
2049	-	71,066	1.405655221	13,490,261	13,479,292
2050	-	72,024	1.413208106	13,562,747	13,563,808
2051	-	-	-	-	13,648,853
2052	-	-	-	-	13,734,431
2053	-	-	-	-	13,820,546
2054	-	-	-	-	13,907,201
2055	-	-	-	-	13,994,399

Table J-1: Estimated Value of Statistical Life 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 Value of Statistical Life ($2022)	Approximated Value of Statistical Life ($2022)
2056	-	-	-	-	14,082,144
2057	-	-	-	-	14,170,439
2058	-	-	-	-	14,259,287
2059	-	-	-	-	14,348,693
2060	-	-	-	-	14,438,660
2061	-	-	-	-	14,529,190
2062	-	-	-	-	14,620,288
2063	-	-	-	-	14,711,957
2064	-	-	-	-	14,804,201
2065	-	-	-	-	14,897,023
2066	-	-	-	-	14,990,428
2067	-	-	-	-	15,084,418
2068	-	-	-	-	15,178,997
2069	-	-	-	-	15,274,169
2070	-	-	-	-	15,369,938
2071	-	-	-	-	15,466,308
2072	-	-	-	-	15,563,282
2073	-	-	-	-	15,660,863
2074	-	-	-	-	15,759,057
2075	-	-	-	-	15,857,866
2076	-	-	-	-	15,957,295
2077	-	-	-	-	16,057,347
2078	-	-	-	-	16,158,027
2079	-	-	-	-	16,259,338
2080	-	-	-	-	16,361,284
2081	-	-	-	-	16,463,869
2082	-	-	-	-	16,567,098
2083	-	-	-	-	16,670,973
2084	-	-	-	-	16,775,500
2085	-	-	-	-	16,880,683
2086	-	-	-	-	16,986,525
2087	-	-	-	-	17,093,030
2088	-	-	-	-	17,200,203
2089	-	-	-	-	17,308,049
2090	-	-	-	-	17,416,570

Table J-1: Estimated Value of Statistical Life 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 Value of Statistical Life ($2022)	Approximated Value of Statistical Life ($2022)
2091	-	-	-	-	17,525,772
2092	-	-	-	-	17,635,659
2093	-	-	-	-	17,746,234
2094	-	-	-	-	17,857,503
2095	-	-	-	-	17,969,470
2096	-	-	-	-	18,082,138
2097	-	-	-	-	18,195,513
2098	-	-	-	-	18,309,599
2099	-	-	-	-	18,424,400
2100	-	-	-	-	18,539,921
2101	-	-	-	-	18,656,167
2102	-	-	-	-	18,773,141
2103	-	-	-	-	18,890,848
2104	-	-	-	-	19,009,294
2105	-	-	-	-	19,128,482

Acronym: PDYPP– personal disposable income per capita.

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. The EPA uses the Value of Statistical Life 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 Value of Statistical Life	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.
Value of Statistical Life 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..2023	BLS 2022 (U.S. Bureau of Labor	Medical cost inflation adjustments were done using annual CPI for medical care (U.S. city average, all urban consumers, series number CUUR0000SAM).

Table J-2: Summary of Inputs and Data Sources Used for Valuation

Data Element	Modeled Variability	Data Source	Notes
		Statistics, 2022a)	
Employment Cost Index	Time: Quarterly, 2001..2022	BLS 2022 (U.S. Bureau of Labor Statistics, 2022b)	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..2022	BEA 2023 (U.S. Bureau of Economic Analysis, 2023)	Value of Statistical Life inflation adjustments were done using annual GDP price deflator index.
Historical income per capita	Time: Annual, 1990..2022	BEA 2021 (U.S. Bureau of Economic Analysis, 2021)	Disposable personal annual income per capita (series number A229RC0A052NBEA). Data are in $2022. The series were converted to constant $2012 to align with US EIA 2021 projections using BLS 2022 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. The 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.

Appendix K. Benefits Sensitivity Analyses

This appendix provides details on the sensitivity analyses implemented by the 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 for the sensitivity analyses. For both alternatives, the 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,[58] 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. The 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).

The EPA notes that relative magnitudes of reductions in PFOA, PFOS, and PFNA may differ from those evaluated in the economic analysis. At EPs where PFOA, PFOS, and PFNA concentrations exceed their respective final MCLs, the EPA expects reductions of 1 ppt or greater. 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 16.5%. The EPA chose to evaluate unit reductions (i.e., 1 ppt each) to demonstrate the effects of and make comparisons between unit changes in

[58] 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.

PFOA, PFOS, and PFNA exposure (U.S. EPA, 2024d). 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

The 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. See the EPA's Github repository for PK modeling[59] and the Final Human Health Toxicity Assessments for PFOA and PFOS for further information on the PFOA/PFOS model (U.S. EPA, 2024b; U.S. EPA, 2024c). 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, the 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 & Bartell, 2020):

[59] https://github.com/USEPA/OW-PFOS-PFOA-MCLG-support-PK-models

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_{∞} = 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). The 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 and Bartell (2020) model assumptions, the 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 and Bartell (2020) model assumptions, the EPA used 100% absorption;

Q = water intake (L/kg body weight per day). Consistent with assumptions used for serum PFOA and PFOS, the 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 and Bartell (2020) model assumptions, the EPA used an estimate of 0.17 L/kg body weight from Zhang et al. (2013).

Using this model, the 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 the EPA meta-analysis-based effect estimates. To this end, the 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 scenario using the 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 the 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 the 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 the 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. The EPA made the following observations:

- Relative to the annualized CVD benefits estimated using the EPA meta-analysis-based slope factors, using the Dong et al. (2019) slope factors increases the annualized CVD benefits by 12.2%, while using the P.-I. D. Lin et al. (2019) slope factors increases the annualized CVD benefits by 6.3%%.
- Inclusion of HDLC effects decreases annualized CVD benefits by 20.5% if the 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 increases annualized benefits by 2.4% and 18.4%, respectively. The wide variation in the impact of HDLC inclusion may be explained by high variance in the slope factor estimates. The 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 2.5% if the EPA meta-analysis slope factors are used. However, estimates decrease by 2.2% and 2.3% 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)	0.091	0.091	0.091	0.091	0.091	0.091	0.091	0.091	0.091	0.091	0.091	0.091
Average reduction in serum PFOS concentration (ng/mL)	0.084	0.084	0.084	0.084	0.084	0.084	0.084	0.084	0.084	0.084	0.084	0.084
Average reduction in TC concentration (mg/dL)	0.150	0.168	0.160	0.150	0.168	0.160	0.150	0.168	0.160	0.150	0.168	0.160
Average reduction in HDLC concentration (mg/dL)	0.000	0.000	0.000	0.014	-0.002	-0.014	0.000	0.000	0.000	0.014	-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]	2.745	3.084	2.920	1.973	3.187	3.654	2.708	3.048	2.883	1.936	3.150	3.618
Non-fatal first IS (total cases avoided)[d]	3.965	4.455	4.218	3.005	4.583	5.130	3.909	4.399	4.161	2.948	4.526	5.073
CVD deaths (total cases avoided)[d]	0.778	0.875	0.828	0.641	0.893	0.958	0.755	0.852	0.804	0.618	0.870	0.935
PDV, non-fatal first MI (2% discount rate, millions $2022)	0.142	0.159	0.151	0.101	0.165	0.189	0.140	0.157	0.149	0.100	0.163	0.188
PDV, non-fatal first IS (2% discount rate, millions $2022)	0.058	0.065	0.062	0.043	0.067	0.076	0.057	0.064	0.061	0.043	0.066	0.075
PDV, CVD deaths (2% discount rate, millions $2022)	6.387	7.169	6.790	5.089	7.341	8.023	6.226	7.009	6.629	4.928	7.181	7.862
PDV, total CVD benefits (2% discount rate, millions $2022)	6.587	7.394	7.003	5.234	7.573	8.288	6.424	7.230	6.839	5.070	7.409	8.124
Annualized CVD benefits (2% discount rate, millions $2022)	**0.164**	**0.184**	**0.174**	**0.130**	**0.189**	**0.206**	**0.160**	**0.180**	**0.170**	**0.126**	**0.185**	**0.202**

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).

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)

[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, and Longnecker (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.

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 scenario using Steenland et al. (2018) for PFOA, Dzierlenga, Crawford, and Longnecker (2020) for PFOS
2-First Trimester	Scenario using first trimester estimates from Steenland et al. (2018) for PFOA and Dzierlenga, Crawford, and Longnecker (2020) for PFOS
3-EA+Lenters	Scenario using Steenland et al. (2018) for PFOA, Dzierlenga, Crawford, and Longnecker (2020) for PFOS, Lenters et al. (2016) for PFNA
4-EA+Valvi	Scenario using Steenland et al. (2018) for PFOA, Dzierlenga, Crawford, and Longnecker (2020) for PFOS, Valvi et al. (2017) for PFNA

Abbreviations: 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, and Longnecker (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, and Longnecker (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. The 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 by a factor of 5.6 to 7.8, 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). The EPA notes that the PFNA slope factor estimates used are orders of magnitude larger than the slope factor estimates used to evaluate the impacts of PFOA/PFOS reductions. The EPA also notes that the PFNA slope factor estimates used are not precise, with 95% CIs covering wide ranges that include zero (i.e., serum PFNA slope factor estimates used 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)	0.089	0.089	0.089	0.089
Average reduction in serum PFOS concentration (ng/mL)	0.081	0.081	0.081	0.081
Average reduction in serum PFNA concentration (ng/mL)	0.000	0.000	0.136	0.136
Total increase in birth weight (g)	1.180	0.404	6.654	9.320
Total number of births affected[c]	102,268	102,268	102,268	102,268
Total number of surviving births affected[c]	101,804	101,803	101,806	101,808
Birth weight-related deaths (total cases avoided)[c]	0.616	0.211	3.462	4.841
PDV, birth weight-related deaths (2% discount rate, millions $2022)	3.943	1.349	22.023	30.779
PDV, birth weight-related morbidity (2% discount rate, millions $2022)	0.117	0.040	0.656	0.918
PDV, total birth weight benefits (2% discount rate, millions $2022)	4.061	1.389	22.679	31.697
Annualized birth weight benefits (2% discount rate, millions $2022)	**0.101**	**0.035**	**0.565**	**0.790**

Abbreviations: PDV – present discounted value; PFNA – perfluorononanoic acid; PFOA – perfluorooctanoic acid; PFOS – perfluorooctane sulfonic acid.
Notes: See Appendix P for results presented at 3 and 7 percent discount rates.
[a]See Table K-1
[b]See Table K-5
[c]Total over the period of analysis.

K.6 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 the EPA (U.S. EPA, 2024c); and
- The use of the serum PFOA central tendency slopes from Vieira et al. (2013) excluding a very high exposure group, as derived by the EPA (U.S. EPA, 2024c).

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 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$_{\text{ExcludeHigh}}$	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% population attributable fraction (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 the EPA (U.S. EPA, 2024c)	0.00178 (CI95: 0.00005, 0.00352)
Vieira et al. (2013), as derived by the EPA (U.S. EPA, 2024c)	0.00007 (CI95: 0.000001, 0.00014)
Vieira et al. (2013) excluding very high exposure group from Vieira et al. (2013), as derived by the EPA (U.S. EPA, 2024c)	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. The 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%.

The EPA also notes that the population attributable fraction (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)	0.085	0.085	0.085
Non-fatal RCC (cases avoided)	9.329	0.365	1.295
RCC-related deaths (cases avoided)[b]	3.762	0.147	0.522
PDV, Non-fatal RCC (2% discount rate, millions $2022)	2.270	0.089	0.315
PDV, RCC-related deaths (2% discount rate, millions $2022)	22.477	0.878	3.118
PDV, total RCC benefits (2% discount rate, millions $2022)	24.747	0.967	3.433
Annualized RCC benefits (2% discount rate, millions $2022)	**0.616**	**0.024**	**0.086**

Abbreviations: PDV – present discounted value; PFOA – perfluorooctanoic acid; RCC – renal cell carcinoma.
Notes: See Appendix P for results presented at 3 and 7 percent discount rates.
[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 other 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 the EPA's approach to modeling these sources of uncertainty.

L.1.1 Total Organic Carbon Concentration Uncertainty

For the national cost analysis, 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 4.3.3.2 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. The EPA used the most recent data obtained in response to the ICR for the fourth Six-Year Review of drinking water regulations. The 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 EPs. TOC levels at systems that have treatment may differ pre- and post-treatment.

The EPA randomly assigned a TOC level to each EP from the corresponding ground water or surface water distribution. The EPA retained that value for each of the 4,000 uncertainty simulations. Thus, the EPA's estimates reflect TOC uncertainty across EPs, 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, 2024e). This input drives the selection of materials for 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, the EPA generated cost curves for low-, medium-, and high-cost options. SafeWater MCBC randomly selects from these cost curves. The 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

The 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 final 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 the 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[a]	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). The EPA meta-analysis of these studies provides a central estimate and a standard error estimate for the slope factors. The 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[a]	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 2003-2012 NHANES cycles. This study provides a central estimate and a standard error estimate for the slope factor. The 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 the EPA reanalysis of Dzierlenga, Crawford, and Longnecker (2020) for PFOS.[b] The meta-analyses provide a central estimate and a standard error estimate for the slope factors. The 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 & Woskie, 2012; Vieira et al., 2013).[c] This study provides a central estimate and a standard error estimate for the slope factor. The 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. The EPA estimated a standard error for this slope factor based on the data reported in Regli et al. (2015). The 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.

Table L-1: Quantified Sources of Uncertainty in Benefits Estimates

Source	Description of Uncertainty
RCC PAF to cap risk reductions for this endpoint	The 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, and Longnecker (2020) estimate, the authors duplicated an estimate from Chen et al. (2017) in the pooled estimate. The 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, the EPA did not characterize the following sources of potential uncertainty: U.S. population life tables (including standard and cause-eliminated life tables; See Section 6.1.4 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 Value of Statistical Life reference value, the Value of Statistical Life income elasticity value used for Value of Statistical Life income growth adjustment, and the gross domestic product per capita projection used to for Value of Statistical Life income growth adjustment (see Appendix J). The 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 (2.5th and 97.5th quantile), and standard errors for the slope factors used in the EPA's assessment of benefits resulting from the final PFAS NPDWR. This table also presents information on the uncertainty distribution used by the 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				Units	Uncertainty Distribution	Data Source
			Central Estimate	LCB	UCB	Standard Error			
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, and Longnecker (2020)
THM4	Bladder cancer	Bladder cancer	0.00427	0.00331	0.00522	0.00	Per µg/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), the EPA placed a PAF-based cap on the estimated RCC risk reductions associated with changes in serum PFOA exposure. The 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%). The EPA used 3.94% (i.e., the mean of this log-uniform distribution) 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 the EPA's environmental justice (EJ) analysis. This includes discussion of results from the EPA's EJ exposure analysis using the EJSCREENbatch R package 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 440 category 4 PWSs serving a population of 959,972, or 0.3% of the overall U.S. population; 97% of category 4 PWSs are small systems, serving 883,187 people. Table M-2 summarizes the demographic profile of category 5 PWS service areas. There are 296 category 5 PWSs serving a population of 1,104,891, or 0.3% of the overall U.S. population. 97% percent of category 5 PWSs are small systems, serving 990,083 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 0.6% of the U.S. population. Compared to the overall U.S. population, the population served by category 4 and 5 PWSs has lower percentages of non-Hispanic American Indian or Alaska Native, non-Hispanic Asian, non-Hispanic Black, non-Hispanic Pacific Islander, and Hispanic populations. Category 4 and 5 PWS service areas also have a lower percentage of populations with income less than twice the poverty level. Category 4 and 5 PWS service areas 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 tribal-owned community water systems.

Table M-1: Number of Category 4 PWSs and Population Served by Size and State

State	Number of Total Service Areas	Number of Small Service Areas	Total Population Served	Population Served in Small Systems[a]	Population Served in Medium and Large Systems
Missouri	37	37	88,025	88,025	
New Jersey	361	347	618,244	554,259	63,985
New York	42	41	253,703	240,903	12,800
TOTAL	**440**	**425**	**959,972**	**883,187**	**76,785**

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 Total Service Areas	Number of Small Service Areas	Total Population Served	Population Served in Small Systems[a]	Population Served in Medium and Large Systems
Alabama	3	3	9,955	9,955	-
Colorado	24	23	94,604	83,737	10,867
Florida	1	1	25	25	-
Illinois	31	31	111,047	111,047	-
Indiana	16	16	67,129	67,129	-
Kentucky	8	8	45,099	45,099	-
Maine	14	14	43,954	43,954	-
Maryland	5	5	17,633	17,633	-
Massachusetts	23	20	127,048	93,072	33,976
Michigan	30	28	130,011	105,728	24,283
Missouri	5	5	12,599	12,599	-
New Hampshire	15	15	28,355	28,355	-
New Jersey	5	5	4,177	4,177	-
New York	45	45	104,808	104,808	-

Table M-2: Number of Category 5 PWSs and Population Served by Size and State

State	Number of Total Service Areas	Number of Small Service Areas	Total Population Served	Population Served in Small Systems[a]	Population Served in Medium and Large Systems
North Dakota	3	3	17,035	17,035	-
Ohio	33	33	123,541	123,541	-
South Carolina	17	16	85,679	73,765	11,914
Vermont	8	8	26,784	26,784	-
Wisconsin	10	7	55,408	21,640	33,768
TOTAL	**296**	**286**	**1,104,891**	**990,083**	**114,808**

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

	Race and Ethnicity						Income		
	Non-Hispanic American Indian or Alaska Native	**Non-Hispanic Asian**	**Non-Hispanic Black**	**Non-Hispanic Pacific Islander**	**Hispanic**	**Non-Hispanic White**	**Below Twice the Poverty Level**	**Above Twice the Poverty Level**	**Total Population Served**
Population Served	6,967	41,639	108,752	943	157,691	1,762,325	556,461	1,563,894	2,120,355
Percent of Total Population Served	0.3%	2.0%	5.1%	0.0%	7.4%	83.1%	26.2%	73.8%	100.00%
U.S. Population Percent by Demographic Group	0.6%	5.6%	12.2%	0.2%	18.2%	60.1%	29.8%	70.2%	
Percent Difference Between Population Served and U.S. Population	-0.3%	-3.6%	-7.1%	-0.2%	-10.8%	23.0%	-3.6%	3.6%	-

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 a trigger level of 2 ppt for each PFAS analyte, which is slightly above the 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 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 PFAS above this threshold (right-hand column). In Table M-4, the highlighted numbers represent where percentages of the population served in a particular demographic group are more than 1 percentage point greater than percentages of the total population. 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, anticipated PFAS exposure above the baseline thresholds is higher for non-Hispanic Asian populations across all PFAS analytes compared to the total population served across all demographic groups. The difference in exposure is even greater when compared to non-Hispanic White populations (28.6% vs. 14.7% for PFOS and 18.1% vs. 12.4% for PFOA). PFAS exposure above baseline thresholds is higher for non-Hispanic Black populations for PFHxS and PFOA and Hispanic populations for all PFAS analytes examined compared to the total population served across all demographic groups. When compared to non-Hispanic White populations instead of the total population served, Hispanic populations face even greater exposure (21.2% vs. 14.7% for PFOS and 16.5% vs. 12.4% for PFOA). In addition, non-Hispanic Pacific Islander populations have a greater percent of the population exposed to all PFAS analytes in comparison to the total population served. The percent of non-Hispanic Pacific Islander populations exposed to PFHpA and PFOA is at least two percentage points higher than the percent of non-Hispanic White populations exposed to these analytes (5.2% vs. 2.9% for PFHpA and 14.8% vs. 12.4% for PFOA). However, it should be noted that the sample size of the non-Hispanic Pacific Islander population included in this analysis is relatively small at only 943 individuals. Exposure for non-Hispanic American Indian or Alaska Native populations is less than or similar to exposure rates for the total population served across all demographic groups for all PFAS analytes. PFAS exposure above the baseline thresholds is generally lower for populations with income below twice the Federal poverty level compared to exposure for the total population served across all demographic groups. Populations with income above twice the Federal poverty level have comparable but slightly higher PFAS exposure 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 demonstrate again that non-Hispanic Asian, non-Hispanic Pacific Islander, and Hispanic populations have higher average exposure to all the PFAS analytes compared to the total population served in category 4 and 5 PWSs. Non-Hispanic American Indian or Alaska Native populations and populations with income below twice the Federal poverty level have higher average exposures to PFHxS

compared to the total population served. Non-Hispanic Black populations have less than or comparable average population-weighted PFAS concentrations across all four analytes in this analysis.

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

PFAS	Race and Ethnicity					Income			Population Served
	Non-Hispanic American Indian or Alaska Native	Non-Hispanic Asian	Non-Hispanic Black	Non-Hispanic Pacific Islander	Hispanic	Non-Hispanic White	Below Twice the Poverty Level	Above Twice the Poverty Level	
Population Served Above Baseline Threshold									
PFOS	552	11,915	16,861	155	33,499	259,771	64,755	263,942	328,697
PFHxS	225	3,322	6,810	56	13,865	89,308	27,740	88,585	116,325
PFHpA	69	3,328	1,399	49	8,725	50,630	9,061	56,760	65,821
PFOA	590	7,545	14,455	140	25,948	217,734	63,857	207,811	271,668
Population Served Above Baseline Threshold as a Percent of Total Population Served									
PFOS	7.9%	***28.6%***	15.5%	***16.4%***	***21.2%***	14.7%	11.6%	***16.9%***	15.5%
PFHxS	3.2%	***8.0%***	***6.3%***	***5.9%***	***8.8%***	5.1%	5.0%	***5.7%***	5.5%
PFHpA	1.0%	***8.0%***	1.3%	***5.2%***	***5.5%***	2.9%	1.6%	***3.6%***	3.1%
PFOA	8.5%	***18.1%***	***13.3%***	***14.8%***	***16.5%***	12.4%	11.5%	***13.3%***	12.8%

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
	Non-Hispanic American Indian or Alaska Native	Non-Hispanic Asian	Non-Hispanic Black	Non-Hispanic Pacific Islander	Hispanic	Non-Hispanic White	Below Twice the Poverty Level	Above Twice the Poverty Level	
PFOS	0.44	2.32	1.07	1.34	1.53	1.04	0.77	1.22	1.10
PFHxS	0.79	0.79	0.53	2.58	1.45	0.51	0.66	0.60	0.62
PFHpA	0.14	0.52	0.16	0.44	0.41	0.26	0.20	0.30	0.28
PFOA	0.74	1.31	0.95	2.05	1.59	0.91	0.94	1.00	0.99

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

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, the EPA assumed that PWSs with PFAS system-level means above the MRL value will reduce PFAS levels to comply with the final rule. The first set of rows in Table M-6 summarizes population served by category 4 and 5 PWS service areas with 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 the 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). In Table M-6, the highlighted numbers represent where percentages of the population served in a particular demographic group are more than 1 percentage point greater than percentages of the total population. 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.

The EPA's EJ exposure analysis shows that anticipated PFAS exposure above the UCMR 5 MRL values at category 4 and 5 systems is higher for non-Hispanic Asian, non-Hispanic Black, and Hispanic populations for almost all PFAS analytes (the exception being exposure to PFHpA for non-Hispanic Black populations) compared to occurrence over the MRL for the total population served across all demographic groups. Exposure to PFOS and PFHpA is also higher for non-Hispanic Pacific Islander populations in comparison to the total population served. PFAS exposures above the UCMR 5 MRL values for non-Hispanic Asian populations are the highest of any demographic group for several PFAS analytes, with PFOA, PFOS, and PFHpA exposure in particular being roughly twice the exposure rate for the total population served across all demographic groups. The percent of non-Hispanic American Indian or Alaska Native populations with exposure above the UCMR 5 MRL values is generally somewhat lower in comparison to the exposure rate for the total population served across all demographic groups. Similarly, a lower percent of populations with income below twice the Federal poverty level have PFAS exposure above the UCMR 5 MRLs values compared to 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. Reductions in all PFAS analytes to UCMR 5 MRL values are larger for Hispanic, non-Hispanic Asian, and non-Hispanic Pacific Islander populations than the total population served across all demographic groups. Non-Hispanic American Indian or Native Alaska populations see larger reductions in PFHxS, while populations with income below twice the Federal poverty level see larger reductions of PFHxS and PFOA compared to the total population served. Non-Hispanic Pacific Islander populations see the greatest reductions in PFOA, PFHpA, and PFHxS of any demographic group.

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, the EPA assumed that PWSs with PFAS system-level means above 10.0 ppt will reduce PFAS levels to comply with the final 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). In Table M-8, the highlighted numbers represent where percentages of the population served in a particular demographic group are more than 1 percentage point greater than percentages of the total population. 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.

The EPA's EJ exposure analysis shows that anticipated PFAS exposure above 10.0 ppt is higher for non-Hispanic Asian, Hispanic, and non-Hispanic Pacific Islander populations for particular PFAS analytes when compared to exposure for the total population served across all demographic groups. Specifically, PFAS exposure above 10.0 ppt is higher for Hispanic populations for PFOA, PFHxS, and PFOS compared to the total population served. Exceedances of 10.0 ppt for non-Hispanic Asian populations are the highest of any demographic group, with PFOS exposure in particular being roughly three times the exposure rate for the total population served across all demographic groups. Exposure to PFOS, PFHxS, and PFOA over 10.0 ppt is substantially higher for non-Hispanic Pacific Islander populations in comparison to the total population, with PFHxS occurrence nearly six times the levels observed in the total population served by category 4 and 5 systems. However, the sample size of Pacific Islander populations is relatively small, and so these differences in population percentages reflect no more than 50 individuals. PFAS exposure above 10.0 ppt is similar or somewhat lower for other populations compared to the exposure rate 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. Table M-9 shows that reductions are higher for non-Hispanic Pacific Islander and Hispanic populations for all three PFAS analytes for which there are exposures above 10.0 ppt in the sample of category 4 and 5 PWSs (PFOA, PFOS, and PFHxS). Reductions for these population groups are highest for PFHxS and PFOA. For instance, reductions in PFHxS and PFOA exposure for non-Hispanic Pacific Islander populations are roughly 10 and four times the exposure rate for the total population served across all demographic groups, respectively (2.09 vs. 0.23 for PFHxS and 1.12 vs. 0.25 for PFOA). Non-Hispanic American Indian or Alaska Native populations served also see greater reductions in PFHxS and PFOA in comparison to the total population served. Reductions PFAS exposure above 10.0 ppt are also higher for non-Hispanic Asian populations for PFOS and for populations with income below twice the Federal poverty level for PFHxS and PFOA.

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

PFAS	Race and Ethnicity						Income		Population Served
	Non-Hispanic American Indian and Alaska Native	Non-Hispanic Asian	Non-Hispanic Black	Non-Hispanic Pacific Islander	Hispanic	Non-Hispanic White	Below Twice the Poverty Level	Above Twice the Poverty Level	
Population Served Above UCMR 5 MRL									
PFOS	176	9067	13162	116	20464	169469	41499	175155	216,654
PFHxS	209	2814	6172	29	11266	58040	19574	61082	80,656
PFHpA	53	2314	676	29	6077	26539	5263	31685	36,948
PFOA	238	5703	10018	58	17925	113903	32348	118765	151,113
Population Served Above UCMR 5 MRL as a Percent of Total Population Served									
PFOS	2.5%	***21.8%***	***12.1%***	***12.3%***	***13.0%***	9.6%	7.5%	***11.2%***	10.2%
PFHxS	3.0%	***6.8%***	***5.7%***	3.1%	***7.1%***	3.3%	3.5%	***3.9%***	3.8%
PFHpA	0.8%	***5.6%***	0.6%	***3.1%***	***3.9%***	1.5%	0.9%	***2.0%***	1.7%
PFOA	3.4%	***13.7%***	***9.2%***	6.2%	***11.4%***	6.5%	5.8%	***7.6%***	7.1%

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

	Race and Ethnicity						Income		
PFAS	**Non-Hispanic American Indian or Alaska Native**	**Non-Hispanic Asian**	**Non-Hispanic Black**	**Non-Hispanic Pacific Islander**	**Hispanic**	**Non-Hispanic White**	**Below Twice the Poverty Level**	**Above Twice the Poverty Level**	**Total Population Served**
PFOS	0.13	1.14	0.27	0.71	0.61	0.38	0.23	0.47	0.41
PFHxS	0.59	0.36	0.21	2.27	1.01	0.23	0.40	0.28	0.32
PFHpA	0.03	0.08	0.02	0.13	0.09	0.03	0.03	0.04	0.03
PFOA	0.39	0.49	0.37	1.40	0.85	0.37	0.47	0.40	0.42

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

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

PFAS	Race and Ethnicity					Income		Population Served
	Non-Hispanic American Indian and Alaska Native	Non-Hispanic Asian	Non-Hispanic Black	Non-Hispanic Pacific Islander	Hispanic	Non-Hispanic White	Below Twice the Poverty Level	Above Twice the Poverty Level	
Population Served Above 10.0 ppt									
PFOS	59	2,397	891	49	5,396	32,632	5,465	37,385	42,850
PFHxS	59	162	494	29	1,997	7,662	4,306	6,879	11,185
PFHpA	0	0	0	0	0	0	0	0	0
PFOA	66	553	1,027	36	4,269	20,842	6,824	20,906	27,730
Population Served Above 10.0 ppt as a Percent of Total Population Served									
PFOS	0.8%	***5.8%***	0.8%	***5.2%***	***3.4%***	1.9%	1.0%	***2.4%***	2.0%
PFHxS	0.8%	0.4%	0.5%	***3.1%***	***1.3%***	0.4%	***0.8%***	0.4%	0.5%
PFHpA	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
PFOA	0.9%	1.3%	0.9%	***3.8%***	***2.7%***	1.2%	1.2%	1.3%	1.3%

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
	Non-Hispanic American Indian or Alaska Native	Non-Hispanic Asian	Non-Hispanic Black	Non-Hispanic Pacific Islander	Hispanic	Non-Hispanic White	Below Twice the Poverty Level	Above Twice the Poverty Level	
PFOS	0.04	0.31	0.04	0.25	0.17	0.09	0.04	0.11	0.10
PFHxS	0.51	0.21	0.17	2.09	0.81	0.16	0.32	0.2	0.23
PFHpA	0	0	0	0	0	0	0	0	0
PFOA	0.32	0.2	0.2	1.12	0.56	0.21	0.32	0.22	0.25

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

Appendix N. Supplemental Cost Analyses

Section N.1 discusses the approach the 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 PFNA, perfluorobutane sulfonic acid (PFBS), HFPO-DA occurrence data on national cost estimates.

N.1 Cost Analysis for Very Large Systems

The 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 EPs; 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; PWSID – public water system identification; 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, the EPA reviewed UCMR3 data and recent system consumer confidence reports to obtain EP PFAS values. Given the type of sources used there were not enough data to confidently estimate running annual averages (RAA). As a result, the EPA used these values to determine which EPs at these systems exceed the MCLs and/or HI for the final rule and alternative options.

Any value reported above relevant limit was interpreted as an exceedance. This approach likely overestimates treatment costs at a national level, since maximum individual reported values are typically higher than RAAs. For example, if a system were to observe four values with one PFOA result at 6 ppt and three PFOA results at 3 ppt, for purposes of calculating an RAA, this EP would be below the PFOA MCL and would not be compelled to take action. However, using the methodology here, because the single value is above the MCL, the EPA treated that EP as needing to take action such as installing treatment.

PFOA and PFOS levels at multiple EPs for two systems exceeded one or more MCLs for the final rule and alternative options (no HI exceedances occurred). The EPA used these reported PFAS values as the baseline occurrence estimates for the cost analysis. The EPA applied the cost estimating methods described in Chapter 5 to these systems to derive estimates of the costs to meet each MCL.

N.2 Hazardous Waste Disposal Cost Impacts

The national cost analysis reflects the assumption that PFAS-contaminated wastes are not considered RCRA regulatory or characteristic hazardous wastes. Stakeholders have expressed concern to the EPA that a hazardous substance designation for certain PFAS may limit their disposal options for drinking water treatment residuals (e.g., spent media, concentrated waste streams) and/or potentially increase costs. Designation of PFOA and PFOS as CERCLA hazardous substances would not require waste (e.g., biosolids, treatment residuals, etc.) to be treated in any particular fashion, nor disposed of at any specific particular type of landfill. The designation also would not restrict, change, or recommend any specific activity or type of waste at landfills. Although designating chemicals as hazardous substances under CERCLA would not result in new requirements for disposal of PFAS drinking water treatment residuals, to address stakeholder concerns, including those raised during the SBREFA process, the EPA conducted a sensitivity analysis with an assumption of hazardous waste disposal for illustrative purposes only. As part of this analysis, the 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. The EPA acknowledges that if PFAS-contaminated wastes are required to be handled 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 landfill 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 final rule. At a 2 percent discount rate, the annualized cost would be $98.90 million (7%) 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, Final Rule (PFOA and PFOS MCLs of 4.0 ppt each, PFHxS, PFNA, and HFPO-DA MCLs of 10 ppt each and HI of 1) (Million $2022)

	2% Discount Rate		
	5th Percentile	**Mean**	**95th Percentile**
Non-Hazardous Disposal	$1,395.23	$1,506.44	$1,627.65
Hazardous Disposal	$1,487.73	$1,605.34	$1,731.75
Increase due to Hazardous Disposal		**$98.90**	

Note: Percentiles cannot be subtracted. See Appendix P for results presented at 3 and 7 percent discount rates.

N.3 National Level Sensitivity Analysis of Incremental Treatment Cost of PFNA, PFBS and HFPO-DA

The EPA has estimated the national level costs of the final rule using occurrence data for PFOA, PFOS and PFHxS. As discussed in Chapter 4 of the EA, there are limitations with nationally representative occurrence information for the other compounds in the final rule (PFNA, HFPO-DA and PFBS), therefore the additional treatment costs associated with the occurrence of PFNA, HFPO-DA, PFBS, are not reported in the national cost estimates. Instead, quantified cost estimates for PFNA, HFPO-DA, and PFBS are considered here as part of this sensitivity analysis. When available, nationally representative occurrence information is preferable for an economic analysis of the national level costs and benefits. However, this does not mean that non-nationally representative occurrence data cannot be used to meaningfully inform regulatory development of drinking water standards and they often represent the best available science and information.

In the case of PFOA, PFOS, and PFHxS, the EPA has a sufficiently robust nationally representative dataset from UCMR3. UCMR3 required all large community and non-transient non-community water systems serving more than 10,000 people to monitor and also required monitoring by a nationally representative sample of small systems (i.e., those serving 10,000 or fewer people). The survey sample design for small systems uses a statistically-derived set of systems for the nationally representative sample that is population-weighted within each system size and source water category so that any PWS within a category has an equivalent likelihood of selection (77 FR 26072). The EPA used additional state data that were available at systems that were part of this UCMR3 set of systems to fit the MCMC occurrence model that informed cost estimates for PFOA, PFOS, and PFHxS. When incorporating the additional state data, the EPA used QC measures to ensure that the data represented finished drinking water, to verify that the majority of data were analyzed using EPA approved drinking water methods[60] and that the set of systems used to inform the model maintained the nationally representative structure. Further details on the MCMC model are available in Cadwallader et al. (2022). For more information on the application of the model in this analysis, see Section 4.4 and Appendix A. For more information on the data and analyses that the EPA used to develop national estimates of PFAS occurrence in public drinking water systems see U.S. EPA (2024a).

In the case of PFNA, HFPO-DA, and PFBS, EPA lacks the same level of precision as described above. While PFNA and PFBS were included in UCMR3, the amount of results above the UCMR3 MRLs was insufficient for incorporation into the MCMC occurrence model and prevented direct quantification through model extrapolation. However, a substantial amount of data (about 36,000 samples from 10,000 systems or more per contaminant) were collected from states. These state data also underwent QC measures to ensure that the data represented finished drinking water and to verify that the majority of data were analyzed using EPA approved drinking water methods.[60] While the state-led data collection efforts provided valuable information about occurrence for PFNA, HFPO-DA, and PFBS, they did not provide the nationally representative foundation provided by UCMR 3 for PFOA, PFOS, and PFHxS to be incorporated into the MCMC model. Therefore, because there is somewhat greater uncertainty in

[60] The EPA was able to verify that approximately 97% of the state data were analyzed using EPA approved methods.

the number of systems that are likely to exceed the MCLs, the quantified cost estimates for PFNA, HFPO-DA, and PFBS are discussed in the context of this sensitivity analysis. For HFPO-DA, PFBS, and PFNA, the EPA extrapolated system level maximums from non-targeted state datasets as part of a conservative approach to estimate occurrence for PFAS without a nationally representative dataset. EPA presents these cost results separately from the results for PFOA, PFOS, and PFHxS to recognize the higher level of uncertainty associated with the occurrence of PFNA, HFPO-DA and PFBS and the different approaches taken to derive occurrence estimates.

In the EA for the proposed PFAS NPDWR, the EPA used a model system approach to illustrate the potential incremental costs for removing PFAS not included in the national economic model. After considering public comments on the incremental cost analysis, the EPA decided to further explore the incremental costs associated with the HI and MCLs with a national level sensitivity analysis in the final rule.

To inform this sensitivity analysis, the EPA estimated the occurrence of HFPO-DA, PFBS, and PFNA, using available state-level data. The EPA then used these estimates to determine the potential impact of exceedance of the HI (mixtures of two or more of PFHxS, PFNA, HFPO-DA, and PFBS) and individual PFNA and HFPO-DA MCLs in addition to exceedances of the PFOA, PFOS and PFHxS MCLs. For more information on the occurrence model output used in this sensitivity analysis, including its development and results, See Section 10.3.2. of *Per- and Polyfluoroalkyl Substances (PFAS) Occurrence & Contaminant Background Support Document* (U.S. EPA, 2024d).

This sensitivity analysis has two major limitations that are important to note. They are:

1. The occurrence data for HFPO-DA, PFBS, and PFNA are modeled using limited available aggregated state-level data that is extrapolated to the nation. Specifically, HFPO-DA does not currently have a completed nationally representative dataset while PFNA and PFBS were not included in the national occurrence model because of the limited reported values above the minimum reporting levels in UCMR 3. As described in the Technical Support Document for PFAS Occurrence and Contaminant Background Chapter 10.3, non-targeted state monitoring datasets were used for extrapolation of PFNA, HFPO-DA, and PFBS in lieu of a nationally representative dataset.

2. The EPA has insufficient quantitative data to include HFPO-DA in the linear equations used to estimate bed life for IX. In this analysis, the EPA assumes the bed life is the same as PFHxA, the contaminant for which quantitative data are available that is the most difficult to remove by IX. The EPA has insufficient quantitative data to include PFNA in the linear equations used to estimate bed life for GAC and IX. For GAC, the EPA assumes the bed life for PFNA is the same as PFOS. For IX, the 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 will result in the EPA estimating higher costs than will actually be realized for this part of the estimate.

When the modeled occurrence data for PFNA, HFPO-DA, PFBS is incorporated into the SafeWater MCBC model, the estimated number of EPs exceeding one or more MCLs, and therefore required to treat or use a different water source, increases to 9,471 from 9,043. This results in an increase in the expected national costs. Under the primary analyses (see Chapter 5) the expected total national cost at a 2 percent discount rate is $1,548.64 million. Under the

sensitivity analysis, the expected national costs increase to $1,631.05 million, or approximately a 5 percent increase in national costs. Broken out by system size, expected national rule costs increase from $275.84 million to $293.09 million (6 percent increase) and $1,272.83 million to $1,337.93 million (5 percent increase) for small and large systems, respectively. This small increase in costs would not change the Administrator's determination at proposal that the EPA is reaffirming for the final rule that the benefits of the rule justify its costs.

N.4 National Level Sensitivity Analysis Considering PFNA and HFPO-DA MCLs

The final rule consists of PFOA and PFOS MCLs of 4.0 ppt each, PFHxS, PFNA, HFPO-DA MCLs of 10 ppt each and an HI MCL of 1 (unitless). To evaluate the costs of the rulemaking in the absence of the HI MCL, the EPA estimated the cost of an MCL only scenario which included only the PFOA and PFOS MCLs of 4.0 ppt each, and the PFHxS, PFNA, HFPO-DA MCLs of 10 ppt each. The EPA then examined the marginal costs of two individual contaminant MCLs (i.e., PFNA, and HFPO-DA) using the MCL only scenario as the base cost. As discussed in Section N.3 above and Section 10.3 of *Per- and Polyfluoroalkyl Substances (PFAS) Occurrence & Contaminant Background Support Document* (U.S. EPA, 2024d) the total estimated annualized cost for the MCL only rule was estimated using combined information from the national occurrence model (PFOA, PFOS, and PFHxS) and state level occurrence information for HFPO-DA and PFNA. For the HFPO-DA and PFNA MCLs the EPA estimated system level maximums using several methods due to uncertainty as part of a conservative approach to estimate occurrence for PFAS without a nationally representative dataset. Results presented below use the method that selects equal percentages of systems among systems that a) are already exceeding an MCL for PFOA or PFOS and b) are not exceeding an MCL for PFOA or PFOS. Within a group, the probability of being selected is proportionate to the system's maximum sum of modeled PFAS. Therefore, these cost estimates can be considered cost conservative. In Section 5.1.3, the EPA discusses the marginal costs associated with PFHxS MCL exceedances. Computationally the EPA first modeled the costs of the MCL only scenario considering the individual MCLs for PFOA (4.0 ppt), PFOS (4.0 ppt), PFNA (10 ppt), HFPO-DA (10 ppt), and PFHxS (10 ppt). The estimated mean total annualized MCL only scenario cost is $1,545.35 ($2022, 2 percent discount rate). The EPA then modeled the costs of the rule without the MCLs for PFNA and HFPO-DA one at a time. The difference between the cost for all analyte MCLs and the cost for all analyte MCLs except the one removed from the model is the marginal costs of the removed MCL. Table N-3 shows the marginal costs of the rulemaking associated with MCLs for PFNA and HFPO-DA.

Table N-3. Marginal Mean Annualized Rule Costs Associated with Individual MCLs of 10 ppt each for PFNA, HFPO-DA (Million $2022)

PFNA	$40.45
HFPO-DA	$14.87

The PFNA MCL is estimated to affect 208 PWSs (393 EPs), 191 PWSs (346 EPs) of which need to take corrective action for PFNA alone and 17 PWSs (46 EPs) will take corrective action due to more than one PFAS MCL. The HFPO-DA MCL is estimated to affect 44 PWSs (84 EPs), 40

PWSs (73 EPs) of which need to take corrective action for HFPO-DA alone, and 4 PWSs (11 EPs) will take corrective action due to more than one PFAS MCL. As demonstrated by these results, the EPA expects that the more unique systems triggered into corrective action by a given MCL, the higher its marginal cost will be.

Considering the MCL only scenario, total annualized costs of $1,545.35 million ($2022, 2 percent discount rate), the PFNA MCL contributes 2.6 percent of the overall costs and the HFPO-DA MCL contributes 0.9 percent of the overall costs.

Appendix O. Supplemental Benefits Analyses

O.1 Supplemental Liver Cancer Analysis

This section presents an analysis that considers potential changes in liver cancer cases and deaths associated with reduced exposures to PFOS considered under the final rule. This analysis is presented as a supplemental analysis for the final rule to respond to public comments received on the proposed rule requesting that the EPA quantify additional health benefits.

O.1.1 Overview of the Liver Cancer Risk Reduction Analysis

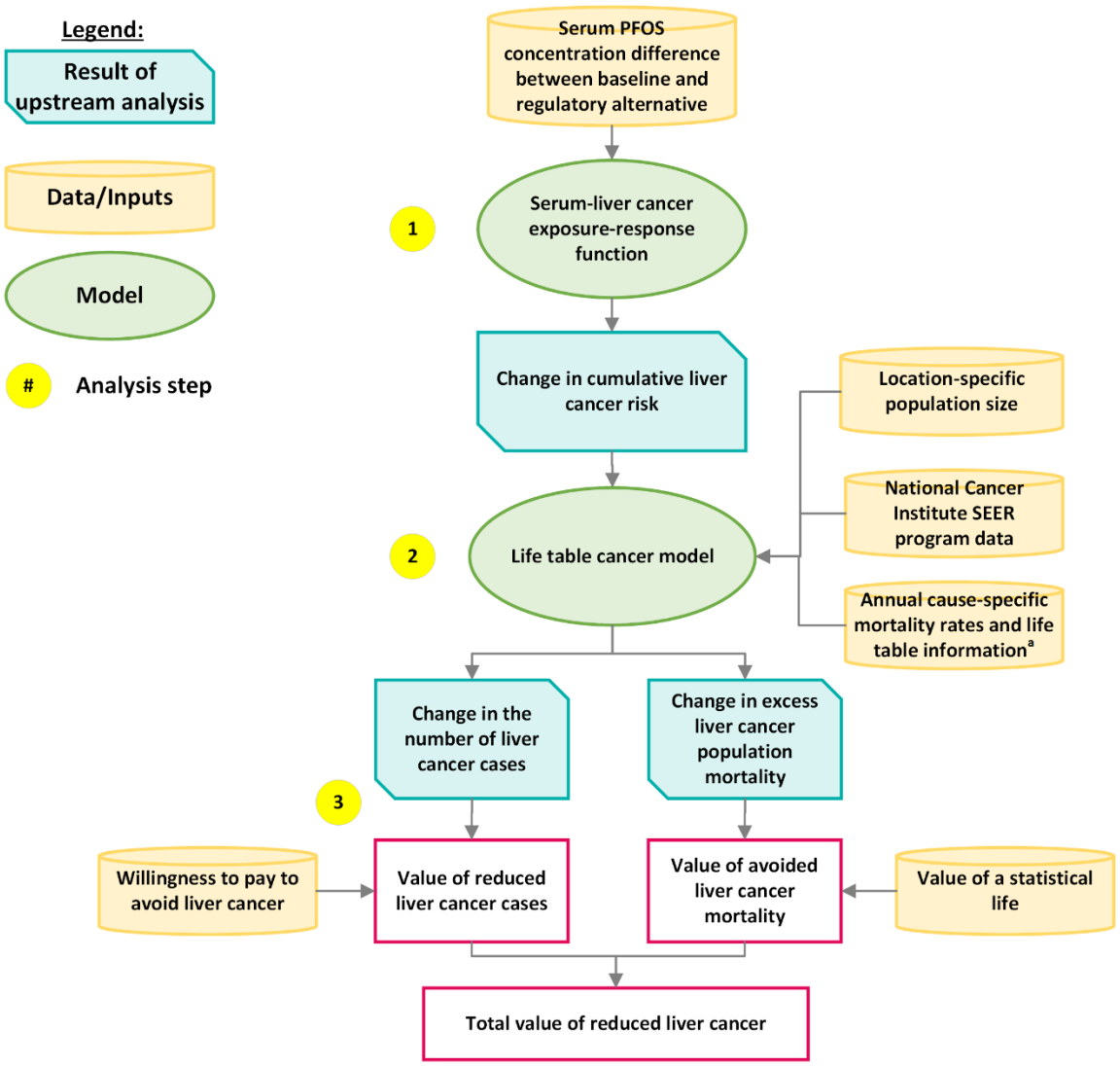
Figure O-1 illustrates the approach used to quantify and value the changes in liver cancer risk associated with decreased serum PFOS levels from reductions in drinking water PFOS concentrations under the regulatory alternatives. Section 4.4 and Section 6.3 detail the PWS EP-specific PFOS drinking water occurrence estimation and modeling of serum PFOS concentrations, respectively. PWS EP-specific time series of the differences between serum PFOS concentrations under baseline and regulatory alternatives are inputs into this analysis. For each PWS EP, evaluation of the changes in liver cancer impacts involves the following key steps:

1. Estimating the changes in liver cancer risk based on modeled changes in serum PFOS levels and the exposure-response function for the effect of serum PFOS on liver cancer;

2. Estimating the annual incidence of liver cancer cases and excess mortality among those with liver cancer in all populations corresponding to baseline and regulatory alternative liver cancer risk levels, as well as estimating the regulatory alternative-specific reduction in cases relative to the baseline; and

3. Estimating the economic value of reducing liver cancer mortality and morbidity from baseline to regulatory alternative levels, using the Value of Statistical Life and willingness to pay measures, respectively.

Section O.1.2 discusses the exposure-response modeling for liver cancer. Section O.1.3 summarizes the life table-based approach for estimation of liver cancer risk reductions. Section O.1.4 discusses the EPA's valuation methodology for liver cancer mortality and morbidity. Section O.1.5 presents the results of the analysis.



Abbreviations: PFOS – perfluorooctane sulfonic acid, SEER - Surveillance, Epidemiology, and End Results program
Notes:
[a]Data from the Centers for Disease Control (CDC) and Prevention.

Figure O-1. Overview of Analysis of Reduced Liver Cancer Risk

O.1.2 Liver Cancer Exposure-Response Modeling

Evidence of the association between PFOA and PFOS exposure and liver cancer in humans was considered inconclusive based on occupational and general population epidemiology studies (U.S. EPA, 2024b; U.S. EPA, 2024c). However, the EPA found evidence of a positive association between PFOS exposure and hepatocellular tumors in animal studies. Butenhoff et al. (2012)/Thomford (2002) reported a statistically significant increase in combined hepatocellular adenomas and carcinomas tumor incidence in female Sprague-Dawley rats exposed to high doses of PFOS. The study reported a statistically significant trend of increased incidence with

increasing PFOS concentrations across dose groups. The EPA reviewed the weight of the evidence and determined that PFOS is Likely to Be Carcinogenic to Humans, as "the evidence is adequate to demonstrate carcinogenic potential to humans but does not reach the weight of evidence for the descriptor Carcinogenic to Humans." The EPA evaluated the effects of the final rule on liver cancer using the relationships between PFOS exposure and hepatocellular adenomas and carcinomas in female rats.

To evaluate changes between baseline and regulatory alternative liver cancer risk resulting from reduced exposure to PFOS, the EPA relied on the estimated time series of changes in serum PFOS concentrations (Section 6.3) and the cancer slope factor calculated based on the EPA's benchmark dose (BMD) modeling results for hepatocellular adenomas and carcinomas in female rats following exposure to PFOS. The EPA carried forward the animal BMD of 37.2 mg/L (Table E-46 of the PFOS MCLG Appendix; U.S. EPA, 2024a), which corresponds to the internal human BMD. This value represents the internal human BMD because the animal BMD was based on area under the curve (AUC) normalized per day (AUCavg), equivalent to mean serum concentration during the duration of the study, which as selected for this model; the AUC accounts for the accumulation of effects expected to precede the increased incidence of adenomas and/or carcinomas (U.S. EPA, 2005a). The EPA then applied the linear extrapolation approach to calculate the human cancer risk factor by dividing the benchmark response (BMR) of 10% by the human BMD, which resulted in $2.69*10^{-6}$ per ng/mL. This linear slope factor enables estimation of the changes in lifetime and relative liver cancer risk associated with reduced lifetime serum PFOS levels, as described in Equations 15, 16, and 27 of Section 6.6.2.

O.1.3 Estimation of Liver Cancer Risk Reductions

The EPA relies on the life table approach to estimate liver cancer risk reductions because:

- Changes in serum PFOS in response to changes in drinking water PFOS occur over multiple years;
- Annual risk of new liver cancer should be quantified only among those not already experiencing this chronic condition; and
- Liver cancer has elevated mortality implications.

The EPA used recurrent life table calculations to estimate PWS EP-specific time series of liver cancer incidence for a population cohort characterized by sex, race/ethnicity, birth year, and age at the beginning of the evaluation period (i.e., 2024) under the baseline scenario and the regulatory alternatives. The life table analysis accounts for the gradual changes in lifetime exposures to PFOS following implementation of treatment under the regulatory alternatives compared to the baseline. Details of the life table calculations are provided in Appendix H. The outputs of the life table calculations are the PWS EP-specific estimates of the annual change in the number of liver cancer cases and the annual change in liver cancer population mortality.

Although the change in PFOS exposure likely affects the risk of developing liver cancer beyond the end of the analysis period (the majority of liver cancer cases manifest during the latter half of the average individual lifespan; see Appendix H), the EPA does not capture effects after the end of the period of analysis, 2105. Individuals alive after the end of the period of analysis likely benefit from lower lifetime exposure to PFOS. Lifetime health risk model data sources include SDWIS/Fed; age-, sex-, and race/ethnicity-specific population estimates from the U.S. Census

Bureau (U.S. Census Bureau, 2020); the SEER program database (National Cancer Institute), and the CDC National Center for Health Statistics. Appendix H provides additional detail on the data sources and information used in this analysis as well as baseline liver cancer statistics. Appendix B describes estimation of the affected population.

O.1.4 Valuation of Liver Cancer Risk Reductions

The EPA uses the Value of Statistical Life to estimate the benefits of reducing mortality associated with liver cancer in the population exposed to PFOS in drinking water. Appendix J provides information on updating Value of Statistical Life for inflation and income growth. The EPA uses the willingness to pay estimates per statistical non-site specific nonfatal cancer avoided from Bosworth et al. (2009), which was identified in a literature review from Abt Associates (2022), Estimated Values of Avoiding Cancer Risks by Cancer Site and Population, to value liver cancer morbidity. Bosworth et al. (2009) elicited willingness to pay to avoid illnesses and premature death using a national survey in a choice experiment format. The valuation scenarios presented to survey respondents described a proposed public policy that will reduce community-level risk of both illness and death for these diseases by improving air pollution, drinking water contamination, and the levels of pesticides in foods. Survey participants were asked to choose between the two offered policies based on the private cost of the policy and the number of avoided illnesses and deaths.

To obtain a willingness to pay value suitable for valuation of liver cancer morbidity risk reductions during 2024-2105, the EPA relies on the base value estimate of $245,000 ($2009, 2009 income year) from Bosworth et al. (2009). The EPA followed the methodology used to adjust the base Value of Statistical Life for inflation and income growth for adjusting willingness to pay estimates (see Appendix J for details). Unlike the Value of Statistical Life, which is adjusted for income growth based on an assumed elasticity of 0.4, willingness to pay values are adjusted based on an assumed elasticity of 0.45, which represents the central elasticity estimate for severe and chronic health effects (U.S. EPA, 2023b). Like Value of Statistical Life, willingness to pay estimates are approximated using the CAGR from 2024 to 2050 (the final year that income growth projections are available) to estimate willingness to pay values for the entire period of analysis, 2024 to 2105. The estimates of willingness to pay per statistical non-site specific cancer morbidity avoided range from $364,060 ($2022) in 2024 to $643,142 ($2022) in 2105. Table O-1 summarizes the projected willingness to pay estimates through 2050 and the approximated willingness to pay estimates through 2105.

Table O-1. Estimated Liver Cancer Willingness to Pay 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 2009 PDYPP to the Power of 0.45)	Projected Willingness to Pay ($2022)	Approximated Willingness to Pay ($2022)
2009	30,327	-	1	328,021	-
2024	-	47,987	1.109868225	364,060	364,060
2025	-	48,917	1.119502162	367,220	366,627
2026	-	49,760	1.128145153	370,055	369,212

Table O-1. Estimated Liver Cancer Willingness to Pay 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 2009 PDYPP to the Power of 0.45)	Projected Willingness to Pay ($2022)	Approximated Willingness to Pay ($2022)
2027	-	50,616	1.136833419	372,905	371,815
2028	-	51,496	1.145687172	375,810	374,436
2029	-	52,407	1.154763474	378,787	377,076
2030	-	53,393	1.164489967	381,977	379,734
2031	-	54,326	1.17359746	384,965	382,411
2032	-	55,258	1.182614732	387,923	385,107
2033	-	56,207	1.191716687	390,908	387,822
2034	-	57,145	1.200625062	393,830	390,556
2035	-	58,072	1.209352808	396,693	393,310
2036	-	58,985	1.217865528	399,486	396,082
2037	-	59,874	1.226099557	402,187	398,875
2038	-	60,753	1.234164989	404,832	401,687
2039	-	61,643	1.242269802	407,491	404,519
2040	-	62,513	1.250121412	410,066	407,371
2041	-	63,408	1.25815293	412,701	410,243
2042	-	64,346	1.266493129	415,437	413,135
2043	-	65,282	1.274745794	418,144	416,047
2044	-	66,210	1.282866035	420,807	418,981
2045	-	67,148	1.291015411	423,480	421,934
2046	-	68,095	1.299174972	426,157	424,909
2047	-	69,069	1.307509356	428,891	427,905
2048	-	70,076	1.316055374	431,694	430,921
2049	-	71,066	1.324386799	434,427	433,959
2050	-	72,024	1.332395223	437,054	437,019
2051	-	-	-	-	440,100
2052	-	-	-	-	443,202
2053	-	-	-	-	446,327
2054	-	-	-	-	449,474
2055	-	-	-	-	452,642
2056	-	-	-	-	455,834
2057	-	-	-	-	459,047
2058	-	-	-	-	462,283
2059	-	-	-	-	465,543
2060	-	-	-	-	468,825
2061	-	-	-	-	472,130

Table O-1. Estimated Liver Cancer Willingness to Pay 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 2009 PDYPP to the Power of 0.45)	Projected Willingness to Pay ($2022)	Approximated Willingness to Pay ($2022)
2062	-	-	-	-	475,458
2063	-	-	-	-	478,810
2064	-	-	-	-	482,186
2065	-	-	-	-	485,585
2066	-	-	-	-	489,009
2067	-	-	-	-	492,456
2068	-	-	-	-	495,928
2069	-	-	-	-	499,424
2070	-	-	-	-	502,945
2071	-	-	-	-	506,491
2072	-	-	-	-	510,062
2073	-	-	-	-	513,658
2074	-	-	-	-	517,279
2075	-	-	-	-	520,926
2076	-	-	-	-	524,598
2077	-	-	-	-	528,297
2078	-	-	-	-	532,021
2079	-	-	-	-	535,772
2080	-	-	-	-	539,549
2081	-	-	-	-	543,353
2082	-	-	-	-	547,184
2083	-	-	-	-	551,041
2084	-	-	-	-	554,926
2085	-	-	-	-	558,838
2086	-	-	-	-	562,778
2087	-	-	-	-	566,746
2088	-	-	-	-	570,741
2089	-	-	-	-	574,765
2090	-	-	-	-	578,817
2091	-	-	-	-	582,898
2092	-	-	-	-	587,007
2093	-	-	-	-	591,146
2094	-	-	-	-	595,313
2095	-	-	-	-	599,510
2096	-	-	-	-	603,737

Table O-1. Estimated Liver Cancer Willingness to Pay 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 2009 PDYPP to the Power of 0.45)	Projected Willingness to Pay ($2022)	Approximated Willingness to Pay ($2022)
2097	-	-	-	-	607,993
2098	-	-	-	-	612,280
2099	-	-	-	-	616,596
2100	-	-	-	-	620,943
2101	-	-	-	-	625,321
2102	-	-	-	-	629,729
2103	-	-	-	-	634,169
2104	-	-	-	-	638,640
2105	-	-	-	-	643,142

Acronym: PDYPP– personal disposable income per capita.

O.1.5 Results

Table O-2 provides the health effects avoided and valuation associated with liver cancer under the final rule MCL and HI assumptions. Modeled uncertainty includes uncertainty regarding the PAF estimation and occurrence estimates. Annualized liver cancer benefits are $4.79 million.

Table O-2. National Liver Cancer Benefits, Final Rule (PFOA and PFOS MCLs of 4.0 ppt each, PFHxS, PFNA, HFPO-DA, of 10 ppt each and HI of 1)

Benefits Category	2% Discount Rate		
	5th Percentile[a]	Expected Value	95th Percentile[a]
Number of Non-Fatal Liver Cancer Cases Avoided	13.30	14.17	15.08
Number of Liver Cancer-Related Deaths Avoided	29.36	31.25	33.29
Total Annualized Liver Cancer Benefits (Million $2022)[b]	**$4.50**	**$4.79**	**$5.10**

Notes: Detail may not add exactly to total due to independent rounding. See Appendix P for results presented at 3 and 7 percent discount rates.
[a]The 5th and 95th percentile range is based on modeled variability and uncertainty related to PAF and occurrence. This range does not include the uncertainty described in Table O-3.
[b]See Table 7-6 for a list of the nonquantifiable benefits, and the potential direction of impact these benefits would have on the estimated monetized total annualized benefits in this table.

O.1.6 Limitations and Uncertainties

Table O-3 describes limitations and uncertainties of the supplemental liver cancer benefits analysis. Limitations and uncertainties that apply to all health benefits analyses are summarized in Table 6-48.

Table O-3. Limitations and Uncertainties in the Analysis of Liver Cancer Benefits

Uncertainty/Assumption	Effect on Benefits Estimate	Notes
Characterizing the Exposed Population		
The analysis uses national-level estimates of liver cancer incidence, prevalence, stage distribution, and relative survival data, as well as national-level life tables.	Uncertain	Using national-level baseline health data may over- or underestimate the effects of regulatory alternatives on liver cancer morbidity and mortality in specific PWSs and well as overall.
Liver cancer risks are estimated for populations for which reductions in PFOS exposures relative to baseline exposures start at different ages, including children.	Uncertain	The relative cancer potency of PFOS in children is unknown, which may bias benefits estimates either upward or downward. Because liver cancer incidence in children is very small, we assess any bias to be negligible.
Modeling Changes in Health Risks		
The analysis relies on associations between PFOS exposure and hepatocellular adenomas and carcinomas in animals.	Uncertain	The cancer slope factor is based on associations between PFOS exposure and hepatocellular adenomas and carcinomas observed in female rats. This relationship may not accurately reflect association be PFOS exposure and risk of liver cancer in humans. The effect of using a cancer slope factor specific to animals to evaluate changes in the incidence of liver cancer in humans is uncertain.

Table O-3. Limitations and Uncertainties in the Analysis of Liver Cancer Benefits

Uncertainty/Assumption	Effect on Benefits Estimate	Notes
The analysis does not explicitly model variability of baseline liver cancer risk by cirrhosis and hepatitis B infection status.	Uncertain	In humans, 95 percent of primary liver tumors are malignant, with hepatocellular carcinoma comprising 90 percent of malignancies in adults (B. B. Anderson et al., 1992). The risk of hepatocellular carcinoma is 33 to 200 times higher in populations with cirrhosis of the liver and populations with hepatitis B infection. While each population represents approximately 1 percent of the U.S. population overall, 75 percent of hepatocellular carcinoma incidence occurs in those affected by cirrhosis/hepatitis B (B. B. Anderson et al., 1992). The cancer slope factor used in the analysis represents an additive change in liver cancer risk and the extent to which it may be modified in the cirrhosis/hepatitis B populations is uncertain. The available association between PFOS exposure and liver cancer risk is linear, implying that the estimated lifetime risk reductions do not depend on the baseline liver cancer risk level. Therefore, modeling cirrhosis/hepatitis B population in this analysis will not generate additional insights.
The analysis assumes that the magnitude of liver cancer risk reductions resulting from reductions in serum PFOA levels will not exceed a PAF of 3.94 percent.	Uncertain	The EPA placed a cap of 3.94 percent on the magnitude of the estimated cumulative liver cancer risk reduction resulting from reductions in serum PFOS levels, based on its analysis of PAF values found in the literature on environmental contaminants and cancers (ICF, 2022). This review found that changes in environmental exposures result in relatively modest PAFs (between 0.2 percent and 17.9%); however, few of the studies provided PAFs related specifically to liver cancer. The EPA characterized the uncertainty surrounding this parameter using a log-uniform distribution with a minimum of 0.2 percent and a maximum of 17.9 percent. For the central estimate of liver cancer benefits, the EPA used a PAF of 3.94 percent, which is the mean of the PAF uncertainty distribution. As such, the EPA assumed that liver cancer risk reduction estimates in excess of the PAF are unreasonable even as a result of large changes in serum PFOS concentrations. Because this PAF cap is not based on liver cancer studies specifically, it is uncertain whether the liver cancer impacts are under- or overestimated.

Table O-3. Limitations and Uncertainties in the Analysis of Liver Cancer Benefits

Uncertainty/Assumption	Effect on Benefits Estimate	Notes
The analysis assumes that there is no lag between changes in serum PFOS concentrations and changes in liver cancer incidence.	Overestimate	The studies estimating the association between serum PFOS and liver cancer are not dynamic, and hence do not provide insights into whether liver cancer incidence may respond gradually to changes in serum PFOS. The PK model estimates daily serum levels, which are averaged annually for the purposes of modeling gradual serum changes for the liver cancer risk reduction analysis. The liver cancer risk reduction analysis assumes immediate liver cancer incidence adjustment within each year, which may overestimate impacts to the exposed population.
The analysis relies on public-access SEER 20 10-year relative liver cancer survival data to model mortality patterns in the liver cancer population.	Uncertain	Reliance on these data generates both a downward and an upward bias. The downward bias is due to the short, 10-year excess mortality follow-up window. Survival rates beyond 10 years following the initial diagnosis are likely to be lower. The upward bias comes from the inability to determine how many of the excess deaths were deaths from liver cancer.
The analysis models the 85+ year old group jointly and applies the average mortality rate for those aged 85+ in this age group.	Uncertain	The effect of this modeling approximation on the liver cancer benefits is not certain because integer age-specific mortality rates may be above or below the average mortality rate.
The analysis models the 85+ year old group jointly and uses serum PFOS estimates for those aged 85 to initiate calculations in this age group.	Underestimate	Because the impacts of changes in PFOS drinking water concentrations on serum PFOS levels increase over time, the use of serum PFOS concentrations at 85 years to model the 85+ age group will underestimate the liver cancer risk impacts in this group.
Economic Valuation of Changes in Health Risk		
The analysis relies on willingness to pay estimates per statistical non-site specific nonfatal cancer avoided to estimate benefits from avoided liver cancer cases.	Uncertain	Primary liver cancer is most treatable if detected early which is not a common situation. Moreover, people who develop liver cancer usually already have an unhealthy liver and would require liver transplant rather than partial hepatectomy. Given the complexity of this organ and a low rate of cure for this type of cancer, the use of willingness to pay for avoiding non-site specific cancer may underestimate the value of avoiding non-fatal liver cancer. On the other hand, Bosworth et al. (2009) found "little heterogeneity of preferences according to the type of illness".

Abbreviations: PFOS – perfluorooctane sulfonic acid; PK – pharmacokinetic.

O.2 Supplemental Analysis Using Willingness to Pay for Cancer Morbidity Risk Reductions

Table O-5 and Table O-6 present results for supplemental national-level estimates of RCC benefits and bladder cancer co-benefits, respectfully, considering willingness to pay metrics for monetization of non-fatal cancer cases. The EPA relies on base willingness to pay estimates from Bosworth et al. (2009) for unspecified cancer in monetizing RCC benefits and for colon/bladder cancer in monetizing bladder cancer co-benefits.[61] The base estimates of willingness to pay per illness avoided based on an affected population of 50,000 for a duration of ten years are $245,000 for unspecified cancer and $400,000 for colon/bladder cancer (reported in $2009). The EPA relied on the approach described in Appendix J to adjust these estimates for inflation and income growth from 2009 to 2024-2050 and calculated the compound annual growth to approximate willingness to pay values during the analysis period (2024 to 2105; see Equations J-1, J-2, and J-3). As described in Section O.1.4, willingness to pay estimates were adjusted for income growth using an assumed elasticity of 0.45, the central elasticity estimate for severe and chronic health effects (U.S. EPA, 2023b). Unspecified cancer willingness to pay estimates range from $364,060 ($2022) in 2024 to $643,142 ($2022), as reported in Table O-1. Colon/bladder cancer willingness to pay estimates range from $594,384 in 2024 to $1,050,028 in 2105 ($2022), as reported below in Table O-4. When using willingness to pay instead of cost of illness values to monetize cancer morbidity impacts, annualized RCC benefits are $360.97 million, whereas annualized bladder cancer benefits are $456.28 million.

Table O-4. Estimated Bladder Cancer Willingness to Pay 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 2009 PDYPP to the Power of 0.45)	Projected Willingness to Pay ($2022)	Approximated Willingness to Pay ($2022)
2009	38,064	-	1	535,545	
2024	-	47,987	1.109868225	594,384	594,384
2025	-	48,917	1.119502162	599,543	598,574
2026	-	49,760	1.128145153	604,172	602,794
2027	-	50,616	1.136833419	608,825	607,044
2028	-	51,496	1.145687172	613,567	611,324
2029	-	52,407	1.154763474	618,427	615,634
2030	-	53,393	1.164489967	623,636	619,974
2031	-	54,326	1.17359746	628,514	624,345
2032	-	55,258	1.182614732	633,343	628,746

[61] The EPA did not identify a willingness to pay estimate specific to kidney cancer in the available literature. Estimates from Bosworth et al. (2009) were implemented in the EPA's Economic Analysis of the Proposed Regulation of Methylene Chloride Under TSCA Section 6(a) (U.S. EPA, 2023a).

Table O-4. Estimated Bladder Cancer Willingness to Pay 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 2009 PDYPP to the Power of 0.45)	Projected Willingness to Pay ($2022)	Approximated Willingness to Pay ($2022)
2033	-	56,207	1.191716687	638,218	633,179
2034	-	57,145	1.200625062	642,988	637,643
2035	-	58,072	1.209352808	647,662	642,138
2036	-	58,985	1.217865528	652,221	646,665
2037	-	59,874	1.226099557	656,631	651,224
2038	-	60,753	1.234164989	660,951	655,815
2039	-	61,643	1.242269802	665,291	660,439
2040	-	62,513	1.250121412	669,496	665,095
2041	-	63,408	1.25815293	673,797	669,784
2042	-	64,346	1.266493129	678,264	674,506
2043	-	65,282	1.274745794	682,683	679,261
2044	-	66,210	1.282866035	687,032	684,050
2045	-	67,148	1.291015411	691,396	688,873
2046	-	68,095	1.299174972	695,766	693,729
2047	-	69,069	1.307509356	700,230	698,620
2048	-	70,076	1.316055374	704,806	703,545
2049	-	71,066	1.324386799	709,268	708,505
2050	-	72,024	1.332395223	713,557	713,500
2051	-	-	-	-	718,530
2052	-	-	-	-	723,596
2053	-	-	-	-	728,697
2054	-	-	-	-	733,835
2055	-	-	-	-	739,008
2056	-	-	-	-	744,218
2057	-	-	-	-	749,465
2058	-	-	-	-	754,749
2059	-	-	-	-	760,070
2060	-	-	-	-	765,428
2061	-	-	-	-	770,824
2062	-	-	-	-	776,259
2063	-	-	-	-	781,731
2064	-	-	-	-	787,242
2065	-	-	-	-	792,792
2066	-	-	-	-	798,382
2067	-	-	-	-	804,010

Table O-4. Estimated Bladder Cancer Willingness to Pay 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 2009 PDYPP to the Power of 0.45)	Projected Willingness to Pay ($2022)	Approximated Willingness to Pay ($2022)
2068	-	-	-	-	809,679
2069	-	-	-	-	815,387
2070	-	-	-	-	821,135
2071	-	-	-	-	826,924
2072	-	-	-	-	832,754
2073	-	-	-	-	838,625
2074	-	-	-	-	844,537
2075	-	-	-	-	850,491
2076	-	-	-	-	856,487
2077	-	-	-	-	862,525
2078	-	-	-	-	868,606
2079	-	-	-	-	874,730
2080	-	-	-	-	880,897
2081	-	-	-	-	887,107
2082	-	-	-	-	893,361
2083	-	-	-	-	899,659
2084	-	-	-	-	906,002
2085	-	-	-	-	912,389
2086	-	-	-	-	918,822
2087	-	-	-	-	925,299
2088	-	-	-	-	931,823
2089	-	-	-	-	938,392
2090	-	-	-	-	945,008
2091	-	-	-	-	951,670
2092	-	-	-	-	958,379
2093	-	-	-	-	965,136
2094	-	-	-	-	971,940
2095	-	-	-	-	978,792
2096	-	-	-	-	985,693
2097	-	-	-	-	992,642
2098	-	-	-	-	999,640
2099	-	-	-	-	1,006,688
2100	-	-	-	-	1,013,785
2101	-	-	-	-	1,020,932
2102	-	-	-	-	1,028,129

Table O-4. Estimated Bladder Cancer Willingness to Pay 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 2009 PDYPP to the Power of 0.45)	Projected Willingness to Pay ($2022)	Approximated Willingness to Pay ($2022)
2103	-	-	-	-	1,035,378
2104	-	-	-	-	1,042,677
2105	-	-	-	-	1,050,028

Acronym: PDYPP– personal disposable income per capita.

Table O-5. National Willingness to Pay-Based RCC Benefits, Final Rule (PFOA and PFOS MCLs of 4.0 ppt each, PFHxS, PFNA, HFPO-DA, of 10 ppt each and HI of 1)

Benefits Category	2% Discount Rate		
	5th Percentile[a]	Expected Value	95th Percentile[a]
Number of Non-Fatal RCC Cases Avoided	1,091.50	6,964.20	17,937.00
Number of RCC-Related Deaths Avoided	320.36	2,028.80	5,206.50
Total Annualized RCC Benefits (Million $2022)[b]	**$62.07**	**$360.97**	**$901.91**

Notes: Detail may not add exactly to total due to independent rounding. See Appendix P for results presented at 3 and 7 percent discount rates.

[a]The 5th and 95th percentile range is based on modeled variability and uncertainty. This range does not include the uncertainty described in Table 6-48.

[b]See Table 7-6 for a list of the nonquantifiable benefits, and the potential direction of impact these benefits would have on the estimated monetized total annualized benefits in this table.

Table O-6. National Willingness to Pay-Based Bladder Cancer Benefits, Final Rule (PFOA and PFOS MCLs of 4.0 ppt each, PFHxS, PFNA, HFPO-DA of 10 ppt each and HI of 1)

Benefits Category	2% Discount Rate		
	5th Percentile[a]	Expected Value	95th Percentile[a]
Number of Non-Fatal Bladder Cancer Cases Avoided	5,781.00	7,313.00	8,912.70
Number of Bladder Cancer-Related Deaths Avoided	2,029.60	2,567.80	3,129.90
Total Annualized Bladder Cancer Benefits (Million $2022)[b]	**$360.61**	**$456.28**	**$556.21**

Notes: Detail may not add exactly to total due to independent rounding. See Appendix P for results presented at 3 and 7 percent discount rates.

[a]The 5th and 95th percentile range is based on modeled variability and uncertainty. This range does not include the uncertainty described in Table 6-48.

[b]See Table 7-6 for a list of the nonquantifiable benefits, and the potential direction of impact these benefits would have on the estimated monetized total annualized benefits in this table.

Appendix P. Additional Model Outputs

In the tables below, the EPA reports additional costs and benefits model outputs. Sections P.1 through P.7 report results at 3 percent and 7 percent discount rates. The EA for the proposed PFAS NPDWR presented costs and benefits consistent with the OMB Circular A-4 guidance at the time of proposal. OMB guidance at the time of proposal indicated that the 3 percent discount rate reflects society's valuation of differences in the timing of consumption; the 7 percent discount rate reflects the opportunity cost of capital to society. In the 2003 Circular A-4, the OMB recommended that 3 percent be used when a regulation affects private consumption, and 7 percent be used when evaluating a regulation that would mainly displace or alter the use of capital in the private sector (OMB, 2003; updated 2009). In this appendix, the EPA presents costs and benefits at both 3 and 7 percent discount rates to allow for a direct comparison for the final quantified cost and benefits to the quantified costs and benefits presented for the proposed rule. The EPA notes that given the updated default social discount rate of 2 percent prescribed in the finalized OMB Circular A-4 (OMB, 2023) and also public input received on the discount rates considered by the EPA in the proposed NPDWR, for this final rule, the EPA estimated national benefits and costs at the 2 percent discount rate for the final rule and incorporated those results into the final economic analysis. The Administrator reaffirms his determination that the benefits of the rule justify the costs. The EPA's determination is based on its analysis under in SDWA Section 1412(b)(3)(C) of the quantifiable benefits and costs at the 2 percent discount rate, in addition to at the 3 and 7 percent discount rate, as well as the nonquantifiable benefits and costs. The EPA found that significant nonquantifiable benefits are likely to occur from the final PFAS NPDWR.

Section P.8 presents undiscounted benefits and costs.

P.1 Total Estimated Benefits and Costs

Table P-1: Quantified Total National Annualized Benefits, All Options (Million $2022)

Option	3% Discount Rate[a]			7% Discount Rate[a]		
	5th Percentile[b]	Expected Value	95th Percentile[b]	5th Percentile[b]	Expected Value	95th Percentile[b]
Final rule[c]	$821.07	$1,393.56	$2,053.30	$536.67	$916.49	$1,328.90
Option 1a[d]	$815.03	$1,387.48	$2,043.00	$534.22	$912.35	$1,321.70
Option 1b[e]	$688.91	$1,167.15	$1,722.70	$450.77	$769.28	$1,117.10
Option 1c[f]	$356.37	$598.63	$872.69	$233.73	$396.05	$572.67

Notes: Detail may not add exactly to total due to independent rounding. Quantified total national annualized benefits do not include quantified sensitivity analysis results for PFNA effects on birth weight and PFOS effects on liver cancer, and as such, the quantified total national annualized benefits may be underestimated. See appendices K and O for PFNA birth weight and PFOS liver cancer sensitivity analysis results, respectively.

[a]See Table 7-6 for a list of the nonquantifiable benefits, and the potential direction of impact these benefits would have on the estimated monetized total annualized benefits in this table.

[b]The 5th and 95th percentile range is based on modeled variability and uncertainty described in Section 6.1.2 and Table 6-1 for benefits. This range does not include the uncertainty described in 6-48 for benefits.

[c]The final rule sets PFOA and PFOS MCLs of 4.0 ppt each, an HI of 1, and MCLs for HFPO-DA, PFNA, and PFHxS of 10 ppt each.

[d]Option 1a sets PFOA and PFOS MCLs only, at 4.0 ppt each.

[e]Option 1b sets PFOA and PFOS MCLs only, at 5.0 ppt each.

[f]Option 1c sets PFOA and PFOS MCLs only, at 10.0 ppt each.

Table P-2: Quantified Total National Annualized Costs, All Options (Million $2022)

Option	3% Discount Rate[a,b]			7% Discount Rate[a,b]		
	5th Percentile[c]	Mean	95th Percentile[c]	5th Percentile[c]	Mean	95th Percentile[c]
Final rule[d,e]	$1,431.50	$1,545.61	$1,670.10	$1,437.00	$1,553.98	$1,688.00
Option 1a[f]	$1,420.30	$1,534.03	$1,658.20	$1,425.50	$1,542.57	$1,676.70
Option 1b[g]	$1,100.10	$1,189.99	$1,290.30	$1,103.90	$1,197.32	$1,304.10
Option 1c[h]	$461.72	$498.64	$540.36	$464.77	$503.02	$547.76

Notes: Detail may not add exactly to total due to independent rounding.
[a]See Table 7-6 for a list of the nonquantifiable costs, and the potential direction of impact these costs would have on the estimated monetized total annualized costs in this table.
[b]PFAS-contaminated wastes are not considered RCRA regulatory or characteristic hazardous wastes at this time and therefore total costs reported in this table do not include costs associated with hazardous waste disposal of spent filtration materials. To address stakeholder concerns about potential costs for disposing PFAS-contaminated wastes as hazardous should they be regulated as such in the future, the EPA conducted a sensitivity analysis with an assumption of hazardous waste disposal for illustrative purposes only. See Appendix N and Section N.2 for additional detail.
[c]The 5th and 95th percentile range is based on modeled variability and uncertainty described in Section 5.1.2 and Table 5-1 for costs. This range does not include the uncertainty described in Table 5-22 for costs.
[d]Quantified national costs do not include quantified sensitivity analysis results for PFNA, PFBS, and HFPO-DA. Including the costs of treating for these compounds increases total annualized cost of the final rule to $1,630.46 million at a 3 percent discount rate and $1,634.56 million at a 7 percent discount rate. These benefits and costs are considered quantitatively in the sensitivity analysis. See Section N.3for more information.
[e]The final rule sets PFOA and PFOS MCLs of 4.0 ppt each, an HI of 1 and MCLs for HFPO-DA, PFNA, and PFHxS of 10 ppt each.
[f]Option 1a sets PFOA and PFOS MCLs of 4.0 ppt each.
[g]Option 1b sets PFOA and PFOS MCLs of 5.0 ppt each.
[h]Option 1c sets PFOA and PFOS MCLs of 10.0 ppt each.

P.2 National Annualized Costs

Table P-3: National Annualized Costs, Final Rule (PFOA and PFOS MCLs of 4.0 ppt each, PFHxS, PFNA, HFPO-DA MCLs of 10 ppt each and HI of 1) (Million $2022)

	3% Discount Rate			7% Discount Rate		
	5th Percentile[a]	Expected Value	95th Percentile[a]	5th Percentile[a]	Expected Value	95th Percentile[a]
Annualized PWS Sampling Costs	$34.45	$37.14	$40.06	$37.71	$40.80	$44.13
Annualized PWS Implementation and Administration Costs	$1.72	$1.72	$1.72	$3.41	$3.41	$3.41
Annualized PWS Treatment Costs	$1,391.16	$1,501.68	$1,624.89	$1,388.69	$1,503.01	$1,634.84
Total Annualized PWS Costs	**$1,426.60**	**$1,540.54**	**$1,665.10**	**$1,431.30**	**$1,547.22**	**$1,680.60**
Primacy Agency Rule Implementation and Administration Cost	$4.73	$5.07	$5.45	$6.26	$6.76	$7.32
Total Annualized Rule Costs[b,c,d]	**$1,431.50**	**$1,545.61**	**$1,670.10**	**$1,437.00**	**$1,553.98**	**$1,688.00**

Abbreviations: PWS – public water system.

Notes: Detail may not add exactly to total due to independent rounding. 5th and 95th percentile values for total rule costs are not additive across cost category as the categories are not completely correlated.

[a]The 5th and 95th percentile range is based on modeled variability and uncertainty described in Section 5.1.2 and Table 5-1. This range does not include the uncertainty described in 5-22.

[b]See Table 7-6 for a list of the nonquantifiable costs, and the potential direction of impact these costs would have on the estimated monetized total annualized costs in this table.

[c]The national level cost estimates for PFHxS are reflective of both the total national cost for PFHxS individual MCL exceedances, and HI MCL exceedances where PFHxS is present above its HBWC while one or more other HI PFAS is also present in that same mixture. Total quantified national cost values do not include the incremental treatment costs associated with the co-occurrence of HFPO-DA, PFBS, and PFNA. EPA has considered the additional national costs of the HI and individual MCLs associated with HFPO-DA, PFNA, and PFBS occurrence in a quantified sensitivity analysis; See Appendix N and Section N.3 for the analysis and more information..

[d]PFAS-contaminated wastes are not considered RCRA regulatory or characteristic hazardous wastes at this time and therefore total costs reported in this table do not include costs associated with hazardous waste disposal of spent filtration materials. To address stakeholder concerns about potential costs for disposing PFAS-contaminated wastes as hazardous should they be regulated as such in the future, the EPA conducted a sensitivity analysis with an assumption of hazardous waste disposal for illustrative purposes only. See Appendix N and Section N.2 for additional detail.

Table P-4: National Annualized Costs, Option 1a (PFOA and PFOS MCLs of 4.0 ppt) (Million $2022)

	3% Discount Rate			7% Discount Rate		
	5th Percentile[a]	Expected Value	95th Percentile[a]	5th Percentile[a]	Expected Value	95th Percentile[a]
Annualized PWS Sampling Costs	$34.17	$36.88	$39.80	$37.42	$40.51	$43.84
Annualized PWS Implementation and Administration Costs	$1.72	$1.72	$1.72	$3.41	$3.41	$3.41
Annualized PWS Treatment Costs	$1,379.26	$1,490.37	$1,612.89	$1,377.38	$1,491.91	$1,623.54
Total Annualized PWS Costs	**$1,415.40**	**$1,528.98**	**$1,653.10**	**$1,419.30**	**$1,535.83**	**$1,669.60**
Primacy Agency Rule Implementation and Administration Cost	$4.71	$5.05	$5.42	$6.24	$6.73	$7.29
Total Annualized Rule Costs[b,c]	**$1,420.30**	**$1,534.03**	**$1,658.20**	**$1,425.50**	**$1,542.57**	**$1,676.70**

Abbreviations: PWS – public water system.

Notes: Detail may not add exactly to total due to independent rounding. 5th and 95th percentile values for total rule costs are not additive across cost category as the categories are not completely correlated.

[a]The 5th and 95th percentile range is based on modeled variability and uncertainty described in Section 5.1.2 and Table 5-1. This range does not include the uncertainty described in Table 5-22.

[b]See Table 7-6 for a list of the nonquantifiable costs, and the potential direction of impact these costs would have on the estimated monetized total annualized costs in this table.

[c]PFAS-contaminated wastes are not considered RCRA regulatory or characteristic hazardous wastes at this time and therefore total costs reported in this table do not include costs associated with hazardous waste disposal of spent filtration materials. To address stakeholder concerns about potential costs for disposing PFAS-contaminated wastes as hazardous should they be regulated as such in the future, the EPA conducted a sensitivity analysis with an assumption of hazardous waste disposal for illustrative purposes only. See Appendix N and Section N.2 for additional detail.

Table P-5: National Annualized Costs, Option 1b (PFOA and PFOS MCLs of 5.0 ppt) (Million $2022)

	3% Discount Rate			7% Discount Rate		
	5th Percentile[a]	Expected Value	95th Percentile[a]	5th Percentile[a]	Expected Value	95th Percentile[a]
Annualized PWS Sampling Costs	$31.75	$34.07	$36.60	$34.62	$37.25	$40.15
Annualized PWS Implementation and Administration Costs	$1.72	$1.72	$1.72	$3.41	$3.41	$3.41
Annualized PWS Treatment Costs	$1,061.02	$1,149.63	$1,248.65	$1,059.22	$1,150.64	$1,254.96
Total Annualized PWS Costs	**$1,095.90**	**$1,185.42**	**$1,285.60**	**$1,098.40**	**$1,191.30**	**$1,298.00**
Primacy Agency Rule Implementation and Administration Cost	$4.31	$4.57	$4.87	$5.63	$6.02	$6.46
Total Annualized Rule Costs[b,c]	**$1,100.10**	**$1,189.99**	**$1,290.30**	**$1,103.90**	**$1,197.32**	**$1,304.10**

Abbreviations: PWS – public water system.

Notes: Detail may not add exactly to total due to independent rounding. 5th and 95th percentile values for total rule costs are not additive across cost category as the categories are not completely correlated.

[a]The 5th and 95th percentile range is based on modeled variability and uncertainty described in Section 5.1.2 and Table 5-1. This range does not include the uncertainty described in Table 5-22.

[b]See Table 7-6 for a list of the nonquantifiable costs, and the potential direction of impact these costs would have on the estimated monetized total annualized costs in this table.

[c]PFAS-contaminated wastes are not considered RCRA regulatory or characteristic hazardous wastes at this time and therefore total costs reported in this table do not include costs associated with hazardous waste disposal of spent filtration materials. To address stakeholder concerns about potential costs for disposing PFAS-contaminated wastes as hazardous should they be regulated as such in the future, the EPA conducted a sensitivity analysis with an assumption of hazardous waste disposal for illustrative purposes only. See Appendix N and Section N.2 for additional detail.

Table P-6: National Annualized Costs, Option 1c (PFOA and PFOS MCLs of 10.0 ppt) (Million $2022)

	3% Discount Rate			7% Discount Rate		
	5th Percentile[a]	**Expected Value**	**95th Percentile[a]**	**5th Percentile[a]**	**Expected Value**	**95th Percentile[a]**
Annualized PWS Sampling Costs	$26.57	$27.99	$29.53	$28.62	$30.22	$31.96
Annualized PWS Implementation and Administration Costs	$1.72	$1.72	$1.72	$3.41	$3.41	$3.41
Annualized PWS Treatment Costs	$429.35	$465.33	$506.21	$427.86	$464.79	$508.64
Total Annualized PWS Costs	**$458.15**	**$495.04**	**$536.59**	**$460.46**	**$498.42**	**$543.00**
Primacy Agency Rule Implementation and Administration Cost	$3.50	$3.60	$3.73	$4.46	$4.61	$4.79
Total Annualized Rule Costs[b,c]	**$461.72**	**$498.64**	**$540.36**	**$464.77**	**$503.02**	**$547.76**

Abbreviations: PWS – public water system.

Notes: Detail may not add exactly to total due to independent rounding. 5th and 95th percentile values for total rule costs are not additive across cost category as the categories are not completely correlated.

[a]The 5th and 95th percentile range is based on modeled variability and uncertainty described in Section 5.1.2 and Table 5-1. This range does not include the uncertainty described in Table 5-22.

[b]See Table 7-6 for a list of the nonquantifiable costs, and the potential direction of impact these costs would have on the estimated monetized total annualized costs in this table.

[c]PFAS-contaminated wastes are not considered RCRA regulatory or characteristic hazardous wastes at this time and therefore total costs reported in this table do not include costs associated with hazardous waste disposal of spent filtration materials. To address stakeholder concerns about potential costs for disposing PFAS-contaminated wastes as hazardous should they be regulated as such in the future, the EPA conducted a sensitivity analysis with an assumption of hazardous waste disposal for illustrative purposes only. See Appendix N and Section N.2 for additional detail.

P.3 National Annualized Benefits

Table P-7: National Annualized Benefits, Final Rule (PFOA and PFOS MCLs of 4.0 ppt each, PFHxS, PFNA, HFPO-DA MCLs of 10 ppt each and HI of 1) (Million $2022)

	3% Discount Rate			7% Discount Rate		
	5th Percentile[a]	Expected Value	95th Percentile[a]	5th Percentile[a]	Expected Value	95th Percentile[a]
Annualized CVD Benefits	$129.38	$557.78	$984.00	$89.33	$392.35	$691.87
Annualized Birth Weight Benefits	$114.45	$191.42	$268.19	$80.26	$134.65	$188.51
Annualized RCC Benefits	$58.61	$317.71	$777.42	$44.40	$206.04	$469.78
Annualized Bladder Cancer Benefits	$258.13	$326.65	$398.24	$144.92	$183.45	$223.73
Total Annualized Rule Benefits[b]	**$821.07**	**$1,393.56**	**$2,053.30**	**$536.67**	**$916.49**	**$1,328.90**

Abbreviations: CVD – cardiovascular disease; RCC – renal cell carcinoma.
Note: Detail may not add exactly to total due to independent rounding. 5th and 95th percentile values for total rule benefits are not additive across benefit category as the categories are not completely correlated. Quantifiable benefits are increased under final rule table results relative to the other options presented because of modeled PFHxS occurrence, which results in additional benefits from co-removed PFOA and PFOS.
[a]The 5th and 95th percentile range is based on modeled variability and uncertainty. This range does not include the uncertainty described in Table 6-48.
[b]See Table 7-6 for a list of the nonquantifiable benefits, and the potential direction of impact these benefits would have on the estimated monetized total annualized benefits in this table.

Table P-8: National Annualized Benefits, Option 1a (PFOA and PFOS MCLs of 4.0 ppt) (Million $2022)

	3% Discount Rate			7% Discount Rate		
	5th Percentile[a]	Expected Value	95th Percentile[a]	5th Percentile[a]	Expected Value	95th Percentile[a]
Annualized CVD Benefits	$128.88	$554.68	$979.99	$88.85	$390.18	$688.72
Annualized Birth Weight Benefits	$113.38	$190.33	$266.56	$80.00	$133.89	$187.59
Annualized RCC Benefits	$58.40	$315.82	$771.62	$44.19	$204.83	$466.90
Annualized Bladder Cancer Benefits	$258.48	$326.65	$397.24	$145.11	$183.45	$223.24
Total Annualized Rule Benefits[b]	**$815.03**	**$1,387.48**	**$2,043.00**	**$534.22**	**$912.35**	**$1,321.70**

Abbreviations: CVD – cardiovascular disease; RCC – renal cell carcinoma.
Note: Detail may not add exactly to total due to independent rounding. 5th and 95th percentile values for total rule benefits are not additive across benefit category as the categories are not completely correlated.
[a]The 5th and 95th percentile range is based on modeled variability and uncertainty. This range does not include the uncertainty described in Table 6-48.
[b]See Table 7-6 for a list of the nonquantifiable benefits, and the potential direction of impact these benefits would have on the estimated monetized total annualized benefits in this table.

Table P-9: National Annualized Benefits, Option 1b (PFOA and PFOS MCLs of 5.0 ppt) (Million $2022)

	3% Discount Rate			7% Discount Rate		
	5th Percentile[a]	Expected Value	95th Percentile[a]	5th Percentile[a]	Expected Value	95th Percentile[a]
Annualized CVD Benefits	$109.42	$472.36	$828.37	$76.25	$332.29	$583.00
Annualized Birth Weight Benefits	$98.27	$163.90	$229.43	$68.86	$115.27	$161.46
Annualized RCC Benefits	$46.81	$261.37	$645.73	$36.03	$170.35	$391.04
Annualized Bladder Cancer Benefits	$211.62	$269.52	$329.18	$118.81	$151.37	$184.69
Total Annualized Rule Benefits[b]	**$688.91**	**$1,167.15**	**$1,722.70**	**$450.77**	**$769.28**	**$1,117.10**

Abbreviations: CVD – cardiovascular disease; RCC – renal cell carcinoma.
Note: Detail may not add exactly to total due to independent rounding. 5th and 95th percentile values for total rule benefits are not additive across benefit category as the categories are not completely correlated.
[a]The 5th and 95th percentile range is based on modeled variability and uncertainty. This range does not include the uncertainty described in Table 6-48.
[b]See Table 7-6 for a list of the nonquantifiable benefits, and the potential direction of impact these benefits would have on the estimated monetized total annualized benefits in this table.

Table P-10: National Annualized Benefits, Option 1c (PFOA and PFOS MCLs of 10.0 ppt) (Million $2022)

	3% Discount Rate			7% Discount Rate		
	5th Percentile[a]	Expected Value	95th Percentile[a]	5th Percentile[a]	Expected Value	95th Percentile[a]
Annualized CVD Benefits	$61.50	$246.21	$431.85	$42.83	$173.14	$302.88
Annualized Birth Weight Benefits	$55.10	$90.63	$126.17	$38.59	$63.70	$88.71
Annualized RCC Benefits	$20.71	$123.87	$310.93	$16.70	$81.75	$189.76
Annualized Bladder Cancer Benefits	$103.85	$137.92	$173.58	$58.35	$77.46	$97.51
Total Annualized Rule Benefits[b]	**$356.37**	**$598.63**	**$872.69**	**$233.73**	**$396.05**	**$572.67**

Abbreviations: CVD – cardiovascular disease; RCC – renal cell carcinoma.
Note: Detail may not add exactly to total due to independent rounding. 5th and 95th percentile values for total rule benefits are not additive across benefit category as the categories are not completely correlated.
[a]The 5th and 95th percentile range is based on modeled variability and uncertainty. This range does not include the uncertainty described in Table 6-48.
[b]See Table 7-6 for a list of the nonquantifiable benefits, and the potential direction of impact these benefits would have on the estimated monetized total annualized benefits in this table.

P.3.1 National Birth Weight Benefits

Table P-11: National Birth Weight Benefits, Final Rule (PFOA and PFOS MCLs of 4.0 ppt each, PFHxS, PFNA, HFPO-DA MCLs of 10 ppt each and HI of 1)

Benefits Category	3% Discount Rate			7% Discount Rate		
	5th Percentile[a]	Expected Value	95th Percentile[a]	5th Percentile[a]	Expected Value	95th Percentile[a]
Increase in Birth Weight (millions of grams)	129.6	216.8	304.1	129.6	216.8	304.1
Number of Birth Weight-Related Deaths Avoided	781.9	1,301.7	1,823.6	781.9	1,301.7	1,823.6
Total Annualized Birth Weight Benefits (Million $2022)[b]	**$114.45**	**$191.42**	**$268.19**	**$80.26**	**$134.65**	**$188.51**

Note: Detail may not add exactly to total due to independent rounding.
[a]The 5th and 95th percentile range is based on modeled variability and uncertainty. This range does not include the uncertainty described in Table 6-48.
[b]See Table 7-6 for a list of the nonquantifiable benefits, and the potential direction of impact these benefits would have on the estimated monetized total annualized benefits in this table.

Table P-12: National Birth Weight Benefits, Option 1a (PFOA and PFOS MCLs of 4.0 ppt)

Benefits Category	3% Discount Rate			7% Discount Rate		
	5th Percentile[a]	Expected Value	95th Percentile[a]	5th Percentile[a]	Expected Value	95th Percentile[a]
Increase in Birth Weight (millions of grams)	128.8	215.6	302.1	128.8	215.6	302.1
Number of Birth Weight-Related Deaths Avoided	777.4	1,294.4	1,812.9	777.4	1,294.4	1,812.9
Total Annualized Birth Weight Benefits (Million $2022)[b]	**$113.38**	**$190.33**	**$266.56**	**$80.00**	**$133.89**	**$187.59**

Note: Detail may not add exactly to total due to independent rounding.
[a]The 5th and 95th percentile range is based on modeled variability and uncertainty. This range does not include the uncertainty described in Table 6-48.
[b]See Table 7-6 for a list of the nonquantifiable benefits, and the potential direction of impact these benefits would have on the estimated monetized total annualized benefits in this table.

Table P-13: National Birth Weight Benefits, Option 1b (PFOA and PFOS MCLs of 5.0 ppt)

Benefits Category	3% Discount Rate			7% Discount Rate		
	5th Percentile[a]	Expected Value	95th Percentile[a]	5th Percentile[a]	Expected Value	95th Percentile[a]
Increase in Birth Weight (millions of grams)	111.3	185.6	260.3	111.3	185.6	260.3
Number of Birth Weight-Related Deaths Avoided	668.9	1,114.7	1,561.2	668.9	1,114.7	1,561.2
Total Annualized Birth Weight Benefits (Million $2022)[b]	**$98.27**	**$163.90**	**$229.43**	**$68.86**	**$115.27**	**$161.46**

Note: Detail may not add exactly to total due to independent rounding.
[a]The 5th and 95th percentile range is based on modeled variability and uncertainty. This range does not include the uncertainty described in Table 6-48.
[b]See Table 7-6 for a list of the nonquantifiable benefits, and the potential direction of impact these benefits would have on the estimated monetized total annualized benefits in this table.

Table P-14: National Birth Weight Benefits, Option 1c (PFOA and PFOS MCLs of 10.0 ppt)

Benefits Category	3% Discount Rate			7% Discount Rate		
	5th Percentile[a]	Expected Value	95th Percentile[a]	5th Percentile[a]	Expected Value	95th Percentile[a]
Increase in Birth Weight (millions of grams)	62.1	102.0	142.4	62.1	102.0	142.4
Number of Birth Weight-Related Deaths Avoided	375.8	616.6	859.1	375.8	616.6	859.1
Total Annualized Birth Weight Benefits (Million $2022)[b]	**$55.10**	**$90.63**	**$126.17**	**$38.59**	**$63.70**	**$88.71**

Note: Detail may not add exactly to total due to independent rounding.
[a]The 5th and 95th percentile range is based on modeled variability and uncertainty. This range does not include the uncertainty described in Table 6-48.
[b]See Table 7-6 for a list of the nonquantifiable benefits, and the potential direction of impact these benefits would have on the estimated monetized total annualized benefits in this table.

P.3.2 National CVD Benefits

Table P-15: National CVD Benefits, Final Rule (PFOA and PFOS MCLs of 4.0 ppt each, PFHxS, PFNA, HFPO-DA MCLs of 10 ppt each and HI of 1)

Benefits Category	3% Discount Rate			7% Discount Rate		
	5th Percentile[a]	Expected Value	95th Percentile[a]	5th Percentile[a]	Expected Value	95th Percentile[a]
Number of Non-Fatal MI Cases Avoided	1,407.7	6,333.1	11,189.0	1,407.7	6,333.1	11,189.0
Number of Non-Fatal IS Cases Avoided	2,074.8	9,247.6	16,279.0	2,074.8	9,247.6	16,279.0
Number of CVD Deaths Avoided	845.5	3,715.8	6,555.6	845.5	3,715.8	6,555.6
Total Annualized CVD Benefits (Million $2022)[b]	**$129.38**	**$557.78**	**$984.00**	**$89.33**	**$392.35**	**$691.87**

Abbreviations: CVD – cardiovascular disease, MI – myocardial infarction, IS – Ischemic Stroke.
Notes: Detail may not add exactly to total due to independent rounding.
[a]The 5th and 95th percentile range is based on modeled variability and uncertainty. This range does not include the uncertainty described in Table 6-48.
[b]See Table 7-6 for a list of the nonquantifiable benefits, and the potential direction of impact these benefits would have on the estimated monetized total annualized benefits in this table.

Table P-16: National CVD Benefits, Option 1a (PFOA and PFOS MCLs of 4.0 ppt)

Benefits Category	3% Discount Rate			7% Discount Rate		
	5th Percentile[a]	Expected Value	95th Percentile[a]	5th Percentile[a]	Expected Value	95th Percentile[a]
Number of Non-Fatal MI Cases Avoided	1,400.8	6,296.0	11,115.0	1,400.8	6,296.0	11,115.0
Number of Non-Fatal IS Cases Avoided	2,065.0	9,194.8	16,203.0	2,065.0	9,194.8	16,203.0
Number of CVD Deaths Avoided	839.9	3,695.1	6,484.4	839.9	3,695.1	6,484.4
Total Annualized CVD Benefits (Million $2022)[b]	**$128.88**	**$554.68**	**$979.99**	**$88.85**	**$390.18**	**$688.72**

Abbreviations: CVD – cardiovascular disease, MI – myocardial infarction, IS – Ischemic Stroke.
Notes: Detail may not add exactly to total due to independent rounding.
[a]The 5th and 95th percentile range is based on modeled variability and uncertainty. This range does not include the uncertainty described in Table 6-48.
[b]See Table 7-6 for a list of the nonquantifiable benefits, and the potential direction of impact these benefits would have on the estimated monetized total annualized benefits in this table.

Table P-17: National CVD Benefits, Option 1b (PFOA and PFOS MCLs of 5.0 ppt)

Benefits Category	3% Discount Rate			7% Discount Rate		
	5th Percentile[a]	Expected Value	95th Percentile[a]	5th Percentile[a]	Expected Value	95th Percentile[a]
Number of Non-Fatal MI Cases Avoided	1,209.2	5,352.0	9,417.5	1,209.2	5,352.0	9,417.5
Number of Non-Fatal IS Cases Avoided	1,778.3	7,826.9	13,778.0	1,778.3	7,826.9	13,778.0
Number of CVD Deaths Avoided	733.1	3,146.8	5,518.0	733.1	3,146.8	5,518.0
Total Annualized CVD Benefits (Million $2022)[b]	**$109.42**	**$472.36**	**$828.37**	**$76.25**	**$332.29**	**$583.00**

Abbreviations: CVD – cardiovascular disease, MI – myocardial infarction, IS – Ischemic Stroke.
Notes: Detail may not add exactly to total due to independent rounding.
[a]The 5th and 95th percentile range is based on modeled variability and uncertainty. This range does not include the uncertainty described in Table 6-48.
[b]See Table 7-6 for a list of the nonquantifiable costs, and the potential direction of impact these costs would have on the estimated monetized total annualized costs in this table.

Table P-18: National CVD Benefits, Option 1c (PFOA and PFOS MCLs of 10.0 ppt)

Benefits Category	3% Discount Rate			7% Discount Rate		
	5th Percentile[a]	Expected Value	95th Percentile[a]	5th Percentile[a]	Expected Value	95th Percentile[a]
Number of Non-Fatal MI Cases Avoided	673.7	2,776.5	4,872.8	673.7	2,776.5	4,872.8
Number of Non-Fatal IS Cases Avoided	987.0	4,079.2	7,145.6	987.0	4,079.2	7,145.6
Number of CVD Deaths Avoided	411.6	1,640.9	2,878.1	411.6	1,640.9	2,878.1
Total Annualized CVD Benefits (Million $2022)[b]	**$61.50**	**$246.21**	**$431.85**	**$42.83**	**$173.14**	**$302.88**

Abbreviations: CVD – cardiovascular disease, MI – myocardial infarction, IS – Ischemic Stroke.
Notes: Detail may not add exactly to total due to independent rounding.
[a]The 5th and 95th percentile range is based on modeled variability and uncertainty. This range does not include the uncertainty described in Table 6-48.
[b]See Table 7-6 for a list of the nonquantifiable benefits, and the potential direction of impact these benefits would have on the estimated monetized total annualized benefits in this table.

P.3.3 National RCC Benefits

Table P-19: National RCC Benefits, Final Rule (PFOA and PFOS MCLs of 4.0 ppt each, PFHxS, PFNA, HFPO-DA MCLs of 10 ppt each and HI of 1)

Benefits Category	3% Discount Rate			7% Discount Rate		
	5th Percentile[a]	Expected Value	95th Percentile[a]	5th Percentile[a]	Expected Value	95th Percentile[a]
Number of Non-Fatal RCC Cases Avoided	1,091.5	6,964.2	17,937.0	1,091.5	6,964.2	17,937.0
Number of RCC-Related Deaths Avoided	320.4	2,028.8	5,206.5	320.4	2,028.8	5,206.5
Total Annualized RCC Benefits (Million $2022)[b,c]	**$58.61**	**$317.71**	**$777.42**	**$44.40**	**$206.04**	**$469.78**

Abbreviations: RCC – renal cell carcinoma.
Notes: Detail may not add exactly to total due to independent rounding.
[a]The 5th and 95th percentile range is based on modeled variability and uncertainty. This range does not include the uncertainty described in Table 6-48.
[b]See Table 7-6 for a list of the nonquantifiable benefits, and the potential direction of impact these benefits would have on the estimated monetized total annualized benefits in this table.
[c]When using willingness to pay metrics to monetize morbidity benefits, total annualized RCC benefits are increased by $5.7 million at a 3 percent discount rate and by $2.6 million at a 7 percent discount rate (see Appendix O).

Table P-20: National RCC Benefits, Option 1a (PFOA and PFOS MCLs of 4.0 ppt)

Benefits Category	3% Discount Rate			7% Discount Rate		
	5th Percentile[a]	Expected Value	95th Percentile[a]	5th Percentile[a]	Expected Value	95th Percentile[a]
Number of Non-Fatal RCC Cases Avoided	1,082.0	6,922.4	17,870.0	1,082.0	6,922.4	17,870.0
Number of RCC-Related Deaths Avoided	319.1	2,016.7	5,190.9	319.1	2,016.7	5,190.9
Total Annualized RCC Benefits (Million $2022)[b]	**$58.40**	**$315.82**	**$771.62**	**$44.19**	**$204.83**	**$466.90**

Abbreviations: RCC – renal cell carcinoma.
Notes: Detail may not add exactly to total due to independent rounding.
[a]The 5th and 95th percentile range is based on modeled variability and uncertainty. This range does not include the uncertainty described in Table 6-48.
[b]See Table 7-6 for a list of the nonquantifiable benefits, and the potential direction of impact these benefits would have on the estimated monetized total annualized benefits in this table.

Table P-21: National RCC Benefits, Option 1b (PFOA and PFOS MCLs of 5.0 ppt)

Benefits Category	3% Discount Rate			7% Discount Rate		
	5th Percentile[a]	Expected Value	95th Percentile[a]	5th Percentile[a]	Expected Value	95th Percentile[a]
Number of Non-Fatal RCC Cases Avoided	851.9	5,696.1	14,906.0	851.9	5,696.1	14,906.0
Number of RCC-Related Deaths Avoided	251.6	1,663.8	4,328.4	251.6	1,663.8	4,328.4
Total Annualized RCC Benefits (Million $2022)[b]	**$46.81**	**$261.37**	**$645.73**	**$36.03**	**$170.35**	**$391.04**

Abbreviations: RCC – renal cell carcinoma.
Notes: Detail may not add exactly to total due to independent rounding.
[a]The 5th and 95th percentile range is based on modeled variability and uncertainty. This range does not include the uncertainty described in Table 6-48.
[b]See Table 7-6 for a list of the nonquantifiable benefits, and the potential direction of impact these benefits would have on the estimated monetized total annualized benefits in this table.

Table P-22: National RCC Benefits, Option 1c (PFOA and PFOS MCLs of 10.0 ppt)

Benefits Category	3% Discount Rate			7% Discount Rate		
	5th Percentile[a]	Expected Value	95th Percentile[a]	5th Percentile[a]	Expected Value	95th Percentile[a]
Number of Non-Fatal RCC Cases Avoided	372.1	2,648.1	6,967.4	372.1	2,648.1	6,967.4
Number of RCC-Related Deaths Avoided	111.5	782.8	2,057.3	111.5	782.8	2,057.3
Total Annualized RCC Benefits (Million $2022)[b]	**$20.71**	**$123.87**	**$310.93**	**$16.70**	**$81.75**	**$189.76**

Abbreviations: RCC – renal cell carcinoma.
Notes: Detail may not add exactly to total due to independent rounding.
[a]The 5th and 95th percentile range is based on modeled variability and uncertainty. This range does not include the uncertainty described in Table 6-48.
[b]See Table 7-6 for a list of the nonquantifiable benefits, and the potential direction of impact these benefits would have on the estimated monetized total annualized benefits in this table.

P.3.4 National Bladder Cancer Benefits

Table P-23: National Bladder Cancer Benefits, Final Rule (PFOA and PFOS MCLs of 4.0 ppt each, PFHxS, PFNA, HFPO-DA MCLs of 10 ppt each and HI of 1)

Benefits Category	3% Discount Rate			7% Discount Rate		
	5th Percentile[a]	Expected Value	95th Percentile[a]	5th Percentile[a]	Expected Value	95th Percentile[a]
Number of Non-Fatal Bladder Cancer Cases Avoided	5,781.0	7,313.0	8,912.7	5,781.0	7,313.0	8,912.7
Number of Bladder Cancer-Related Deaths Avoided	2,029.6	2,567.8	3,129.9	2,029.6	2,567.8	3,129.9
Total Annualized Bladder Cancer Benefits (Million $2022)[b,c]	**$258.13**	**$326.65**	**$398.24**	**$144.92**	**$183.45**	**$223.73**

Notes:
[a]The 5th and 95th percentile range is based on modeled variability and uncertainty. This range does not include the uncertainty described in Table 6-48.
[b]See Table 7-6 for a list of the nonquantifiable benefits, and the potential direction of impact these benefits would have on the estimated monetized total annualized benefits in this table.
[c]When using willingness to pay metrics to monetize morbidity benefits, total annualized bladder cancer benefits are increased by $65.7 million at a 3 percent discount rate and by $38.6 million at a 7 percent discount rate (see Appendix O).

Table P-24: National Bladder Cancer Benefits, Option 1a (PFOA and PFOS MCLs of 4.0 ppt)

Benefits Category	3% Discount Rate			7% Discount Rate		
	5th Percentile[a]	Expected Value	95th Percentile[a]	5th Percentile[a]	Expected Value	95th Percentile[a]
Number of Non-Fatal Bladder Cancer Cases Avoided	5,789.3	7,312.9	8,896.0	5,789.3	7,312.9	8,896.0
Number of Bladder Cancer-Related Deaths Avoided	2,032.5	2,567.8	3,123.2	2,032.5	2,567.8	3,123.2
Total Annualized Bladder Cancer Benefits (Million $2022)[b]	**$258.48**	**$326.65**	**$397.24**	**$145.11**	**$183.45**	**$223.24**

Notes:
[a]The 5th and 95th percentile range is based on modeled variability and uncertainty. This range does not include the uncertainty described in Table 6-48.
[b]See Table 7-6 for a list of the nonquantifiable benefits, and the potential direction of impact these benefits would have on the estimated monetized total annualized benefits in this table.

Table P-25: National Bladder Cancer Benefits, Option 1b (PFOA and PFOS MCLs of 5.0 ppt)

Benefits Category	3% Discount Rate			7% Discount Rate		
	5th Percentile[a]	Expected Value	95th Percentile[a]	5th Percentile[a]	Expected Value	95th Percentile[a]
Number of Non-Fatal Bladder Cancer Cases Avoided	4,739.4	6,034.0	7,367.1	4,739.4	6,034.0	7,367.1
Number of Bladder Cancer-Related Deaths Avoided	1,664.0	2,118.7	2,587.1	1,664.0	2,118.7	2,587.1
Total Annualized Bladder Cancer Benefits (Million $2022)[b]	**$211.62**	**$269.52**	**$329.18**	**$118.81**	**$151.37**	**$184.69**

Notes:
[a]The 5th and 95th percentile range is based on modeled variability and uncertainty. This range does not include the uncertainty described in Table 6-48.
[b]See Table 7-6 for a list of the nonquantifiable benefits, and the potential direction of impact these benefits would have on the estimated monetized total annualized benefits in this table.

Table P-26: National Bladder Cancer Benefits, Option 1c (PFOA and PFOS MCLs of 10.0 ppt)

Benefits Category	3% Discount Rate			7% Discount Rate		
	5th Percentile[a]	Expected Value	95th Percentile[a]	5th Percentile[a]	Expected Value	95th Percentile[a]
Number of Non-Fatal Bladder Cancer Cases Avoided	2,326.9	3,087.9	3,885.3	2,326.9	3,087.9	3,885.3
Number of Bladder Cancer-Related Deaths Avoided	816.8	1,084.3	1,364.3	816.8	1,084.3	1,364.3
Total Annualized Bladder Cancer Benefits (Million $2022)[b]	**$103.85**	**$137.92**	**$173.58**	**$58.35**	**$77.46**	**$97.51**

Notes:
[a]The 5th and 95th percentile range is based on modeled variability and uncertainty. This range does not include the uncertainty described in Table 6-48.
[b]See Table 7-6 for a list of the nonquantifiable benefits, and the potential direction of impact these benefits would have on the estimated monetized total annualized costs in this table.

P.4 Comparison of Costs and Benefits

Table P-27: Annualized Quantified National Costs and Benefits, Final Rule (PFOA and PFOS MCLs of 4.0 ppt each, PFHxS, PFNA, HFPO-DA MCLs of 10 ppt each and HI of 1) (Million $2022)

	3% Discount Rate			7% Discount Rate		
	5th Percentile[a]	Mean	95th Percentile[a]	5th Percentile[a]	Mean	95th Percentile[a]
Total Annualized Rule Costs	$1,431.50	$1,545.61	$1,670.10	$1,437.00	$1,553.98	$1,688.00
Total Annualized Rule Benefits	$821.07	$1,393.56	$2,053.30	$536.67	$916.49	$1,328.90
Total Net Benefits[b,c,d]	**-$717.96**	**-$152.05**	**$494.34**	**-$1,022.20**	**-$637.49**	**-$224.87**

Notes: Detail may not add exactly to total due to independent rounding. Quantifiable benefits are increased under final rule table results relative to the other options presented because of modeled PFHxS occurrence, which results in additional benefits from co-removed PFOA and PFOS.

[a]The 5th and 95th percentile range is based on modeled variability and uncertainty described in Section 5.1.2 and Table 5-1 for costs and Section 6.1.2 and Table 6-1 for benefits. This range does not include the uncertainty described in 5-22 for costs and Table 6-48 for benefits.

[b]See Table 7-6 for a list of the nonquantifiable benefits and costs, and the potential direction of impact these benefits and costs would have on the estimated monetized total annualized benefits and costs in this table.

[c]The national level cost estimates for PFHxS are reflective of both the total national cost for PFHxS individual MCL exceedances, and HI MCL exceedances where PFHxS is present above its HBWC while one or more other HI PFAS is also present in that same mixture. Total quantified national cost values do not include the incremental treatment costs associated with the co-occurrence of HFPO-DA, PFBS, and PFNA. EPA has considered the additional national costs of the HI and individual MCLs associated with HFPO-DA, PFNA, and PFBS occurrence in a quantified sensitivity analysis; see Appendix N and Section N.3 for the analysis and more information.

[d]PFAS-contaminated wastes are not considered RCRA regulatory or characteristic hazardous wastes at this time and therefore total costs reported in this table do not include costs associated with hazardous waste disposal of spent filtration materials. To address stakeholder concerns about potential costs for disposing PFAS-contaminated wastes as hazardous should they be regulated as such in the future, the EPA conducted a sensitivity analysis with an assumption of hazardous waste disposal for illustrative purposes only. See Appendix N and Section N.2 for additional detail.

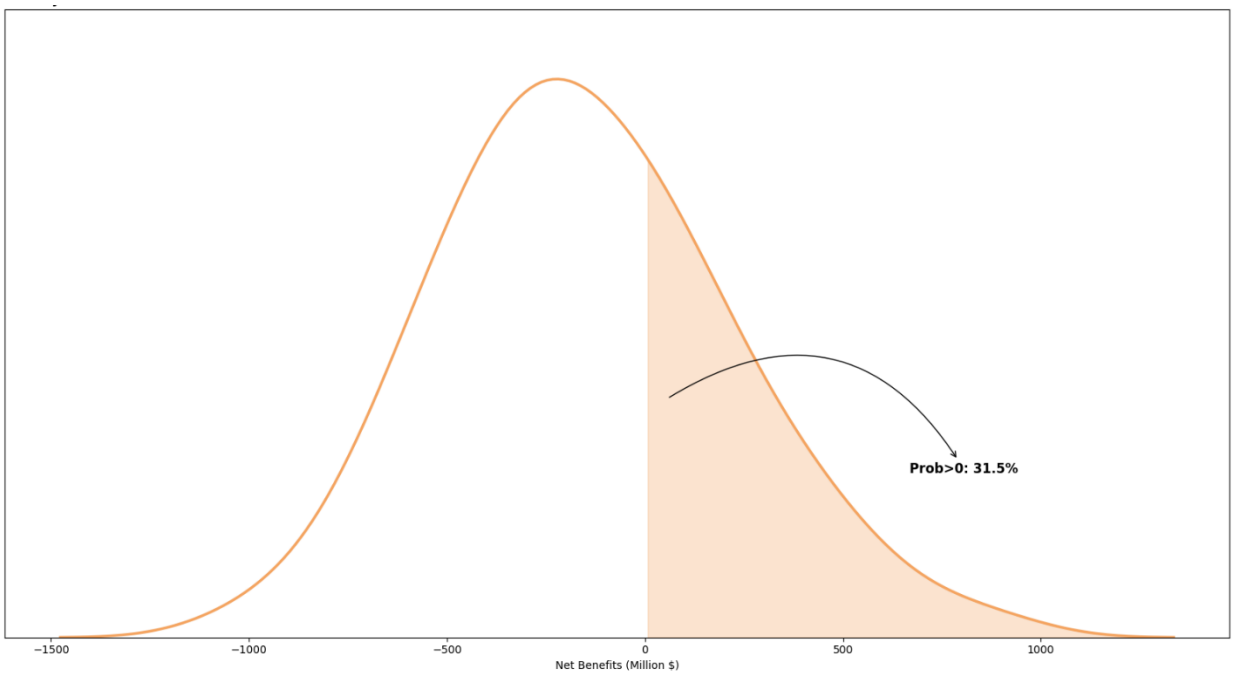


Figure P-1: Distribution of Estimated Net Quantified Benefits, Final Rule (PFOA and PFOS MCLs of 4.0 ppt each, PFHxS, PFNA, HFPO-DA MCLs of 10 ppt each and HI of 1; 3 percent Discount Rate; Million $2022)

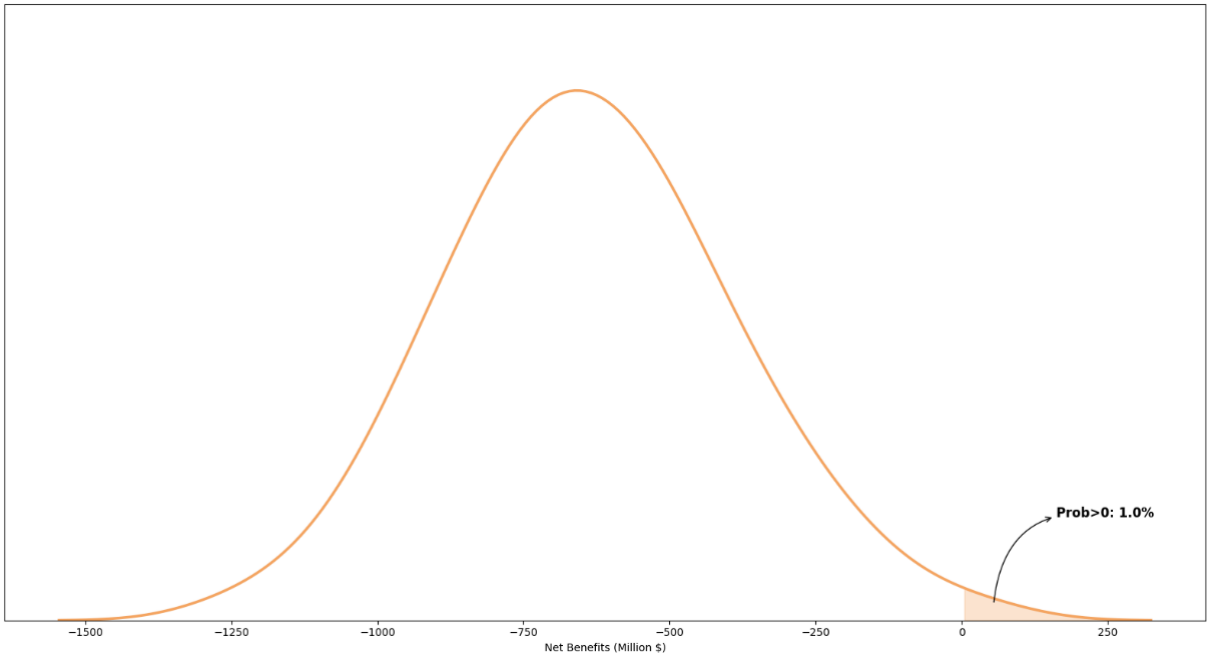


Figure P-2: Distribution of Estimated Net Quantified Benefits, Final Rule (PFOA and PFOS MCLs of 4.0 ppt each, PFHxS, PFNA, HFPO-DA MCLs of 10 ppt each and HI of 1; 7 percent Discount Rate; Million $2022)

Table P-28: Annualized Quantified National Costs and Benefits, Option 1a (PFOA and PFOS MCLs of 4.0 ppt) (Million $2022)

	3% Discount Rate			7% Discount Rate		
	5th Percentile[a]	Mean	95th Percentile[a]	5th Percentile[a]	Mean	95th Percentile[a]
Total Annualized Rule Costs	$1,420.30	$1,534.03	$1,658.20	$1,425.50	$1,542.57	$1,676.70
Total Annualized Rule Benefits	$815.03	$1,387.48	$2,043.00	$534.22	$912.35	$1,321.70
Total Net Benefits[b,c]	**-$709.19**	**-$146.55**	**$498.73**	**-$1,013.40**	**-$630.22**	**-$219.47**

Notes: Detail may not add exactly to total due to independent rounding.
[a]The 5th and 95th percentile range is based on modeled variability and uncertainty described in Section 5.1.2 and Table 5-1 for costs and Section 6.1.2 and Table 6-1 for benefits. This range does not include the uncertainty described in Table 5-22 for costs and Table 6-48 for benefits.
[b]See Table 7-6 for a list of the nonquantifiable benefits and costs, and the potential direction of impact these benefits and costs would have on the estimated monetized total annualized benefits and costs in this table.
[c]PFAS-contaminated wastes are not considered RCRA regulatory or characteristic hazardous wastes at this time and therefore total costs reported in this table do not include costs associated with hazardous waste disposal of spent filtration materials. To address stakeholder concerns about potential costs for disposing PFAS-contaminated wastes as hazardous should they be regulated as such in the future, the EPA conducted a sensitivity analysis with an assumption of hazardous waste disposal for illustrative purposes only. See Appendix N and Section N.2 for additional detail.

Table P-29: Annualized Quantified National Costs and Benefits, Option 1b (PFOA and PFOS MCLs of 5.0 ppt) (Million $2022)

	3% Discount Rate			7% Discount Rate		
	5th Percentile[a]	Mean	95th Percentile[a]	5th Percentile[a]	Mean	95th Percentile[a]
Total Annualized Rule Costs	$1,100.10	$1,189.99	$1,290.30	$1,103.90	$1,197.32	$1,304.10
Total Annualized Rule Benefits	$688.91	$1,167.15	$1,722.70	$450.77	$769.28	$1,117.10
Total Net Benefits[b,c]	**-$496.16**	**-$22.84**	**$517.44**	**-$748.65**	**-$428.04**	**-$79.59**

Notes: Detail may not add exactly to total due to independent rounding.
[a]The 5th and 95th percentile range is based on modeled variability and uncertainty described in Section 5.1.2 and Table 5-1 for costs and Section 6.1.2 and 6-1 for benefits. This range does not include the uncertainty described in Table 5-22 for costs and Table 6-48 for benefits.
[b]See Table 7-6 for a list of the nonquantifiable benefits and costs, and the potential direction of impact these benefits and costs would have on the estimated monetized total annualized benefits and costs in this table.
[c]PFAS-contaminated wastes are not considered RCRA regulatory or characteristic hazardous wastes at this time and therefore total costs reported in this table do not include costs associated with hazardous waste disposal of spent filtration materials. To address stakeholder concerns about potential costs for disposing PFAS-contaminated wastes as hazardous should they be regulated as such in the future, the EPA conducted a sensitivity analysis with an assumption of hazardous waste disposal for illustrative purposes only. See Appendix N and Section N.2 for additional detail.

Table P-30: Annualized Quantified National Costs and Benefits, Option 1c (PFOA and PFOS MCLs of 10.0 ppt) (Million $2022)

	3% Discount Rate			7% Discount Rate		
	5th Percentile[a]	**Mean**	**95th Percentile[a]**	**5th Percentile[a]**	**Mean**	**95th Percentile[a]**
Total Annualized Rule Costs	$461.72	$498.64	$540.36	$464.77	$503.02	$547.76
Total Annualized Rule Benefits	$356.37	$598.63	$872.69	$233.73	$396.05	$572.67
Total Net Benefits[b,c]	**-$136.94**	**$99.99**	**$370.06**	**-$270.13**	**-$106.98**	**$68.02**

Notes: Detail may not add exactly to total due to independent rounding.
[a]The 5th and 95th percentile range is based on modeled variability and uncertainty described in Section 5.1.2 and Table 5-1 for costs and Section 6.1.2 and Table 6-1 for benefits. This range does not include the uncertainty described in Table 5-22 for costs and Table 6-48 for benefits.
[b]See Table 7-6 for a list of the nonquantifiable benefits and costs, and the potential direction of impact these benefits and costs would have on the estimated monetized total annualized benefits and costs in this table.
[c]PFAS-contaminated wastes are not considered RCRA regulatory or characteristic hazardous wastes at this time and therefore total costs reported in this table do not include costs associated with hazardous waste disposal of spent filtration materials. To address stakeholder concerns about potential costs for disposing PFAS-contaminated wastes as hazardous should they be regulated as such in the future, the EPA conducted a sensitivity analysis with an assumption of hazardous waste disposal for illustrative purposes only. See Appendix N and Section N.2 for additional detail.

P.5 Benefits Sensitivity Analyses

Table P-31: 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)	0.091	0.091	0.091	0.091	0.091	0.091	0.091	0.091	0.091	0.091	0.091	0.091
Average reduction in serum PFOS concentration (ng/mL)	0.084	0.084	0.084	0.084	0.084	0.084	0.084	0.084	0.084	0.084	0.084	0.084
Average reduction in TC concentration (mg/dL)	0.150	0.168	0.160	0.150	0.168	0.160	0.150	0.168	0.160	0.150	0.168	0.160
Average reduction in HDLC concentration (mg/dL)	0.000	0.000	0.000	0.014	-0.002	-0.014	0.000	0.000	0.000	0.014	-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]	2.745	3.084	2.920	1.973	3.187	3.654	2.708	3.048	2.883	1.936	3.150	3.618
Non-fatal first IS (total cases avoided)[d]	3.965	4.455	4.218	3.005	4.583	5.130	3.909	4.399	4.161	2.948	4.526	5.073
CVD deaths (total cases avoided)[d]	0.778	0.875	0.828	0.641	0.893	0.958	0.755	0.852	0.804	0.618	0.870	0.935
PDV, non-fatal first MI (3% discount rate, millions $2022)	0.104	0.117	0.111	0.074	0.121	0.139	0.103	0.115	0.109	0.073	0.119	0.138
PDV, non-fatal first IS (3% discount rate, millions $2022)	0.043	0.048	0.046	0.032	0.050	0.056	0.042	0.048	0.045	0.032	0.049	0.056
PDV, CVD deaths (3% discount rate, millions $2022)	5.090	5.707	5.410	3.989	5.854	6.458	4.973	5.590	5.294	3.872	5.737	6.341

Table P-31: 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 (3% discount rate, millions $2022)	5.237	5.872	5.567	4.095	6.024	6.653	5.119	5.753	5.449	3.977	5.906	6.535
Annualized CVD benefits (3% discount rate, millions $2022)	**0.172**	**0.193**	**0.183**	**0.135**	**0.198**	**0.219**	**0.168**	**0.189**	**0.179**	**0.131**	**0.194**	**0.215**
PDV, non-fatal first MI (7% discount rate, millions $2022)	0.040	0.045	0.043	0.029	0.046	0.053	0.039	0.044	0.042	0.028	0.046	0.053
PDV, non-fatal first IS (7% discount rate, millions $2022)	0.017	0.019	0.018	0.013	0.020	0.022	0.017	0.019	0.018	0.012	0.019	0.022
PDV, CVD deaths (7% discount rate, millions $2022)	2.286	2.553	2.429	1.733	2.629	2.957	2.245	2.512	2.388	1.692	2.588	2.916
PDV, total CVD benefits (7% discount rate, millions $2022)	2.343	2.617	2.489	1.774	2.695	3.033	2.301	2.575	2.447	1.732	2.653	2.991
Annualized CVD benefits (7% discount rate, millions $2022)	**0.165**	**0.184**	**0.175**	**0.125**	**0.189**	**0.213**	**0.162**	**0.181**	**0.172**	**0.122**	**0.186**	**0.210**

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.

Table P-32: 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)	0.089	0.089	0.089	0.089
Average reduction in serum PFOS concentration (ng/mL)	0.081	0.081	0.081	0.081
Average reduction in serum PFNA concentration (ng/mL)	0.000	0.000	0.136	0.136
Total increase in birth weight (g)	1.180	0.404	6.654	9.320
Total number of births affected[c]	102,268	102,268	102,268	102,268
Total number of surviving births affected[c]	101,804	101,803	101,806	101,808
Birth weight-related deaths (total cases avoided)[c]	0.616	0.211	4.841	4.841
PDV, birth weight-related deaths (3% discount rate, millions $2022)	2.724	0.932	15.133	21.144
PDV, birth weight-related morbidity (3% discount rate, millions $2022)	0.083	0.028	0.462	0.646
PDV, total birth weight benefits (3% discount rate, millions $2022)	2.807	0.960	15.595	21.791
Annualized birth weight benefits (3% discount rate, millions $2022)	**0.092**	**0.032**	**0.513**	**0.717**
PDV, birth weight-related deaths (7% discount rate, millions $2022)	0.882	0.301	4.804	6.704
PDV, birth weight-related morbidity (7% discount rate, millions $2022)	0.029	0.010	0.157	0.219
PDV, total birth weight benefits (7% discount rate, millions $2022)	0.910	0.311	4.961	6.923
Annualized birth weight benefits (7% discount rate, millions $2022)	**0.064**	**0.022**	**0.349**	**0.487**

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.

Table P-33: Summary of RCC Sensitivity Analysis

Result Description	Exposure-Response Scenario[a]		
	1-EA	2-Vieira	3- Vieira$_{\text{ExcludeHigh}}$
Average reduction in serum PFOA concentration (ng/mL)	0.085	0.085	0.085
Non-fatal RCC (cases avoided)	9.329	0.365	1.295

Table P-33: Summary of RCC Sensitivity Analysis

RCC-related deaths (cases avoided)[b]	3.762	0.147	0.522
PDV, Non-fatal RCC (3% discount rate, millions $2022)	1.530	0.060	0.212
PDV, RCC-related deaths (3% discount rate, millions $2022)	14.696	0.574	2.039
PDV, total RCC benefits (3% discount rate, millions $2022)	16.226	0.634	2.251
Annualized RCC benefits (3% discount rate, millions $2022)	**0.534**	**0.021**	**0.074**
PDV, Non-fatal RCC (7% discount rate, millions $2022)	0.444	0.017	0.062
PDV, RCC-related deaths (7% discount rate, millions $2022)	3.834	0.150	0.532
PDV, total RCC benefits (7% discount rate, millions $2022)	4.278	0.167	0.593
Annualized RCC benefits (7% discount rate, millions $2022)	**0.301**	**0.012**	**0.042**

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.

P.6 Supplemental Cost Analyses

Table P-34: Annualized PWS Treatment Cost Associated with Non-Hazardous and Hazardous Residual Management Requirements, Final Rule (PFOA and PFOS MCLs of 4.0 ppt each, PFHxS, PFNA, and HFPO-DA MCLs of 10 ppt each and HI of 1) (Million $2022)

	3% Discount Rate			7% Discount Rate		
	5th Percentile	**Mean**	**95th Percentile**	**5th Percentile**	**Mean**	**95th Percentile**
Non-Hazardous Disposal	$1,391.16	$1,501.68	$1,624.89	$1,388.69	$1,503.01	$1,634.84
Hazardous Disposal	$1,480.76	$1,598.08	$1,725.79	$1,470.69	$1,590.41	$1,725.64
Increase due to Hazardous Disposal		**$96.40**			**$87.40**	

Note: Percentiles cannot be subtracted.

P.7 Supplemental Benefits Analyses

Table P-35. National Liver Cancer Benefits, Final Rule (PFOA and PFOS MCLs of 4.0 ppt each, PFHxS, PFNA, HFPO-DA, of 10 ppt each and HI of 1)

Benefits Category	3% Discount Rate			7% Discount Rate		
	5th Percentile[a]	Expected Value	95th Percentile[a]	5th Percentile[a]	Expected Value	95th Percentile[a]
Number of Non-Fatal Liver Cancer Cases Avoided	13.3	14.2	15.1	13.3	14.2	15.1
Number of Liver Cancer-Related Deaths Avoided	29.4	31.3	33.3	29.4	31.2	33.3
Total Annualized Liver Cancer Benefits (Million $2022)[b]	**$3.81**	**$4.05**	**$4.31**	**$1.97**	**$2.10**	**$2.23**

Notes: Detail may not add exactly to total due to independent rounding.
[a]The 5th and 95th percentile range is based on modeled variability and uncertainty related to PAF and occurrence. This range does not include the uncertainty described in Table O-3.
[b]See Table 7-6 for a list of the nonquantifiable benefits, and the potential direction of impact these benefits would have on the estimated monetized total annualized benefits in this table.

Table P-36. National Willingness to Pay-Based RCC Benefits, Final Rule (PFOA and PFOS MCLs of 4.0 ppt each, PFHxS, PFNA, HFPO-DA, of 10 ppt each and HI of 1)

Benefits Category	3% Discount Rate			7% Discount Rate		
	5th Percentile[a]	Expected Value	95th Percentile[a]	5th Percentile[a]	Expected Value	95th Percentile[a]
Number of Non-Fatal RCC Cases Avoided	1091.50	6964.20	17937.00	1,091.50	6,964.20	17,937.00
Number of RCC-Related Deaths Avoided	320.36	2028.80	5206.50	320.36	2,028.80	5,206.50
Total Annualized RCC Benefits (Million $2022)[b]	**$59.08**	**$323.40**	**$793.48**	**$44.80**	**$208.56**	**$477.05**

Notes: Detail may not add exactly to total due to independent rounding.
[a]The 5th and 95th percentile range is based on modeled variability and uncertainty. This range does not include the uncertainty described in Table 6-48.
[b]See Table 7-6 for a list of the nonquantifiable benefits, and the potential direction of impact these benefits would have on the estimated monetized total annualized benefits in this table.

Table P-37. National Willingness to Pay-Based Bladder Cancer Benefits, Final Rule (PFOA and PFOS MCLs of 4.0 ppt each, PFHxS, PFNA, HFPO-DA of 10 ppt each and HI of 1)

Benefits Category	3% Discount Rate			7% Discount Rate		
	5th Percentile[a]	Expected Value	95th Percentile[a]	5th Percentile[a]	Expected Value	95th Percentile[a]
Number of Non-Fatal Bladder Cancer Cases Avoided	5,781.00	7,313.00	8,912.70	5,781.00	7,313.00	8,912.70
Number of Bladder Cancer-Related Deaths Avoided	2,029.60	2,567.80	3,129.90	2,029.60	2,567.80	3,129.90
Total Annualized Bladder Cancer Benefits (Million $2022)[b]	**$310.08**	**$392.38**	**$478.37**	**$175.42**	**$222.06**	**$270.81**

Notes: Detail may not add exactly to total due to independent rounding.
[a]The 5th and 95th percentile range is based on modeled variability and uncertainty. This range does not include the uncertainty described in Table 6-48.
[b]See Table 7-6 for a list of the nonquantifiable benefits, and the potential direction of impact these benefits would have on the estimated monetized total annualized benefits in this table.

P.8 Undiscounted Benefits and Costs

Table P-38. Quantified Total National Annual Costs, Final Rule (Undiscounted, Million $2022)

Year	Primacy Agency Administration	Primacy Agency Sampling Review	Primacy Agency Treatment Plan Review	PWS Treatment Capital	PWS Treatment Operations and Maintenance	PWS Administration	PWS Sampling	PWS Treatment Plan Submittal	Primacy Agency Total	PWS Total	Rule Total
2024	$6.48	$9.59	$0.00	$0.00	$0.00	$18.49	$92.76	$0.00	$16.08	$111.25	$127.32
2025	$6.48	$0.00	$0.00	$0.00	$0.00	$18.49	$0.00	$0.00	$6.48	$18.49	$24.97
2026	$6.48	$0.00	$0.00	$0.00	$0.00	$18.49	$0.00	$0.00	$6.48	$18.49	$24.97
2027	$0.00	$10.44	$0.00	$0.00	$0.00	$0.00	$113.71	$0.00	$10.44	$113.71	$124.15
2028	$0.00	$5.00	$35.25	$0.00	$0.00	$0.00	$63.55	$6.21	$40.24	$69.76	$110.01
2029	$0.00	$5.00	$0.00	$14,378.00	$1,023.30	$0.00	$63.55	$0.00	$5.00	$15,464.85	$15,469.85
2030	$0.00	$6.70	$0.00	$0.00	$1,023.30	$0.00	$66.05	$0.00	$6.70	$1,089.35	$1,096.04
2031	$0.00	$1.25	$0.00	$0.00	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,039.19	$1,040.44
2032	$0.00	$1.25	$0.00	$0.00	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,039.19	$1,040.44
2033	$0.00	$6.70	$0.00	$0.00	$1,023.30	$0.00	$66.05	$0.00	$6.70	$1,089.35	$1,096.04
2034	$0.00	$1.25	$0.00	$0.00	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,039.19	$1,040.44
2035	$0.00	$1.25	$0.00	$0.00	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,039.19	$1,040.44
2036	$0.00	$6.70	$0.00	$0.00	$1,023.30	$0.00	$66.05	$0.00	$6.70	$1,089.35	$1,096.04
2037	$0.00	$1.25	$0.00	$0.00	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,039.19	$1,040.44
2038	$0.00	$1.25	$0.00	$0.00	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,039.19	$1,040.44
2039	$0.00	$6.70	$0.00	$0.00	$1,023.30	$0.00	$66.05	$0.00	$6.70	$1,089.35	$1,096.04
2040	$0.00	$1.25	$0.00	$0.00	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,039.19	$1,040.44
2041	$0.00	$1.25	$0.00	$0.00	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,039.19	$1,040.44
2042	$0.00	$6.70	$0.00	$0.00	$1,023.30	$0.00	$66.05	$0.00	$6.70	$1,089.35	$1,096.04
2043	$0.00	$1.25	$0.00	$0.00	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,039.19	$1,040.44
2044	$0.00	$1.25	$0.00	$0.00	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,039.19	$1,040.44
2045	$0.00	$6.70	$0.00	$0.00	$1,023.30	$0.00	$66.05	$0.00	$6.70	$1,089.35	$1,096.04
2046	$0.00	$1.25	$0.00	$0.00	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,039.19	$1,040.44
2047	$0.00	$1.25	$0.00	$363.67	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,402.86	$1,404.11
2048	$0.00	$6.70	$0.00	$405.22	$1,023.30	$0.00	$66.05	$0.00	$6.70	$1,494.57	$1,501.26
2049	$0.00	$1.25	$0.00	$183.95	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,223.14	$1,224.39
2050	$0.00	$1.25	$0.00	$0.00	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,039.19	$1,040.44
2051	$0.00	$6.70	$0.00	$2,095.00	$1,023.30	$0.00	$66.05	$0.00	$6.70	$3,184.35	$3,191.04
2052	$0.00	$1.25	$0.00	$126.49	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,165.68	$1,166.93

Table P-38. Quantified Total National Annual Costs, Final Rule (Undiscounted, Million $2022)

Year	Primacy Agency Administration	Primacy Agency Sampling Review	Primacy Agency Treatment Plan Review	PWS Treatment Capital	PWS Treatment Operations and Maintenance	PWS Administration	PWS Sampling	PWS Treatment Plan Submittal	Primacy Agency Total	PWS Total	Rule Total
2053	$0.00	$1.25	$0.00	$0.00	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,039.19	$1,040.44
2054	$0.00	$6.70	$0.00	$101.26	$1,023.30	$0.00	$66.05	$0.00	$6.70	$1,190.61	$1,197.30
2055	$0.00	$1.25	$0.00	$27.17	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,066.35	$1,067.60
2056	$0.00	$1.25	$0.00	$1.95	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,041.14	$1,042.38
2057	$0.00	$6.70	$0.00	$0.00	$1,023.30	$0.00	$66.05	$0.00	$6.70	$1,089.35	$1,096.04
2058	$0.00	$1.25	$0.00	$27.31	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,066.50	$1,067.75
2059	$0.00	$1.25	$0.00	$40.26	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,079.45	$1,080.69
2060	$0.00	$6.70	$0.00	$23.34	$1,023.30	$0.00	$66.05	$0.00	$6.70	$1,112.68	$1,119.38
2061	$0.00	$1.25	$0.00	$1.00	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,040.19	$1,041.43
2062	$0.00	$1.25	$0.00	$0.00	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,039.19	$1,040.44
2063	$0.00	$6.70	$0.00	$1,960.20	$1,023.30	$0.00	$66.05	$0.00	$6.70	$3,049.55	$3,056.24
2064	$0.00	$1.25	$0.00	$5,851.40	$1,023.30	$0.00	$15.89	$0.00	$1.25	$6,890.59	$6,891.84
2065	$0.00	$1.25	$0.00	$2,373.40	$1,023.30	$0.00	$15.89	$0.00	$1.25	$3,412.59	$3,413.84
2066	$0.00	$6.70	$0.00	$1,151.00	$1,023.30	$0.00	$66.05	$0.00	$6.70	$2,240.35	$2,247.04
2067	$0.00	$1.25	$0.00	$405.22	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,444.41	$1,445.66
2068	$0.00	$1.25	$0.00	$8.97	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,048.16	$1,049.41
2069	$0.00	$6.70	$0.00	$183.95	$1,023.30	$0.00	$66.05	$0.00	$6.70	$1,273.30	$1,279.99
2070	$0.00	$1.25	$0.00	$0.00	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,039.19	$1,040.44
2071	$0.00	$1.25	$0.00	$0.00	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,039.19	$1,040.44
2072	$0.00	$6.70	$0.00	$0.00	$1,023.30	$0.00	$66.05	$0.00	$6.70	$1,089.35	$1,096.04
2073	$0.00	$1.25	$0.00	$2,095.00	$1,023.30	$0.00	$15.89	$0.00	$1.25	$3,134.19	$3,135.44
2074	$0.00	$1.25	$0.00	$0.00	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,039.19	$1,040.44
2075	$0.00	$6.70	$0.00	$126.49	$1,023.30	$0.00	$66.05	$0.00	$6.70	$1,215.84	$1,222.53
2076	$0.00	$1.25	$0.00	$0.00	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,039.19	$1,040.44
2077	$0.00	$1.25	$0.00	$0.00	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,039.19	$1,040.44
2078	$0.00	$6.70	$0.00	$0.00	$1,023.30	$0.00	$66.05	$0.00	$6.70	$1,089.35	$1,096.04
2079	$0.00	$1.25	$0.00	$101.26	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,140.45	$1,141.70
2080	$0.00	$1.25	$0.00	$0.00	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,039.19	$1,040.44
2081	$0.00	$6.70	$0.00	$27.17	$1,023.30	$0.00	$66.05	$0.00	$6.70	$1,116.51	$1,123.21
2082	$0.00	$1.25	$0.00	$0.00	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,039.19	$1,040.44
2083	$0.00	$1.25	$0.00	$365.62	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,404.81	$1,406.06
2084	$0.00	$6.70	$0.00	$0.00	$1,023.30	$0.00	$66.05	$0.00	$6.70	$1,089.35	$1,096.04
2085	$0.00	$1.25	$0.00	$0.00	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,039.19	$1,040.44

Table P-38. Quantified Total National Annual Costs, Final Rule (Undiscounted, Million $2022)

Year	Primacy Agency Administration	Primacy Agency Sampling Review	Primacy Agency Treatment Plan Review	PWS Treatment Capital	PWS Treatment Operations and Maintenance	PWS Administration	PWS Sampling	PWS Treatment Plan Submittal	Primacy Agency Total	PWS Total	Rule Total
2086	$0.00	$1.25	$0.00	$405.22	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,444.41	$1,445.66
2087	$0.00	$6.70	$0.00	$27.31	$1,023.30	$0.00	$66.05	$0.00	$6.70	$1,116.66	$1,123.36
2088	$0.00	$1.25	$0.00	$0.00	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,039.19	$1,040.44
2089	$0.00	$1.25	$0.00	$224.21	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,263.40	$1,264.65
2090	$0.00	$6.70	$0.00	$0.00	$1,023.30	$0.00	$66.05	$0.00	$6.70	$1,089.35	$1,096.04
2091	$0.00	$1.25	$0.00	$23.34	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,062.52	$1,063.77
2092	$0.00	$1.25	$0.00	$0.00	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,039.19	$1,040.44
2093	$0.00	$6.70	$0.00	$1.00	$1,023.30	$0.00	$66.05	$0.00	$6.70	$1,090.34	$1,097.04
2094	$0.00	$1.25	$0.00	$0.00	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,039.19	$1,040.44
2095	$0.00	$1.25	$0.00	$2,095.00	$1,023.30	$0.00	$15.89	$0.00	$1.25	$3,134.19	$3,135.44
2096	$0.00	$6.70	$0.00	$0.00	$1,023.30	$0.00	$66.05	$0.00	$6.70	$1,089.35	$1,096.04
2097	$0.00	$1.25	$0.00	$1,960.20	$1,023.30	$0.00	$15.89	$0.00	$1.25	$2,999.39	$3,000.64
2098	$0.00	$1.25	$0.00	$126.49	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,165.68	$1,166.93
2099	$0.00	$6.70	$0.00	$5,851.40	$1,023.30	$0.00	$66.05	$0.00	$6.70	$6,940.75	$6,947.44
2100	$0.00	$1.25	$0.00	$0.00	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,039.19	$1,040.44
2101	$0.00	$1.25	$0.00	$2,373.40	$1,023.30	$0.00	$15.89	$0.00	$1.25	$3,412.59	$3,413.84
2102	$0.00	$6.70	$0.00	$0.00	$1,023.30	$0.00	$66.05	$0.00	$6.70	$1,089.35	$1,096.04
2103	$0.00	$1.25	$0.00	$1,151.00	$1,023.30	$0.00	$15.89	$0.00	$1.25	$2,190.19	$2,191.44
2104	$0.00	$1.25	$0.00	$101.26	$1,023.30	$0.00	$15.89	$0.00	$1.25	$1,140.45	$1,141.70
2105	$0.00	$6.70	$0.00	$0.00	$1,023.30	$0.00	$66.05	$0.00	$6.70	$1,089.35	$1,096.04

Table P-39. Quantified Total National Annual Benefits, Final Rule (Undiscounted, Million $2022)

Year	Birth Weight	CVD	RCC	Bladder Cancer	Rule Total
2024	$0.00	$0.00	$0.00	$0.00	$0.00
2025	$0.00	$0.00	$0.00	$0.00	$0.00
2026	$0.00	$0.00	$0.00	$0.00	$0.00
2027	$0.00	$0.00	$0.00	$0.00	$0.00
2028	$0.00	$0.00	$0.00	$0.00	$0.00
2029	$29.20	$62.83	$57.07	$61.84	$210.93
2030	$72.24	$156.58	$132.60	$84.70	$446.12
2031	$105.92	$245.95	$191.16	$100.26	$643.29
2032	$132.31	$330.69	$234.03	$115.73	$812.76
2033	$153.04	$410.55	$265.09	$130.92	$959.60
2034	$169.35	$481.69	$288.48	$145.13	$1,084.65
2035	$182.24	$540.26	$307.52	$160.02	$1,190.04
2036	$192.48	$587.20	$322.59	$174.56	$1,276.83
2037	$200.68	$624.79	$335.02	$189.25	$1,349.74
2038	$207.30	$654.85	$345.66	$203.90	$1,411.71
2039	$212.70	$678.67	$355.08	$216.60	$1,463.05
2040	$217.17	$697.45	$364.16	$229.47	$1,508.25
2041	$220.93	$712.55	$372.19	$242.81	$1,548.48
2042	$224.14	$724.65	$379.50	$256.45	$1,584.74
2043	$226.94	$734.33	$386.34	$270.26	$1,617.87
2044	$229.42	$741.94	$392.88	$284.17	$1,648.41
2045	$231.65	$747.55	$399.25	$297.63	$1,676.08
2046	$233.69	$751.89	$405.12	$311.21	$1,701.91
2047	$235.60	$755.25	$410.67	$324.80	$1,726.32
2048	$237.41	$757.81	$416.01	$338.32	$1,749.55
2049	$239.15	$759.72	$421.23	$351.73	$1,771.83
2050	$240.83	$760.91	$426.18	$364.15	$1,792.07
2051	$242.47	$761.71	$430.90	$376.48	$1,811.56
2052	$244.10	$762.35	$435.46	$388.69	$1,830.60
2053	$245.70	$762.94	$439.97	$400.77	$1,849.38
2054	$247.29	$763.58	$444.46	$412.69	$1,868.02
2055	$248.89	$764.30	$448.74	$423.48	$1,885.41
2056	$250.47	$765.15	$452.94	$434.20	$1,902.76
2057	$252.07	$766.25	$457.12	$444.87	$1,920.31
2058	$253.66	$767.67	$461.32	$455.52	$1,938.17
2059	$255.26	$769.49	$465.54	$466.16	$1,956.45
2060	$256.87	$771.70	$469.66	$476.17	$1,974.40
2061	$258.49	$774.19	$473.85	$486.30	$1,992.83
2062	$260.11	$776.97	$478.08	$496.58	$2,011.74
2063	$261.74	$780.07	$482.38	$507.02	$2,031.21
2064	$263.39	$783.51	$486.71	$517.63	$2,051.24
2065	$265.04	$785.85	$490.67	$528.25	$2,069.81
2066	$266.70	$787.99	$494.68	$539.14	$2,088.51
2067	$268.37	$789.88	$498.75	$550.29	$2,107.29
2068	$270.06	$791.52	$502.85	$561.68	$2,126.11
2069	$271.75	$792.96	$506.96	$573.30	$2,144.97
2070	$273.45	$793.98	$510.52	$585.25	$2,163.20
2071	$275.17	$794.94	$514.11	$597.39	$2,181.61
2072	$276.89	$795.80	$517.72	$609.68	$2,200.09
2073	$278.63	$796.58	$521.34	$622.11	$2,218.66

Table P-39. Quantified Total National Annual Benefits, Final Rule (Undiscounted, Million $2022)

Year	Birth Weight	CVD	RCC	Bladder Cancer	Rule Total
2074	$280.37	$797.24	$524.98	$634.64	$2,237.23
2075	$282.13	$797.63	$527.76	$647.13	$2,254.65
2076	$283.90	$797.89	$530.56	$659.50	$2,271.85
2077	$285.68	$798.07	$533.39	$671.79	$2,288.93
2078	$287.47	$798.17	$536.25	$684.00	$2,305.89
2079	$289.27	$798.20	$539.16	$696.13	$2,322.76
2080	$291.09	$798.11	$540.87	$707.46	$2,337.53
2081	$292.91	$798.00	$542.68	$718.38	$2,351.97
2082	$294.75	$797.97	$544.59	$729.05	$2,366.36
2083	$296.60	$798.04	$546.63	$739.55	$2,380.82
2084	$298.46	$798.30	$548.75	$749.90	$2,395.41
2085	$300.33	$798.60	$549.73	$759.15	$2,407.81
2086	$302.21	$798.99	$550.95	$767.94	$2,420.09
2087	$304.10	$799.55	$552.41	$776.54	$2,432.60
2088	$306.01	$800.29	$554.06	$785.06	$2,445.42
2089	$307.93	$801.27	$555.89	$793.57	$2,458.66
2090	$309.86	$802.03	$556.61	$800.58	$2,469.08
2091	$311.80	$803.04	$557.67	$807.24	$2,479.75
2092	$313.76	$804.29	$559.02	$813.78	$2,490.85
2093	$315.72	$805.75	$560.63	$820.25	$2,502.35
2094	$317.70	$807.44	$562.49	$826.80	$2,514.43
2095	$319.70	$809.23	$564.20	$832.04	$2,525.17
2096	$321.70	$811.09	$566.42	$836.97	$2,536.18
2097	$323.72	$813.13	$558.61	$841.87	$2,537.33
2098	$325.75	$815.33	$552.43	$846.86	$2,540.37
2099	$327.79	$817.72	$544.46	$852.01	$2,541.98
2100	$329.84	$820.26	$529.89	$853.24	$2,533.23
2101	$331.91	$822.92	$514.44	$854.25	$2,523.52
2102	$333.99	$825.67	$493.80	$855.62	$2,509.08
2103	$336.09	$828.47	$466.19	$857.60	$2,488.35
2104	$338.19	$831.38	$426.39	$860.23	$2,456.19
2105	$340.31	$834.39	$357.62	$862.30	$2,394.62

Appendix Q. Appendix References

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