eAppendix 1

eTable 1. Crude and Adjusted[a] Association of Maternal Characteristics with Pregnancy Outcome among Singleton Pregnancies, Mid-Ohio Valley, 1990-2006

	Miscarriage			Stillbirth			Preeclampsia		
Maternal Characteristic	N	Crude OR	Adjusted[a] OR (95% CI)	N	Crude OR	Adjusted[a] OR (95% CI)	N	Crude OR	Adjusted[a] OR (95% CI)
Exposure Year									
1990 – 1994	445	1.0	1.0	35	1.0	1.0	179	1.0	1.0
1995 – 1999	450	1.0	1.0 (0.9, 1.2)	31	0.9	0.9 (0.5, 1.4)	235	1.2	1.3 (1.1, 1.6)
2000 – 2005	548	1.2	1.2 (1.0, 1.4)	39	1.1	1.1 (0.7, 1.8)	316	1.6	1.9 (1.5, 2.3)
Age, years									
14 – 20	229	1.1	0.6 (0.5, 0.8)	26	1.6	0.9 (0.5, 1.6)	123	1.1	0.8 (0.7, 1.1)
20 – 24	418	1.0	1.0	32	1.0	1.0	246	1.0	1.0
25 – 29	374	1.0	1.5 (1.3, 1.8)	24	0.9	1.4 (0.8, 2.5)	215	1.0	1.2 (1.0, 1.5)
30 – 34	257	1.3	2.4 (2.0, 3.0)	15	1.0	2.0 (1.0, 4.0)	112	1.0	1.3 (1.0, 1.6)
35 – 45	165	2.5	5.3 (4.2, 6.8)	8	1.6	3.3 (1.5, 7.4)	34	0.9	1.2 (0.8, 1.7)
Parity									
0	1121	1.0	1.0	79	1.0	1.0	459	1.0	1.0
1	230	0.3	0.2 (0.2, 0.2)	18	0.3	0.2 (0.1, 0.4)	180	0.5	0.4 (0.4, 0.5)
2+	92	0.2	0.1 (0.1, 0.1)	8	0.2	0.2 (0.1, 0.3)	91	0.5	0.4 (0.3, 0.5)
Education at interview, years									
<12	113	1.1	1.3 (1.0, 1.7)	15	1.5	1.7 (0.9, 3.4)	43	0.8	0.9 (0.6, 1.3)
12	438	1.0	1.0	39	1.0	1.0	210	1.0	1.0
13 – 15	646	1.2	1.1 (0.9, 1.3)	42	0.8	0.8 (0.5, 1.3)	354	1.3	1.2 (1.0, 1.5)
≥16	246	1.2	0.8 (0.7, 1.0)	9	0.5	0.4 (0.2, 0.9)	123	1.3	1.0 (0.7, 1.3)
Smoking status at interview									
Never smoker	630	1.0	1.0	42	1.0	1.0	368	1.0	1.0
Former smoker	318	1.2	1.2 (1.0, 1.4)	18	1.0	0.9 (0.5, 1.6)	168	1.0	1.0 (0.8, 1.3)
Current smoker	495	1.1	1.4 (1.2, 1.6)	45	1.5	1.4 (0.9, 2.2)	194	0.8	0.8 (0.7, 1.0)

[a] Adjusted for exposure year, maternal age, parity, education level at interview, smoking status at interview

eTable 1, continued. Crude and Adjusted[a] Association of Maternal Characteristics with Pregnancy Outcome among Singleton Pregnancies, Mid-Ohio Valley, 1990-2006

	Preterm Birth			Term Low Birthweight			Birth Defect		
Maternal Characteristic	N	Crude OR	Adjusted[a] OR (95% CI)	N	Crude OR	Adjusted[a] OR (95% CI)	N	Crude OR	Adjusted[a] OR (95% CI)
Exposure Year									
1990 – 1994	474	1.0	1.0	50	1.0	1.0	157	1.0	1.0
1995 – 1999	574	1.3	1.3 (1.1, 1.4)	42	0.9	0.9 (0.6, 1.4)	147	1.0	1.0 (0.8, 1.2)
2000 – 2005	795	1.8	1.9 (1.6, 2.1)	41	0.9	0.9 (0.6, 1.4)	145	0.9	0.9 (0.7, 1.2)
Age, years									
14 – 20	337	1.0	1.0 (0.8, 1.1)	36	1.7	1.4 (0.9, 2.2)	94	1.2	1.0 (0.7, 1.3)
20 – 24	632	1.0	1.0	39	1.0	1.0	157	1.0	1.0
25 – 29	504	1.0	1.0 (0.9, 1.2)	37	1.1	1.4 (0.9, 2.2)	114	0.9	1.0 (0.8, 1.3)
30 – 34	276	1.0	1.1 (0.9, 1.3)	16	0.9	1.2 (0.7, 2.2)	56	0.8	1.0 (0.7, 1.4)
35 – 45	94	1.0	1.1 (0.9, 1.4)	5	0.9	1.2 (0.5, 3.3)	28	1.2	1.5 (0.9, 2.3)
Parity									
0	887	1.0	1.0	56	1.0	1.0	223	1.0	1.0
1	661	1.0	0.9 (0.8, 1.0)	49	1.1	1.1 (0.8, 1.6)	150	0.8	0.8 (0.7, 1.0)
2+	295	0.8	0.7 (0.6, 0.8)	28	1.1	1.1 (0.6, 1.8)	76	0.8	0.7 (0.5, 1.0)
Education at interview, years									
<12	170	1.1	1.0 (0.8, 1.3)	26	1.9	1.4 (0.8, 2.4)	54	1.3	1.2 (0.9, 1.7)
12	631	1.0	1.0	58	1.0	1.0	164	1.0	1.0
13 – 15	781	1.0	1.0 (0.8, 1.1)	40	0.5	0.6 (0.4, 0.9)	187	0.9	0.9 (0.7, 1.1)
≥16	261	0.9	0.9 (0.7, 1.0)	9	0.3	0.5 (0.2, 1.0)	44	0.6	0.6 (0.4, 0.9)
Smoking status at interview									
Never smoker	819	1.0	1.0	30	1.0	1.0	178	1.0	1.0
Former smoker	365	1.0	1.0 (0.9, 1.2)	19	1.5	1.4 (0.8, 2.6)	92	1.2	1.2 (0.9, 1.5)
Current smoker	659	1.2	1.1 (1.0, 1.3)	84	4.1	3.3 (2.1, 5.3)	179	1.4	1.3 (1.0, 1.6)

[a] Adjusted for exposure year, maternal age, parity, education level at interview, smoking status at interview

eTable 2. Crude and Adjusted[a] Association of Estimated Maternal PFOA Serum Concentration Using Standard or Bayesian Calibration with Pregnancy Outcome among Singleton Pregnancies, Mid-Ohio Valley, 1990-2006

	Miscarriage			Stillbirth			Preeclampsia		
	N	Crude OR	Adjusted[a] OR (95% CI)	N	Crude OR	Adjusted[a] OR (95% CI)	N	Crude OR	Adjusted[a] OR (95% CI)
Standard Calibration									
IQR(lnPFOA)[b] increase	1443	1.01	0.97 (0.89, 1.05)	105	1.00	1.01 (0.80, 1.26)	730	1.09	1.09 (0.98, 1.21)
100 ng/mL increase	1443	1.00	1.00 (0.94, 1.05)	105	0.89	0.90 (0.69, 1.17)	730	0.98	1.02 (0.96, 1.09)
<40th percentile 0.05 – <9.6 ng/mL	558	1.0	1.0	37	1.0	1.0	253	1.0	1.0
40 – <60th percentile 9.6 – <17.0 ng/mL	303	1.1	1.0 (0.8, 1.2)	23	1.3	1.3 (0.8, 2.2)	149	1.2	1.1 (0.9, 1.4)
60 – <80th percentile 17.0 – <39.6 ng/mL	286	1.0	0.9 (0.7, 1.1)	30	1.6	1.6 (0.9, 2.7)	172	1.3	1.1 (0.9, 1.4)
≥80th percentile 39.6 – 3971.2 ng/mL	296	1.1	1.0 (0.9, 1.2)	15	0.8	0.9 (0.5, 1.6)	156	1.2	1.2 (1.0, 1.5)
Bayesian Calibration									
IQR(lnPFOA)[c] increase	1443	0.98	0.94 (0.86, 1.04)	105	0.95	0.97 (0.75, 1.26)	730	1.16	1.16 (1.03, 1.30)
100 ng/mL increase	1443	0.98	0.99 (0.93, 1.05)	105	0.83	0.85 (0.65, 1.13)	730	1.01	1.05 (0.99, 1.12)
<40th percentile 3.9 – <6.9 ng/mL	570	1.0	1.0	36	1.0	1.0	228	1.0	1.0
40 – <60th percentile 6.9 – <15.1 ng/mL	295	1.0	0.9 (0.8, 1.1)	24	1.3	1.3 (0.8, 2.3)	157	1.4	1.2 (1.0, 1.5)
60 – <80th percentile 15.1 – <40.1 ng/mL	299	1.0	0.9 (0.7, 1.0)	29	1.6	1.6 (0.9, 2.8)	181	1.6	1.3 (1.1, 1.7)
≥80th percentile 40.1 – 3531.8 ng/mL	279	1.0	0.9 (0.8, 1.1)	16	0.9	0.9 (0.5, 1.7)	164	1.4	1.4 (1.1, 1.7)

[a] Adjusted for exposure year, maternal age, parity, education level at interview, smoking status at interview

[b] Effect estimates represent the change in outcome for a shift from the 25th percentile to the 75th percentile in estimated PFOA serum levels (IQR (lnPFOA) = 1.60)

[c] Effect estimates represent the change in outcome for a shift from the 25th percentile to the 75th percentile in estimated PFOA serum levels (IQR (lnPFOA) = 1,81)

eTable 2, continued. Crude and Adjusted[a] Association of Estimated Maternal PFOA Serum Concentration Using Standard or Bayesian Calibration with Pregnancy Outcome among Singleton Pregnancies, Mid-Ohio Valley, 1990-2006

	Preterm Birth			Term Low Birthweight			Birth Defect		
	N	Crude OR	Adjusted[a] OR (95% CI)	N	Crude OR	Adjusted[a] OR (95% CI)	N	Crude OR	Adjusted[a] OR (95% CI)
Standard Calibration									
IQR(lnPFOA)[b] increase	1843	1.00	0.98 (0.91, 1.05)	133	0.86	0.92 (0.73, 1.15)	449	1.00	1.02 (0.90, 1.15)
100 ng/mL increase	1843	0.98	1.00 (0.93, 1.08)	133	0.84	0.88 (0.67, 1.14)	449	1.03	1.03 (0.94, 1.13)
<40th percentile 0.05 – <9.6 ng/mL	720	1.0	1.0	56	1.0	1.0	179	1.0	1.0
40 – <60th percentile 9.6 – <17.0 ng/mL	384	1.1	1.0 (0.9, 1.2)	30	1.1	1.1 (0.7, 1.7)	90	1.0	1.0 (0.8, 1.3)
60 – <80th percentile 17.0 – <39.6 ng/mL	411	1.2	1.1 (0.9, 1.3)	23	0.8	0.8 (0.5, 1.4)	88	1.0	1.0 (0.8, 1.3)
≥80th percentile 39.6 – 3971.2 ng/mL	328	0.9	0.9 (0.8, 1.1)	24	0.7	0.9 (0.5, 1.4)	92	1.0	1.1 (0.8, 1.4)
Bayesian Calibration									
IQR(lnPFOA)[c] increase	1843	0.99	0.98 (0.91, 1.07)	133	0.86	0.95 (0.71, 1.27)	449	1.02	1.04 (0.90, 1.20)
100 ng/mL increase	1843	0.98	1.02 (0.95, 1.08)	133	0.94	0.99 (0.81, 1.22)	449	1.05	1.05 (0.97, 1.14)
<40th percentile 3.9 – <6.9 ng/mL	696	1.0	1.0	62	1.0	1.0	183	1.0	1.0
40 – <60th percentile 6.9 – <15.1 ng/mL	394	1.2	1.0 (0.9, 1.2)	27	0.9	0.9 (0.6, 1.5)	86	0.9	0.9 (0.7, 1.2)
60 – <80th percentile 15.1 – <40.1 ng/mL	416	1.2	1.1 (0.9, 1.3)	19	0.6	0.7 (0.4, 1.2)	87	0.9	0.9 (0.7, 1.2)
≥80th percentile 40.1 – 3531.8 ng/mL	337	1.0	1.0 (0.8, 1.1)	25	0.7	0.9 (0.5, 1.4)	93	1.0	1.0 (0.8, 1.4)

[a] Adjusted for exposure year, maternal age, parity, education level at interview, smoking status at interview

[b] Effect estimates represent the change in outcome for a shift from the 25th percentile to the 75th percentile in estimated PFOA serum levels (IQR (lnPFOA) = 1.60)

[c] Effect estimates represent the change in outcome for a shift from the 25th percentile to the 75th percentile in estimated PFOA serum levels (IQR (lnPFOA) = 1,81)

eTable 3. Crude and Adjusted[a] Association of Estimated Maternal PFOA Serum Concentration with Pregnancy Outcome among Singleton Pregnancies with Varying Duration of Highest Quality Exposure Measures, Mid-Ohio Valley, 1990-2006

	Miscarriage			Stillbirth			Preeclampsia		
	N	Crude OR	Adjusted[a] OR (95% CI)	N	Crude OR	Adjusted[a] OR (95% CI)	N	Crude OR	Adjusted[a] OR (95% CI)
6 years, n=6,358									
IQR(lnPFOA)[b] increase	799	0.96	0.94 (0.83, 1.07)	52	0.98	1.01 (0.69, 1.48)	407	1.23	1.22 (1.03, 1.43)
100 ng/mL increase	799	1.00	0.99 (0.94, 1.05)	52	0.89	0.91 (0.69, 1.20)	407	1.08	1.10 (1.02, 1.18)
<40th percentile 3.9 – <6.2 ng/mL	326	1.0	1.0	19	1.0	1.0	129	1.0	1.0
40 – <60th percentile 6.2 – <18.3 ng/mL	154	0.9	0.9 (0.7, 1.1)	10	1.1	0.9 (0.4, 2.0)	96	1.4	1.4 (1.0, 1.8)
60 – <80th percentile 18.3 – <66.4 ng/mL	167	1.0	0.9 (0.7, 1.1)	16	1.7	1.6 (0.8, 3.2)	84	1.3	1.2 (0.9, 1.6)
≥80th percentile 66.4 – 934.3 ng/mL	152	0.9	0.9 (0.7, 1.1)	7	0.7	0.8 (0.3, 1.8)	98	1.5	1.4 (1.1, 1.9)
16 years, n=4,253									
IQR(lnPFOA)[c] increase	536	0.98	0.94 (0.81, 1.10)	32	1.05	1.07 (0.70, 1.64)	288	1.28	1.26 (1.05, 1.51)
100 ng/mL increase	536	1.00	0.99 (0.92, 1.07)	32	0.96	0.96 (0.67, 1.38)	288	1.12	1.12 (1.02, 1.22)
<40th percentile 3.9 – <5.7 ng/mL	213	1.0	1.0	10	1.0	1.0	92	1.0	1.0
40 – <60th percentile 5.7 – <15.6 ng/mL	104	1.0	0.9 (0.7, 1.2)	8	1.6	1.6 (0.6, 4.2)	57	1.2	1.2 (0.8, 1.7)
60 – <80th percentile 15.6 – <55.6 ng/mL	116	1.1	0.9 (0.7, 1.3)	11	2.2	2.4 (0.9, 6.4)	68	1.5	1.4 (1.0, 2.0)
≥80th percentile 55.6 – 934.3 ng/mL	103	1.0	0.9 (0.7, 1.2)	3	0.6	0.6 (0.2, 2.3)	71	1.5	1.4 (1.0, 2.0)

[a] Adjusted for exposure year, maternal age, parity, education level at interview, smoking status at interview

[b] Effect estimates represent the change in outcome for a shift from the 25th percentile to the 75th percentile in estimated PFOA serum levels (IQR (lnPFOA) = 2.27)

[c] Effect estimates represent the change in outcome for a shift from the 25th percentile to the 75th percentile in estimated PFOA serum levels (IQR (lnPFOA) = 2.08)

eTable 3, continued. Crude and Adjusted[a] Association of Estimated Maternal PFOA Serum Concentration with Pregnancy Outcome among Singleton Pregnancies with Varying Duration of Highest Quality Exposure Measures, Mid-Ohio Valley, 1990-2006

	Preterm Birth			Term Low Birthweight			Birth Defect		
	N	Crude OR	Adjusted[a] OR (95% CI)	N	Crude OR	Adjusted[a] OR (95% CI)	N	Crude OR	Adjusted[a] OR (95% CI)
6 years, n=6,358									
IQR(lnPFOA)[b] increase	1011	1.04	0.99 (0.88, 1.11)	76	0.85	0.97 (0.65, 1.43)	247	0.97	0.98 (0.81, 1.19)
100 ng/mL increase	1011	1.00	0.99 (0.94, 1.05)	76	0.89	0.96 (0.78, 1.18)	247	0.96	0.97 (0.88, 1.07)
<40th percentile 3.9 – <6.2 ng/mL	379	1.0	1.0	28	1.0	1.0	97	1.0	1.0
40 – <60th percentile 6.2 – <18.3 ng/mL	232	1.3	1.1 (0.9, 1.3)	19	1.4	1.4 (0.8, 2.5)	53	1.1	1.1 (0.8, 1.5)
60 – <80th percentile 18.3 – <66.4 ng/mL	196	1.1	0.9 (0.7, 1.1)	16	1.1	1.2 (0.6, 2.3)	50	1.0	1.0 (0.7, 1.4)
≥80th percentile 66.4 – 934.3 ng/mL	204	1.1	1.0 (0.8, 1.2)	13	0.9	1.1 (0.5, 2.3)	47	1.0	1.0 (0.7, 1.4)
16 years, n=4,253									
IQR(lnPFOA)[c] increase	696	1.05	0.97 (0.84, 1.11)	45	0.70	0.80 (0.49, 1.29)	171	0.90	0.94 (0.75, 1.18)
100 ng/mL increase	696	1.00	0.99 (0.92, 1.07)	45	0.72	0.79 (0.54, 1.17)	171	0.93	0.94 (0.82, 1.08)
<40th percentile 3.9 – <5.7 ng/mL	259	1.0	1.0	17	1.0	1.0	72	1.0	1.0
40 – <60th percentile 5.7 – <15.6 ng/mL	157	1.3	1.1 (0.9, 1.4)	15	1.9	1.8 (0.9, 3.8)	37	1.0	1.1 (0.7, 1.7)
60 – <80th percentile 15.6 – <55.6 ng/mL	141	1.2	1.0 (0.8, 1.2)	7	0.8	0.8 (0.3, 2.3)	32	0.9	0.9 (0.6, 1.5)
≥80th percentile 55.6 – 934.33 ng/mL	139	1.1	1.0 (0.7, 1.2)	6	0.7	0.9 (0.3, 2.4)	30	0.8	0.9 (0.6, 1.4)

[a] Adjusted for exposure year, maternal age, parity, education level at interview, smoking status at interview

[b] Effect estimates represent the change in outcome for a shift from the 25th percentile to the 75th percentile in estimated PFOA serum levels (IQR (lnPFOA) = 2.27)

[c] Effect estimates represent the change in outcome for a shift from the 25th percentile to the 75th percentile in estimated PFOA serum levels (IQR (lnPFOA) = 2.08)

eTable 4. Crude and Adjusted[a] Association of Estimated Maternal PFOA Serum Concentration with Preeclampsia stratified by year, among Singleton Live Births, Mid-Ohio Valley, 1990-2006

	1990-1994			1995-1999			2000-2005		
Estimated PFOA	N	Crude OR	Adjusted[a] OR (95% CI)	N	Crude OR	Adjusted[a] OR (95% CI)	N	Crude OR	Adjusted[a] OR (95% CI)
IQR(lnPFOA)[b] increase	179	1.05	1.07 (0.85, 1.35)	235	1.18	1.16 (0.94, 1.42)	316	1.20	1.17 (0.97, 1.42)
100 ng/mL increase	179	1.01	1.04 (0.92, 1.17)	235	1.09	1.09 (0.96, 1.24)	316	1.10	1.09 (1.00, 1.19)
<40th percentile 3.9 – <6.8 ng/mL	94	1.0	1.0	75	1.0	1.0	68	1.0	1.0
40 – <60th percentile 6.8 – <16.6 ng/mL	31	1.0	1.0 (0.7, 1.6)	54	1.4	1.3 (0.9, 1.9)	87	1.5	1.5 (1.1, 2.2)
60 – <80th percentile 16.6 – <63.1 ng/mL	18	0.8	0.8 (0.5, 1.3)	52	1.4	1.4 (0.9, 2.0)	84	1.3	1.3 (0.9, 1.8)
≥80th percentile 63.1 – 934.3 ng/mL	36	1.2	1.2 (0.8, 1.9)	54	1.3	1.3 (0.9, 1.8)	77	1.5	1.4 (1.0, 2.0)

[a] Adjusted for exposure year, maternal age, parity, education level at interview, smoking status at interview

[b] Effect estimates represent the change in outcome for a shift from the 25th percentile to the 75th percentile in estimated PFOA serum levels (IQR (lnPFOA) = 2.19)

eTable 5. Crude and Adjusted[a] Association of Estimated Maternal PFOA Serum Concentration with Birth Defects among Singleton Live Births, Mid-Ohio Valley, 1990-2006

	Congenital Heart Defect			Club or Other Foot Defect			Oral Clefts			Genital or Urinary Defect			Eye Defect		
Estimated PFOA	N	Crude OR	Adjusted[a] OR (95% CI)	N	Crude OR	Adjusted[a] OR (95% CI)	N	Crude OR	Adjusted[a] OR (95% CI)	N	Crude OR	Adjusted[a] OR (95% CI)	N	Crude OR	Adjusted[a] OR (95% CI)
IQR(lnPFOA)[b] increase	79	1.27	1.31 (0.95, 1.79)	17	0.99	0.99 (0.46, 2.13)	16	0.91	0.94 (0.44, 1.97)	31	1.23	1.18 (0.76,1.84)	31	1.11	1.06 (0.59,1.93)
100 ng/mL increase	79	1.11	1.13 (0.96, 1.33)	17	0.93	0.94 (0.65, 1.35)	16	0.97	0.97 (0.65, 1.43)	31	1.00	0.98 (0.79, 1.20)	31	1.15	1.15 (0.89, 1.49)
<40th percentile 3.9 – <6.8 ng/mL	25	1.0	1.0	6	1.0	1.0	5	1.0	1.0	12	1.0	1.0	13	1.0	1.0
≥40th percentile 6.8 – 934.3 ng/mL	54	1.4	1.5 (0.9, 2.4)	11	1.2	1.1 (0.4, 3.1)	11	1.5	1.6 (0.6, 4.6)	19	1.0	1.0 (0.5, 2.0)	18	0.9	0.9 (0.4, 1.9)

[a] Adjusted for exposure year, maternal age, parity, education level at interview, smoking status at interview

[b] Effect estimates represent the change in outcome for a shift from the 25th percentile to the 75th percentile in estimated PFOA serum levels (IQR (lnPFOA) = 2.19)

eAppendix 2: Bayesian calibration with a multivariate normal prior distribution and standard calibration methods

Overview

The idea of calibration is to take advantage of the 2005-2006 serum measurements, adjusting the historical exposure estimates to make them more closely match the observed serum concentrations. However, PFOA serum concentrations mostly reflect PFOA exposures experience during the 5 or 10 years prior to the time of measurement, and some participants' water consumption behaviors likely changed after they became aware of local water contamination. Rather than adjusting the entire history of exposure estimates by some constant fraction (a traditional form of calibration), we developed a time-dependent Bayesian calibration that relies on a pharmacokinetic model, resulting in larger adjustments to more recent exposure estimates and smaller adjustments to exposure estimates for years farther in the past.

We performed Bayesian calibration of the annual exposure estimates for each individual, using the annual fate and transport model predictions as the prior mean and the measured 2005-2006 PFOA serum concentration as the updating datum. The model for the likelihood function is a discrete-time single compartment pharmacokinetic model, previously used for PFOA and other contaminants (Bartell et al., 2004; Hoffman et al., 2010; Shin et al., 2011, under review):

$$C_t|I \sim N\left(\sum_{j=1}^{n} w_j I_j, \sigma_\varepsilon^2\right) \sim N(W'I, \sigma_\varepsilon^2)$$

where C_t is the observed serum concentration at the sampling year t, I is an m-length vector of PFOA exposure rates I_j for each year of m years of life, W is a m-length vector of weights w_j

reflecting the relative contribution of PFOA exposure in year *j* to the serum concentration in year *t*, and σ^2_ε is the error variance. The error term is assumed to be normally distributed, and the weights are determined by the following function:

$$w_j = \left(\frac{1-e^{-k}}{k}\right)e^{-k(t-j)}$$

where *k* is an elimination rate constant (= 0.2) corresponding to a half-life of 3.5 years (Olsen et al. 2007).

Prior information from the fate and transport model is incorporated through a multivariate normal prior:

$$I \sim N_m(\mu, \Sigma)$$

where μ is the *m*-length vector of year-by-year fate and transport model based exposure estimates, and $\sum$ is an $m \times m$ covariance matrix describing the prior uncertainty regarding those exposure estimates. The posterior distribution of the exposure vector, determined from the prior and likelihood, is also multivariate normal:

$$I \mid C_t \sim N_m(M, S)$$

where $\mathrm{M} = \mathrm{S}'\Sigma^{-1}\mu + \mathrm{S}'\mathrm{W} \cdot \sigma_\varepsilon^{-2} \cdot \mathrm{C_t} = \mathrm{S}'\left(\Sigma^{-1}\mu + \mathrm{WC_t} \cdot \sigma_\varepsilon^{-2}\right)$

and $\mathrm{S} = \left(\Sigma^{-1} + \mathrm{W} \cdot \mathrm{W}' \cdot \sigma_\varepsilon^{-2}\right)^{-1}$.

We also rely on a prior estimate of σ^2_ε, assumed here to be the square of 10 % of C_t, and $\sum$, assumed here to be a diagonal matrix with variances equal to the square of 400 % of μ. The posterior mean vector, *M*, expresses the calibrated annual exposure estimates for the participant. In some cases *M* includes one or more negative values; we substituted zeros for these values in order to ensure that all annual exposure estimates were non-negative.

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Derivation

Using the fact that posterior probability density (ρ) for the vector of annual exposures is proportional to the product of the prior density (π) and likelihood function (L), we derive the posterior distribution below:

$$\rho(I|C_t) \propto \pi(I) \cdot L(C_t|I)$$

1. Multiply probability density functions of prior and likelihood.

$$\propto \left[|\Sigma|^{-\frac{1}{2}} \cdot e^{-\frac{1}{2}(I-\mu)'\Sigma^{-1}(I-\mu)}\right] \cdot \left[\sigma_\varepsilon^{-1} \cdot e^{-\frac{1}{2}(C_t-W'I)^2/\sigma_\varepsilon^2}\right]$$

2. Drop multiplicative constants ($|\Sigma|^{-\frac{1}{2}}$, σ_ε^{-1}) and combine the two expressions.

$$\propto e^{-\frac{1}{2}\left[(I-\mu)'\Sigma^{-1}(I-\mu) + (C_t-W'I)^2 \cdot \sigma_\varepsilon^{-2}\right]}$$

3. Expand the first term and the square.

$$\propto e^{-\frac{1}{2}\left[(I'\Sigma^{-1} - \mu'\Sigma^{-1})(I-\mu) + C_t^2\sigma_\varepsilon^{-2} - 2C_t \cdot W'I \cdot \sigma_\varepsilon^{-2} + (W'I)^2 \cdot \sigma_\varepsilon^{-2}\right]}$$

4. Expand all terms.

$$\propto e^{-\frac{1}{2}\left[I'\Sigma^{-1}I - 2\mu'\Sigma^{-1}I + \mu'\Sigma^{-1}\mu + C_t^2\sigma_\varepsilon^{-2} - 2C_t \cdot W'I \cdot \sigma_\varepsilon^{-2} + W'I \cdot W'I \cdot \sigma_\varepsilon^{-2}\right]}$$

5. Drop constants $\mu'\Sigma^{-1}\mu + C_t^2\sigma_\varepsilon^{-2}$.

$$\propto e^{-\frac{1}{2}\left[I'\Sigma^{-1}I - 2\mu'\Sigma^{-1}I - 2C_t \cdot W'I \cdot \sigma_\varepsilon^{-2} + W'I \cdot W'I \cdot \sigma_\varepsilon^{-2}\right]}$$

6. Rearrange the terms so as to be combined.

$$\propto e^{-\frac{1}{2}\left[I'\Sigma^{-1}I + I'W \cdot W' \cdot \sigma_\varepsilon^{-2} \cdot I - 2\mu'\Sigma^{-1}I - 2C_t \cdot W'I \cdot \sigma_\varepsilon^{-2}\right]}$$

7. Collect the terms.

$$\propto e^{-\frac{1}{2}\left[I'\left(\Sigma^{-1} + W\cdot W'\cdot\sigma_\varepsilon^{-2}\right)I \; - \; 2\left(\mu'\Sigma^{-1}+C_t\cdot W'\cdot\sigma_\varepsilon^{-2}\right)I\right]}$$

8. Write in a simpler form to see the kernel of an *m*-dimensional multivariate normal distribution.

$$\propto e^{-\frac{1}{2}[X'S^{-1}X - 2M'S^{-1}X]}$$

where

$$S = \left(\Sigma^{-1} \; + \; W\cdot W'\cdot\sigma_\varepsilon^{-2}\right)^{-1}$$

$$M = S'\Sigma^{-1}\mu + S'W\cdot\sigma_\varepsilon^{-2}\cdot C_t = S'\left(\Sigma^{-1}\mu + WC_t\cdot\sigma_\varepsilon^{-2}\right)$$

Thus, the posterior exposure estimates follow a multivariate normal distribution with mean *M* and variance *S*.

Standard calibration

We conducted a limited single-parameter optimization to calibrate groundwater concentrations for six public wells in Shin et al. (2011b), by scaling retrospective predictions by the same multiplicative factor over the entire time course of 1951-2008 in order to best match observed water concentrations in 2000-2008. Here, we refer to that scaling factor approach as "traditional calibration". We computed a multiplicative scaling factor, φ_i, for each participant *i* by the following equation.

$$\varphi_i C_{pred,i,2005} - C_{obs,i,2005}$$

where φ_i is a calibration coefficient for a participant *i*, $C_{obs,i,2005}$ is the observed serum concentration for a participant *i* taken at the serum sampling event in either 2005 or 2006, and $C_{pred,i,2005}$ is the corresponding prediction of the serum concentration for a participant *i* from our exposure and pharmacokinetic models. Since we have one-time observation (t = 2005), φ_i is

simply computed as $C_{obs,i,2005} / C_{pred,i,2005}$ from the above equation and multiplied to prior predicted serum concentration ($C_{pred,i,t}$) to make new predictions. This approach scales the predictions for each participant according to his or her one serum concentration measurement, while retaining the shape of each prediction curve generated from the linked exposure and pharmacokinetic model.

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