SUPPLEMENTAL MATERIAL to:

A Multi-Individual Pharmacokinetic Model Framework for Interpreting Time Trends of Persistent Chemicals in Human Populations: Application to a Post-Ban Situation

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Integration of the Model Equation

Our base model of an average person is represented by the inhomogeneous ordinary differential equation (ODE) given in eq. 2 in the main text (here eq. S1). We integrate it using the method of variation of the constant.

$$\frac{dC(t)}{dt} = -k_{\text{elim}} \cdot C(t) + \frac{U \cdot E_{\text{a}} \cdot I_0}{bw \cdot f_{\text{lipid}}} \cdot e^{-k_{\text{dec}} \cdot t} \qquad \text{eq. S1}$$

To simplify the notation we introduce P_1 as a placeholder constant as:

$$P_1 = \frac{U \cdot E_{\text{a}} \cdot I_0}{bw \cdot f_{\text{lipid}}} \qquad \text{eq. S2}$$

and rewrite eq. S1 as:

$$\frac{dC(t)}{dt} = -k_{\text{elim}} \cdot C(t) + P_1 \cdot e^{-k_{\text{dec}} \cdot t} \qquad \text{eq. S3}$$

As a first step we integrate the corresponding homogeneous ODE by separation of the variables.

$$\frac{dC(t)}{dt} = -k_{\text{elim}} \cdot C(t) \qquad \text{eq. S4}$$

And obtain:

$$C(t) = K \cdot e^{-k_{\text{elim}} \cdot t} \qquad \text{eq. S5}$$

with K being the initial value of eq. S5. We use the method of the variation of the constant to derive the solution of the inhomogeneous ODE.

$$C(t) = K(t) \cdot e^{-k_{\text{elim}} \cdot t} \qquad \text{eq. S6}$$

Taking the derivative with respect to t leads to:

$$\frac{dC(t)}{dt} = \frac{dK}{dt} \cdot e^{-k_{\text{elim}} \cdot t} - k_{\text{elim}} \cdot K(t) \cdot e^{-k_{\text{elim}} \cdot t} \qquad \text{eq. S7}$$

After rearranging eq. S3 to

$$\frac{dC(t)}{dt} + k_{\text{elim}} \cdot C(t) = P_1 \cdot e^{-k_{\text{dec}} \cdot t} \qquad \text{eq. S8}$$

we insert eq. S6 and S7 into eq. S8, and obtain:

$$\frac{dK}{dt} \cdot e^{-k_{\text{elim}} \cdot t} - k_{\text{elim}} \cdot K(t) \cdot e^{-k_{\text{elim}} \cdot t} + k_{\text{elim}} \cdot K(t) \cdot e^{-k_{\text{elim}} \cdot t} = P_1 \cdot e^{-k_{\text{dec}} \cdot t} \qquad \text{eq. S9}$$

Which simplifies to:

$$K'(t) = P_1 \cdot e^{-k_{\text{dec}} \cdot t} \cdot e^{k_{\text{elim}} \cdot t} \qquad \text{eq. S10}$$

To obtain *K(t)*, we integrate eq. S10:

$$\begin{aligned} K(t) &= P_1 \cdot \int e^{-k_{\text{dec}} \cdot t} \cdot e^{k_{\text{elim}} \cdot t} \cdot dt + \alpha = P_1 \cdot \int e^{(k_{\text{elim}} - k_{\text{dec}}) \cdot t} \cdot dt + \alpha \\ &= \frac{P_1}{k_{\text{elim}} - k_{\text{dec}}} e^{(k_{\text{elim}} - k_{\text{dec}}) \cdot t} + \alpha \end{aligned} \qquad \text{eq. S11}$$

with α as an integration constant. After insertion of eq. S11 into eq. S6, we obtain the general solution of the inhomogeneous ODE as:

$$C(t) = \left(\frac{P_1}{k_{\text{elim}} - k_{\text{dec}}} e^{(k_{\text{elim}} - k_{\text{dec}}) \cdot t} + \alpha\right) \cdot e^{-k_{\text{elim}} \cdot t} = \frac{P_1}{k_{\text{elim}} - k_{\text{dec}}} \cdot e^{-k_{\text{dec}} \cdot t} + \alpha \cdot e^{-k_{\text{elim}} \cdot t} \qquad \text{eq. S12}$$

To obtain the particular solution of the inhomogeneous ODE, we use the initial condition $C(t = 0) = 0$ to determine the integration constant, α:

$$C(t = 0) = 0 = \frac{P_1}{k_{\text{elim}} - k_{\text{dec}}} + \alpha \qquad \text{eq. S13}$$

$$\alpha = -\frac{P_1}{k_{\text{elim}} - k_{\text{dec}}} \qquad \text{eq. S14}$$

After insertion of eq. S14 into eq. S12 we obtain:

$$C(t) = \frac{P_1}{k_{\text{elim}} - k_{\text{dec}}} (e^{-k_{\text{dec}} \cdot t} - e^{-k_{\text{elim}} \cdot t}) \qquad \text{eq. S15}$$

Resubstitution of the placeholder constant P_1 leads to the particular solution of the inhomogeneous ODE in the form presented in the main text (eq. 3):

$$C(t) = \frac{U \cdot E_{\text{a}} \cdot I_0}{(k_{\text{elim}} - k_{\text{dec}}) \cdot bw \cdot f_{\text{lipid}}} (e^{-k_{\text{dec}} \cdot t} - e^{-k_{\text{elim}} \cdot t}) \qquad \text{eq. S16}$$

Removable Discontinuities for the Case $k_{elim} = k_{dec}$

Convergence properties of the basic model equation. Eq. S16 exhibits a definition gap for the case $k_{elim} = k_{dec}$. In order to determine the limit of convergence at this specific case, we apply L'Hospital's rule, which is given in general form in eq. S17.

$$\lim_{x \to c} \frac{f(x)}{g(x)} = \lim_{x \to c} \frac{f'(x)}{g'(x)} \qquad \text{eq. S17}$$

If $\lim_{x \to c} f(x) = \lim_{x \to c} g(x) = 0$ or $\lim_{x \to c} g(x) = \pm\infty$

First, we simplify eq. S16 to:

$$C(t) = \frac{P_1}{(k_{elim} - k_{dec})} (e^{-k_{dec} \cdot t} - e^{-k_{elim} \cdot t}) \qquad \text{eq. S18}$$

$$\text{With: } P_1 = \frac{U \cdot E_a \cdot I_0}{bw \cdot f_{lipid}} \qquad \text{eq. S19}$$

To apply eq. S17 to eq. S18 we define: $f(x) = f(k_{elim}) = P_1 \cdot (e^{-k_{dec} \cdot t} - e^{-k_{elim} \cdot t})$ and $g(x) = g(k_{elim}) = (k_{elim} - k_{dec})$ and write:

$$\lim_{k_{elim} \to k_{dec}} \frac{f'(k_{elim})}{g'(k_{elim})} = \lim_{k_{elim} \to k_{dec}} \frac{P_1 \cdot t \cdot e^{-k_{elim} \cdot t}}{1} = P_1 \cdot t \cdot e^{-k_{elim} \cdot t} \qquad \text{eq. S20}$$

This means that for $k_{elim} = k_{dec}$ $C(t)$ is given by $P_1 \cdot t \cdot e^{-k_{elim} \cdot t}$

Convergence properties of the CSTD function. We apply L'Hospital's rule also to eq. 7 in the main publication in order to investigate the convergence properties. We can rewrite eq. 7 using the placeholder constant P_1 to:

$$C^{CSTD}(t^{birth}) = \frac{P_1 \cdot e^{-k_{dec} \cdot t^{birth}} \cdot \left(e^{-k_{dec} \cdot t_c^{age}} - e^{-k_{elim} \cdot t_c^{age}}\right)}{\left(k_{elim} - k_{dec}\right)} \qquad \text{eq. S21}$$

We define:

$$\lim_{k_{\text{elim}} \to k_{\text{dec}}} \frac{f(k_{\text{elim}})}{g(k_{\text{elim}})} = \lim_{k_{\text{elim}} \to k_{\text{dec}}} \frac{P_1 \cdot e^{-k_{\text{dec}} \cdot t^{\text{birth}}} \cdot \left(e^{-k_{\text{dec}} \cdot t_{\text{c}}^{\text{age}}} - e^{-k_{\text{elim}} \cdot t_{\text{c}}^{\text{age}}} \right)}{(k_{\text{elim}} - k_{\text{dec}})} \qquad \text{eq. S22}$$

Applying eq. S17 we obtain:

$$\begin{aligned} \lim_{k_{\text{elim}} \to k_{\text{dec}}} \frac{f(k_{\text{elim}})}{g(k_{\text{elim}})} &= \lim_{k_{\text{elim}} \to k_{\text{dec}}} \frac{f'(k_{\text{elim}})}{g'(k_{\text{elim}})} = \lim_{k_{\text{elim}} \to k_{\text{dec}}} -P_1 \cdot e^{-k_{\text{dec}} \cdot t^{\text{birth}}} \cdot t_{\text{c}}^{\text{age}} \cdot e^{-k_{\text{elim}} \cdot t_{\text{c}}^{\text{age}}} \\ &= -P_1 \cdot e^{-k_{\text{dec}} \cdot t_{\text{c}}^{\text{age}}} \cdot t_{\text{c}}^{\text{age}} \cdot e^{-k_{\text{dec}} \cdot t^{\text{birth}}} \end{aligned} \qquad \text{eq. S23}$$

Convergence properties of the CSD function. Similarly, the equation describing CSD, eq. 9 in the main text, here given as eq. S24, exhibits a definition gap for the case $k_{\text{elim}} = k_{\text{dec}}$.

$$C^{\text{CSD}}(t^{\text{age}}) = \frac{U \cdot E_{\text{a}}}{\left(k_{\text{elim}} - k_{\text{dec}}\right) \cdot bw \cdot f_{\text{lipid}}} \cdot I_0 \cdot e^{-k_{\text{dec}} \cdot t_{\text{m}}} \cdot \left(1 - e^{-(k_{\text{elim}} - k_{\text{dec}}) \cdot t^{\text{age}}}\right) \qquad \text{eq. S24}$$

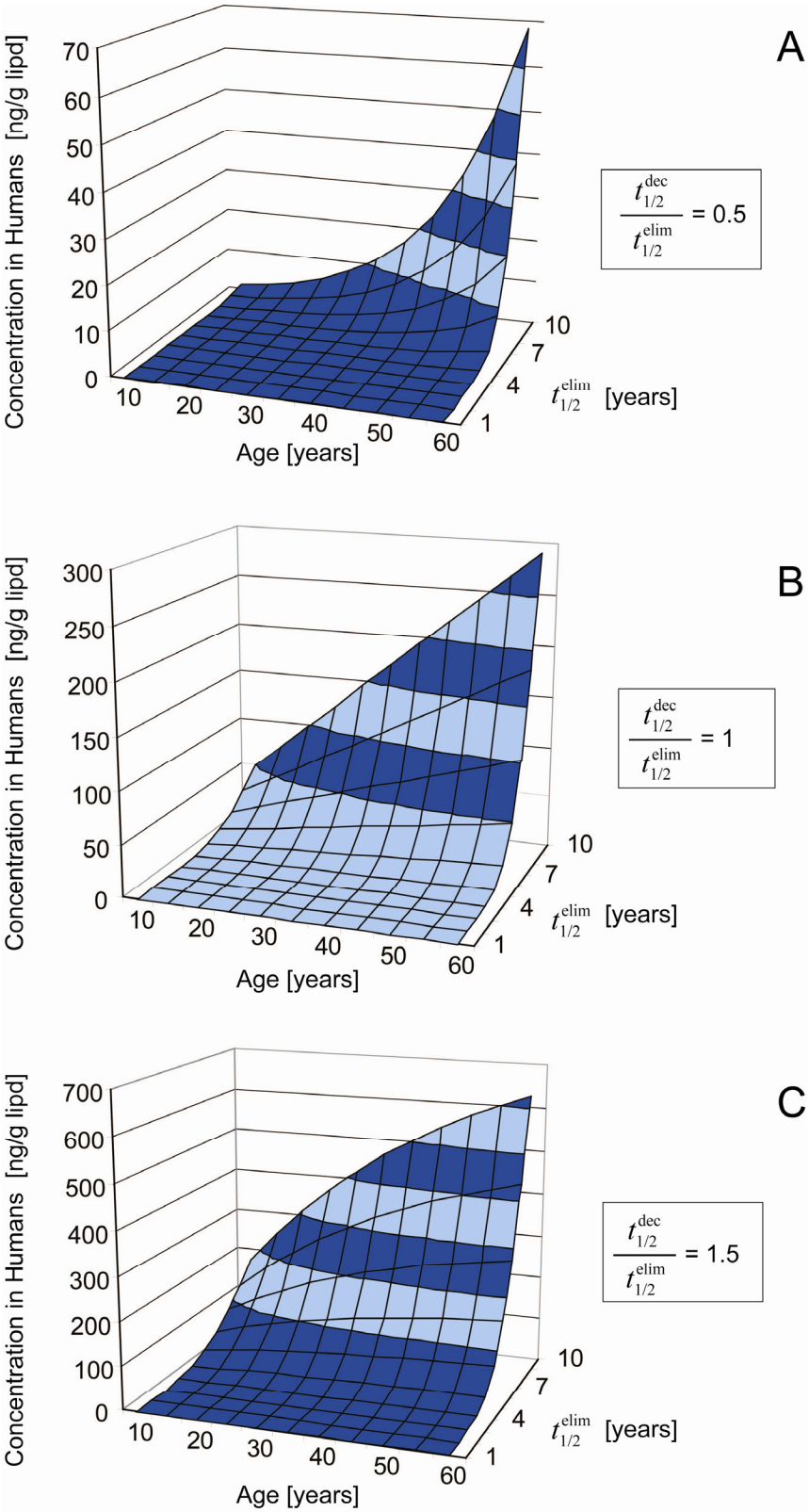
We introduce a placeholder constant, $P_2 = \dfrac{U \cdot E_{\text{a}} \cdot I_0 \cdot e^{-k_{\text{dec}} \cdot t_{\text{m}}}}{bw \cdot f_{\text{lipid}}}$ in order to simplify the notation:

$$C^{\text{CSD}}(t^{\text{age}}) = P_2 \cdot \frac{1}{(k_{\text{elim}} - k_{\text{dec}})} \cdot \left(1 - e^{-(k_{\text{elim}} - k_{\text{dec}}) \cdot t^{\text{age}}}\right) \qquad \text{eq. S25}$$

We again calculate the limit:

$$\lim_{k_{\text{elim}} \to k_{\text{dec}}} \frac{f(k_{\text{elim}})}{g(k_{\text{elim}})} = \lim_{k_{\text{elim}} \to k_{\text{dec}}} P_2 \cdot \frac{1 - e^{-(k_{\text{elim}} - k_{\text{dec}}) \cdot t^{\text{age}}}}{(k_{\text{elim}} - k_{\text{dec}})} = \lim_{k_{\text{elim}} \to k_{\text{dec}}} P_2 \cdot t^{\text{age}} e^{-(k_{\text{elim}} - k_{\text{dec}}) \cdot t^{\text{age}}} = P_2 \cdot t^{\text{age}} \qquad \text{eq. S26}$$

Hence, if $k_{\text{elim}} = k_{\text{dec}}$, the correlation between the body burden and age becomes a linear function. This is illustrated in Figure S1.



Supplemental Material, Figure S1: Properties of the CSD function, $C(t^{age})$, given in eq. 9 in the main text and for the case $k_{elim} = k_{dec}$ given in eq. S26 in this Supplemental Material. For details refer to the text.

Proportionality-Assumption of Background Intake and Body Weight

Breast-feeding causes an important increase in the dietary intake of persistent organic pollutants (POPs) of infants. As a consequence, large differences in the concentration of POPs between breast-fed children and formula-fed children can be observed. However, these differences have been shown to level out between the age of 10 and 20 years (Verner et al. 2008). In contrast to the "peak" intake during the period of breast-feeding, background intake is usually assumed proportional to the body weight, i.e. it is expressed in units such as [ng kg bw^{-1} day^{-1}] (e.g. Verner et al. 2008). Using P_3 as a placeholder constant, we restate eq. S1 as follows:

$$\frac{dC(t)}{dt} = -k_{\text{elim}} \cdot C(t) + P_3 \cdot \frac{I_0}{bw} \cdot e^{-k_{\text{dec}} \cdot t} \qquad \text{eq. S27}$$

$$with: P_3 = \frac{U \cdot E_{\text{a}}}{f_{\text{lipid}}} \qquad \text{eq. S28}$$

In our formulation, the term $\frac{I_0[\text{ng} \cdot \text{person}^{-1} \cdot \text{day}^{-1}]}{bw[\text{kg} \cdot \text{person}^{-1}]}$ represents intake and body weight of an average adult person. Hence, I_0 and bw are both constants. Alternatively, the differential equation can also be formulated with the body weight being a function of time (i.e. age). However, since background intake is assumed to be proportional to the body weight, background intake would increase with time as body weight does and the ratio of I_0 and bw would again be constant.

Sources of Empirical Data

Supplemental Material, Table S1. Measurements in humans of p,p'-DDE and p,p'-DDT used to assemble CSTD

Chemical	Country	Sampling Period	Tissue	*N*	Concentration (mean or median) [ng/g lipid]	Age Structure [years]	Source/ References	Remarks
p,p'-DDE	UK	1990-91	adipose tissue	19 [1)]	584[1)]	20-41 [1)]	Duarte-Davidson et al. 1994	Welsh population
p,p'-DDE	UK	1997-98	human milk	168	283	17-39	Harris et al. 1999	14 Hospitals in England, Wales, Scotland and Northern Ireland
p,p'-DDE	UK	2001-03	human milk	54	150	24-34	Kalantzi et al. 2004	Lancaster and London
p,p'-DDE	UK	2003	blood serum	76	68.5	22-40[2)]	Thomas et al. 2006	13 regions across the UK
p,p'-DDT	UK	1990-91	adipose tissue	75[3)]	27[3)]	14-79 [3)]	Duarte-Davidson et al. 1994	Welsh population
p,p'-DDT	UK	1997-98	human milk	168	4.8 [4)]	17-39	Harris et al. 1999	14 Hospitals in England, Wales, Scotland and Northern Ireland
p,p'-DDT	UK	2001-03	human milk	54	6.2	24-34	Kalantzi et al. 2004	Lancaster and London
p,p'-DDT	UK	2003	blood serum	76	2.1	22-40[2)]	Thomas et al. 2006	13 regions across the UK
p,p'-DDE	Sweden	1996	human milk	20	159 [5)]	28.8	Glynn et al. 2007 (Report)	Primiparous women from Uppsala County
p,p'-DDE	Sweden	1997	human milk	67	137 [5)]	28.8	Glynn et al. 2007 (Report)	Primiparous women from Uppsala County
p,p'-DDE	Sweden	1998	human milk	90	119 [5)]	28.8	Glynn et al. 2007 (Report)	Primiparous women from Uppsala County
p,p'-DDE	Sweden	1999	human milk	26	108 [5)]	28.8	Glynn et al. 2007 (Report)	Primiparous women from Uppsala County
p,p'-DDE	Sweden	2000-01	human milk	29	90 [5)]	28.8	Glynn et al. 2007 (Report)	Primiparous women from Uppsala County
p,p'-DDE	Sweden	2002-03	human milk	31	68.6 [5)]	28.8	Glynn et al. 2007 (Report)	Primiparous women from Uppsala County
p,p'-DDE	Sweden	2004	human milk	32	69.5 [5)]	28.8	Glynn et al. 2007 (Report)	Primiparous women from Uppsala County
p,p'-DDE	Sweden	2006	human milk	30	81.6 [5)]	28.8	Glynn et al. 2007 (Report)	Primiparous women from Uppsala County

Table S1. (continued)

p,p'-DDT	Sweden	1996	human milk	20	11.2 [5)]	28.8	Glynn et al. 2007 (Report)	Primiparous women from Uppsala County
p,p'-DDT	Sweden	1997	human milk	67	14.4 [5)]	28.8	Glynn et al. 2007 (Report)	Primiparous women from Uppsala County
p,p'-DDT	Sweden	1998	human milk	90	7.9 [5)]	28.8	Glynn et al. 2007 (Report)	Primiparous women from Uppsala County
p,p'-DDT	Sweden	1999	human milk	26	5.8 [5)]	28.8	Glynn et al. 2007 (Report)	Primiparous women from Uppsala County
p,p'-DDT	Sweden	2000-01	human milk	29	6.1 [5)]	28.8	Glynn et al. 2007 (Report)	Primiparous women from Uppsala County
p,p'-DDT	Sweden	2002-03	human milk	31	4.5 [5)]	28.8	Glynn et al. 2007 (Report)	Primiparous women from Uppsala County
p,p'-DDT	Sweden	2004	human milk	32	5.2 [5)]	28.8	Glynn et al. 2007 (Report)	Primiparous women from Uppsala County
p,p'-DDT	Sweden	2006	human milk	30	4 [5)]	28.8	Glynn et al. 2007 (Report)	Primiparous women from Uppsala County

[1)] Data subset for ΣDDT with women aged between 20-41 years was used to better reflect the age-structure of the other studies included in the CSTD (Data where extrapolated from the graph)
[2)] Data subset with women aged between 22-40 years was used to better reflect the age-structure of the other studies included in the CSTD (Data kindly provided by the authors)
[3)] Calculation of data-subset with a reduced range in individual's ages (as in [1)]) was not possible based on the published data
[4)] Only 3.6% of data were over the limit of detection (LOD); we used substitution with half LOD and the median of the detects to approximate the value
[5)] Numerical values from Figure 4, p. 15, of Glynn et al. (2007) have been kindly provided by the authors

Supplemental Material, Table S2. Sources of empirical estimates for the dietary intake of p,p-DDE, p,p-DDT and ΣDDT

chemical	country	year	daily intake per person [ng/person/day]	references	remarks
ΣDDT	Sweden	1975	4400	Vaz et al. 1995	Food from animal origin
ΣDDT	Sweden	1980	3000	Vaz et al. 1995	Food from animal origin
ΣDDT	Sweden	1985	2100	Vaz et al. 1995	Food from animal origin
ΣDDT	Sweden	1990	2200	Vaz et al. 1995	Food from animal origin
ΣDDT	Sweden	1999	523	Darnerud et al. 2006	Market-based data
ΣDDT	Sweden	2005	292	Ankarberg et al. 2006 (Report)	Market-based data
p,p'-DDE	Sweden	1999	306	Darnerud et al. 2006	Market-based data
p,p'-DDE	Sweden	2005	210	Ankarberg et al. 2006 (Report)	Market-based data
ΣDDT	UK	1965	56000	Robinson and McGill 1966	
ΣDDT	UK	1966-1967	44400	Abbott et al. 1969	
ΣDDT	UK	1970-1971	15000	Egan et al. 1977	
ΣDDT	UK	1974-1975	12000	Egan et al. 1977	
ΣDDT	UK	1980	3000	Kannan et al. 1997	
ΣDDT	UK	1985	3000	Kannan et al. 1997	
ΣDDT	UK	1984-1985	500	Food Standard Agency 2002	
ΣDDT	UK	1989-1990	100	Food Standard Agency 2002	
ΣDDT	UK	1996-1997	300	Food Standard Agency 2002	
p,p'-DDE	UK	1966-1967	23800	Abbott et al. 1969	Approximated by the difference of ΣDDT and p,p'-DDT intakes
p,p'-DDE	UK	1970-1971	8500	Egan et al. 1977	Approximated by the difference of ΣDDT and p,p'-DDT intakes
p,p'-DDE	UK	1974-1975	9200	Egan et al. 1977	Approximated by the difference of ΣDDT and p,p'-DDT intakes
p,p'-DDE	UK	1984-1985	500	Food Standard Agency 2002	Identical values as ΣDDT have been reported
p,p'-DDE	UK	1989-1990	100	Food Standard Agency 2002	Identical values as ΣDDT have been reported
p,p'-DDE	UK	1996-1997	300	Food Standard Agency 2002	Identical values as ΣDDT have been reported
p,p'-DDT	UK	1966-1967	20600	Abbott et al. 1969	
p,p'-DDT	UK	1970-1971	6500	Egan et al. 1977	
p,p'-DDT	UK	1974-1975	2800	Egan et al. 1977	

Model Parameterization for the DDT Case Studies (Sweden and UK)

Table S3 lists human elimination half-lives, $t_{1/2}^{elim}$, for p,p'-DDE and p,p'-DDT as inferred from CSTD sets from Sweden and the UK according to the procedure described in the main text. CSTD from different countries were fitted with eq. 7 in the main text, which yields k_{dec} and $t_{1/2}^{dec} = \ln 2/k_{dec}$. Table S3 further lists model parameters specific to each set of CSTD and used in the estimation procedure, such as daily-intake at time t_0, I_0, the year of ban, and the characteristic age, t_c^{age}. The following standard parameterization has been applied in all model calculations: bw = 70 kg, f_{lipid} = 0.25 (Alcock et al. 2000; Aylward and Hays 2002), and E_a = 0.9 (Moser and McLachlan 2001).

Supplemental Material, Table S3. Country-specific input parameters and estimated elimination half-lives for Sweden and the UK.

chemical	country	year of ban [years]	t_0 [years]	I_0 [ng/person/day]	t_c^{age} [years]	$t_{1/2}^{dec}$ [years]	$t_{1/2}^{elim}$ **[years]**
p,p'-DDE	Sweden	1970	1967	4000	29	8.8	**6.2**
p,p'-DDE	UK	1964/84[1)]	1961	42000	30	4.3	**7.6**
p,p'-DDT	Sweden	1970	1967	3000	29	6.3	**2.2**
p,p'-DDT	UK	1964/84[1)]	1961	33000	30	4.1	**2.1**

[1)] Severely restricted in 1964/ officially banned in 1984 (Gillespie et al. 1994)

In the case study the model framework has been employed to estimate human elimination half-lives, $t_{1/2}^{elim}$, from CSTD sets and empirical intake estimates from Sweden and the UK. Elimination half-life estimates from both countries compare well and are consistent with estimates based on longitudinal data for DDT and DDE (see main text). Consistency between estimates of $t_{1/2}^{elim}$ that are based on CSTD from different countries is expected since elimination is a process determined by human physiology and the properties of the chemical to be eliminated. The population exposure half-life, $t_{1/2}^{dec}$, in contrast, shows larger differences between both countries. This is plausible because many different environmental (e.g. initial contamination, climate) and behavioral factors (e.g. different dietary habits) determine the

daily intake of a population. These factors are likely to differ between populations in different countries.

Negligible Conversion to p,p'-DDE Within the Human Body

The applications of the model to p,p'-DDE assumes negligible conversion of p,p'-DDT to p,p'-DDE within the human body. This assumption is based on experimental data that demonstrated that conversion p,p'-DDT to p,p'-DDE is extremely limited in the human body (Morgan and Roan 1971). As a result, p,p'-DDE in the human body is mainly derived from intake of DDE previously degraded in the environment (Kutz et al., 1976).

Properties of the CSD Function

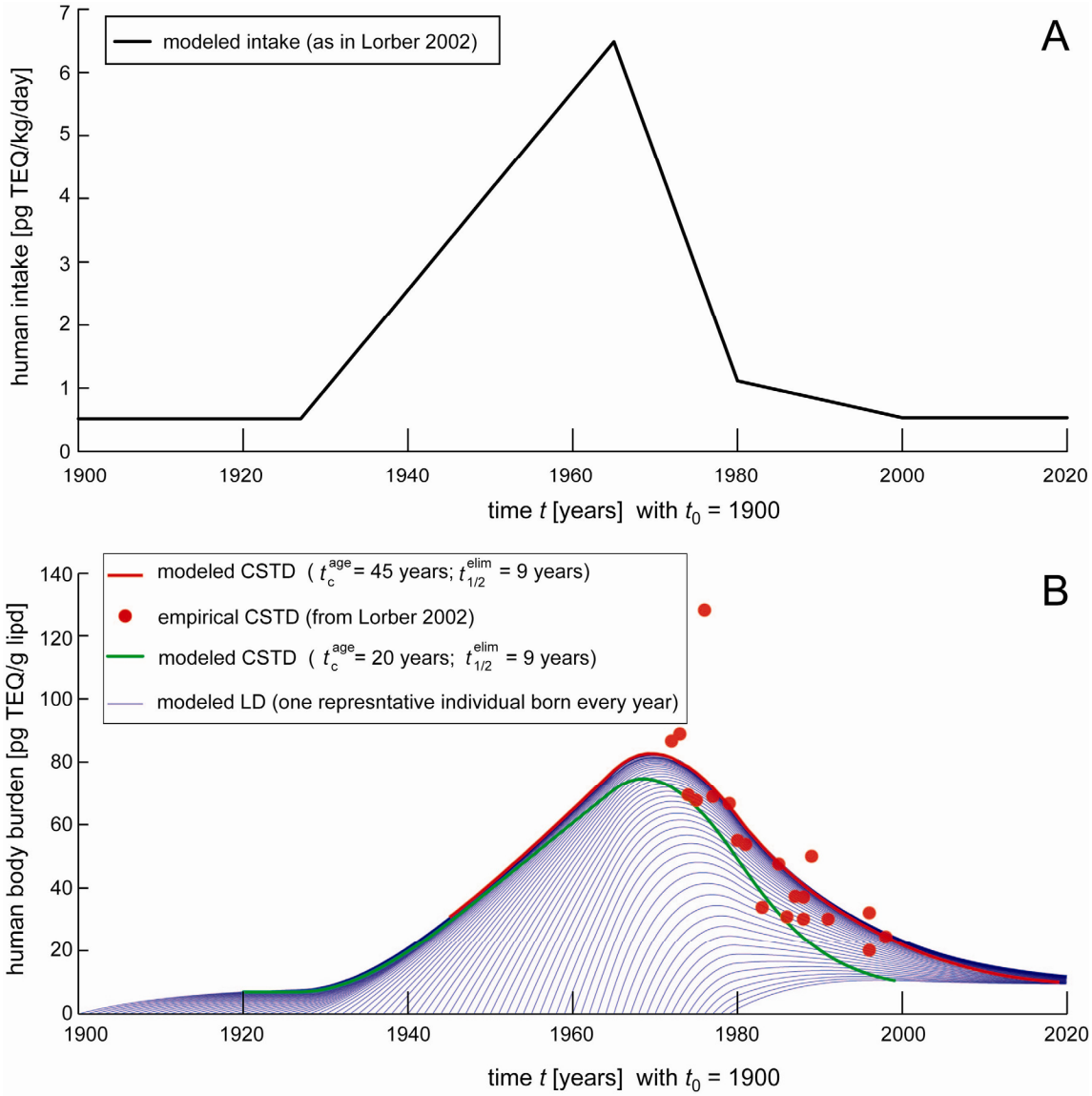
Figure S1 illustrates that the relationship between body burden and age as described by eq. 9 in the main text (eq. S24 in this Supplemental Material) is not only determined by the human elimination half-life alone. The elimination half-life determines the general strength of this relationship: the larger $t_{1/2}^{\text{elim}}$, the more the concentration or body burden increases with increasing age. However, the shape of this relationship is determined by the relative size of the population exposure half-life, $t_{1/2}^{\text{dec}}$, and the human elimination half-life. Three cases can be distinguished: (i) if $t_{1/2}^{\text{dec}}$ is smaller than $t_{1/2}^{\text{elim}}$ (e.g. $t_{1/2}^{\text{dec}} / t_{1/2}^{\text{elim}} = 0.5$), a convex non-linear relationship is observed (Panel A of Figure S1). (ii) if $t_{1/2}^{\text{dec}} = t_{1/2}^{\text{elim}}$, a linear relationship is observed (Panel B of Figure S1), which has been formally demonstrated in eq. S26. (iii) if $t_{1/2}^{\text{dec}}$ is larger than $t_{1/2}^{\text{elim}}$ (e.g. $t_{1/2}^{\text{dec}} / t_{1/2}^{\text{elim}} = 1.5$), a concave non-linear relationship is observed. In practice, linear regression is often used to interpret the age-concentration relationship (e.g. Hue et al. 2007; Thomas et al. 2006). Different modeling studies have also obtained concave non-linear relationships (Alcock et al. 2000; Moser and McLachlan 2002).

Generalization of the Model Framework

In the main text we present explicit analytical solutions to our multi-individual PK model framework that are obtained under the assumption of exponentially declining intakes, which is empirically observed for persistent organic chemicals in a post-ban phase (Morisawa et al. 2002; De Mul et al. 2008). However, our conceptual model-framework is not limited to this case and can be applied to any intake function if the model equations are integrated numerically. To provide an example of this type of application, we use the intake function for intake of dioxin-like compounds reported by Lorber (2002), which is given in Figure S2A below. Lorber (2002) uses a multi-individual PK modeling approach where population averages of chemical concentrations are calculated as the average TEQ from 11 individuals aged 20 to 70 years with an average age of 45 years. To reproduce this case, we parameterize our model by using 45 years as the characteristic age, $t_{\mathrm{c}}^{\mathrm{age}}$. Furthermore, Lorber (2002) uses age-dependent elimination kinetics in his model. We parameterize our model with the approximate average elimination half-life, $t_{1/2}^{\mathrm{elim}}$, of 9 years for a 45 year old person according to Lorber (2002). Figure S2B shows longitudinal data for individuals born in different years (shown by blue thin lines in Figure S2B; plotted for illustrational purposes) and CSTD obtained under the intake trend plotted in Figure S2A. The CSTD obtained from the model exactly reproduce the "population body concentration" obtained by Lorber 2002 (red curve in Figure S2B); this curve is identical to the curve in Figure 7 of the publication by Lorber (2002), p. 92. This demonstrates that our framework can be used to model CSTD from a population that experiences a "complex" intake trend including a pre-ban phase.

In addition to reproducing the case reported by Lorber (2002) we have also plotted the CSTD obtained from our model with a characteristic age of 20 years instead of 45 years (green curve in Figure S2B). This shows that in a mixed pre-ban and post-ban case a change in the characteristic age influences the slope of the CSTD curve. (An additional analysis in the log-

space shows that the slope of the logarithmic form of the green line in Figure S2B is steeper than that of the red line). This is in contrast to the parallel shift of the CSTD curve (no change of slope) that is observed for a pure post-ban case if the characteristic age is changed (see Figure S2A in the main text). Similarly, a change in elimination half-life (e.g. using 2 years instead of 9 years) affects the slope of the CSTD curve in the log-space whereas, in a pure post-ban case, it causes a parallel shift of the CSTD line, see Figure S2A in the main text. This demonstrates that the slope of CSTD under a "complex" intake scenario (i.e. including pre-ban intake) reflects influences of the intake trend, the elimination half-life and the characteristic age of the sampled population. The relative contribution of either of these parameters will depend on the temporal course of the "complex" intake scenario.



Supplemental Material, Figure S2. Application of our multi-individual model framework to a more general intake function $I(t)$ taken from Lorber (2002). A: intake function $I(t)$, taken from Figure 6 of Lorber (2002, p. 91). B: empirical body burden data from Lorber (2002) (red dots), model results for longitudinal data of individuals born every year (blue lines), model results for cross-sectional trend data (CSTD) for a characteristic age of 45 years (red line) and for a characteristic age of 20 years (green line).

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