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Polychlorinated biphenyl (PCB) half-lives in humans: A systematic review

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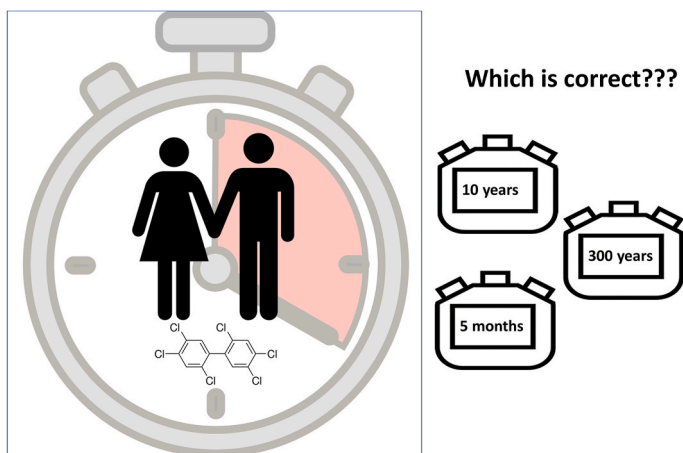
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HIGHLIGHTS

- Reported half-lives for the same PCB can vary by nearly 4 orders of magnitude.
- Half-lives in highly exposed individuals are shorter than those in the general population.
- Manuscript provides harmonization of half-life terminology.
- Apparent half-life is reflective of observed changes in PCB blood concentrations over time.
- Intrinsic half-life accounts for the effects of ongoing exposure and several factors.

GRAPHICAL ABSTRACT



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ABSTRACT

This manuscript presents a systematic review of PCB half-lives reported in the scientific literature. The review was completed in accordance with PRISMA guidelines and included a review of almost 1000 peer-reviewed publications. In total, 26 articles were found to report half-lives in humans, with the majority of data coming from studies performed in North America on individuals suspected to have been exposed to PCBs. Terminology for reporting PCB half-lives was inconsistent, so we have attempted to consolidate this and recommend using either “apparent half-life” or “intrinsic half-life” in future studies. Within the literature, values for reported half-lives varied considerably for different PCBs. Less chlorinated PCBs generally have shorter half-lives than more chlorinated PCBs. It was interesting to note the large variability of half-lives reported for the same PCB. For example, the reported half-life for PCB 180 varied by nearly 3 orders of magnitude (0.34 years–300 years).

Our review identified that the half-lives estimated were largely dependent on the studied cohort. We discuss the importance of PCB body burden, degree of chlorination and PCB structure, gender, age, breastfeeding, BMI, and smoking status on half-life estimations. We also identified significantly shorter half-lives for some PCBs in

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occupationally exposed individuals compared to results reported from the general population. PCB half-lives are not the same for every PCB or every individual. Therefore, careful consideration is needed when these values are used in human exposure studies.

1. Introduction

Polychlorinated biphenyls (PCBs) are some of our most extensively studied environmental pollutants. They are stable compounds containing one to ten chlorines with a general formula, $C_{12}H_{10-x}Cl_x$. PCBs are lipophilic with varying solubility in fats, oils, and organic solvents but low solubility in water. They are semi-volatile, are found in the atmosphere, and can be transported over long distances in the air (Carlsson et al., 2018; Uhl et al., 2012). PCBs have also been shown to bioaccumulate through food chains and have been found in humans all over the globe (Breivik et al., 2002a, 2002b, 2007; Beyer and Biziuk, 2009; Fernandez-Gonzalez et al., 2015). The manufacturing of PCBs as technical mixtures started in the 1920s (Johnson et al., 2006), and production was phased out in the US in the late 1970s (US EPA, 1976). There are also releases from inadvertently produced PCBs, such as in the production of paints and pigments and waste incineration and electrical waste (Anh et al., 2021; Carpenter, 2015; Hannah et al., 2022). The increased importance of by-product PCBs (PCBs formed inadvertently in chemical processes) is widely reported in the recent scientific literature (Panero et al., 2005; Herkert et al., 2018; Megson et al., 2022, 2023).

PCBs are still routinely detected in humans (Esser et al., 2021a; Björvang et al., 2021; Plaku-Alakbarova et al., 2021). There are three primary routes of exposure: ingestion, inhalation, and dermal contact. The main recognized route of exposure to PCBs is through diet (Duar-te-Davidson and Jones, 1994). Dietary exposure to PCBs occurs primarily by ingesting high-fat foods such as dairy products, eggs, fish, and wildlife. Although the environmental release of PCBs from technical mixtures is at an all-time low, attention has been given to inhalation from environmental exposures, especially for occupants living or working in contaminated buildings in recent years (Johansson et al., 2003; Schettgen et al., 2012a; Meyer et al., 2013; Hornbuckle, 2022; Herkert et al., 2018). Dermal exposure occurs through direct contact with contaminated surfaces. Due to the lipophilic nature of PCBs, they can be absorbed when in touch with the skin. This route of exposure can be a concern for workers who are in close contact with surfaces with oils containing PCBs or their family members who are in contact with their clothing or office gear (Schettgen et al., 2012b). Historically, there have been several instances where humans have been exposed to elevated concentrations of PCBs in their workplace. Exposure to PCBs at the workplace is referred to as occupation exposure. This exposure is relevant in workers occupying PCB-contaminated buildings or workers of capacitor or waste recycling plants (Megson et al., 2015; Esser et al., 2021a, 2021b; Quinete et al., 2017; Seegal et al., 2011; Brown and Lawton, 2001; Aylward et al., 2014). Historical incidents of accidental exposure through diet have been reported in Yusho, Japan, in 1968 and Yucheng, Taiwan, in 1979, after thousands of people consumed rice oil contaminated with PCB (Kashimoto et al., 1985; Miyata et al., 1985; Masuda et al., 1985). In addition to occupational and incidental exposures, there are also general population (background) exposures due to the global presence of PCBs. These are the normal, everyday background levels of PCBs found in humans (ATSDR, 2000).

PCBs are biotransformed and eliminated from humans by activating the P450 cytochrome system. This eliminates PCBs from the body as they are transformed into more water-soluble derivatives (Letcher et al., 1999; Sandau, 2001). The presence of certain chemicals (including PCBs themselves) can activate the P450 cytochrome system to increase the rate PCBs are removed from the body. This removal rate is estimated as a half-life (the number of years for PCB concentration to decrease by half). Initial studies evaluating the removal rates of PCBs in humans were reported based on the commercial mixtures of PCBs rather than

individual PCBs congeners (Steele et al., 1986). However, later studies focusing on individual PCB congeners show that the half-life of individual PCB congeners can vary widely depending on their degree of chlorination and the position of chlorination. The half-life will also vary in individuals based on their age, lifestyle, gender, dietary habits, living environment, and occupation (Axelrad et al., 2009; Brown and Lawton, 2001; Jain and Wang, 2011; Weintraub and Birnbaum, 2008; Megson et al., 2013). This has resulted in a wide range of different PCB half-life values quoted in the scientific literature and the use of various terminologies to define half-life. As a result, it is now recognized that the half-life of PCBs in humans is complex and highly dependent on variable parameters that are influenced by several factors (Shirai and Kissel, 1996).

This study aims to summarise the current knowledge on PCB half-lives in humans. A systematic literature review was performed to comprehensively record and review PCB half-lives and cohort information documented in the scientific literature. This study documents: publication trends, reported half-lives, half-life terminologies, factors affecting half-lives, methods for calculating half-lives, and a comparison of half-lives from exposed and background or general population exposed cohorts.

2. Methods

2.1. Study selection

Scientific manuscripts were selected following the guidelines set by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Page et al., 2021). Manuscripts were identified from two different search engines, Scopus and Web of Science, using a combination of keywords “polychlorinated” AND “biphenyls”, “half” AND “lives”, “half” AND “life” and “human” (and not “cancer” for Web of Science). Google Scholar was used to cross-check any papers that may have been missed during the initial two searches. However, as Google Scholar delivered over 18,000 hits, only the first ten (10) pages (One hundred (100) papers) were screened.

Studies were included for this review based on the following inclusion criteria: studies were published in English, were on PCBs (no other POPs were included in this review), and they estimated PCB half-lives and/or past or future PCB concentrations. Manuscripts were also included if they estimated PCB elimination rates. Manuscripts were collected from all years up until June 2023. Studies were excluded if they were not peer-reviewed (grey literature), not written in English, or not available online. Data was not collated for studies that estimated average PCB concentrations or half-lives based on the sum of several PCB congeners. In total, 966 articles were identified, 874 were excluded from a review of the title, 6 were excluded from the review of the abstract, and 7 were excluded following a review of the entire manuscript. These manuscripts were excluded as a review of the title/abstract/body revealed that they were not relevant as they did not include information on polychlorinated biphenyl half-lives. This resulted in 26 manuscripts for inclusion in this review (Fig. 1).

2.2. Data collection

For all 26 studies included in the final review, general information was collected, including the author(s), the year the study was published, title, journal name, issue, volume, and page numbers (where applicable), and source (Scopus, Web of Science, Google Scholar or other). Information was also collected on; the study area (country), study

population including ethnicity (where specified) and occupation/industry (where appropriate), year(s) of data collection, age(s) and age group of participants, number of participants, gender, cohort/exposure type (e.g., background, occupational exposure), the specific PCBs included in the study, the terminology used in the study to describe the half-life and, the sample matrix. This data is presented in the supplementary information (S.I. 1a).

In addition to general information, data was collected on; the concentration of PCBs reported (S.I. 1b), the apparent half-lives (S.I. 1c), the intrinsic half-life (S.I. 1d), and elimination rates (S.I. 1e). There was a lack of consistency in reporting PCB half-life units across the scientific literature. Some literature reported in days and months, while the majority were reported in years. To allow for easier comparison of datasets, units were recorded and converted into one standard unit (where possible). A unified unit, years, was used for half life values, and all data is presented in an Excel spreadsheet in the supplementary information (S.I. 1b, S.I. 1c, S.I. 1d).

3. Results and discussion

3.1. Publication trends

Twenty-six (26) manuscripts were identified that satisfied the search terms outlined in the methodology. Half-life data has been reported in individuals from 13 different countries (S.I. 1a & Fig. 2). Most research has focused on economically developed Western countries, with no data reported for Africa or South America. Half-life data on U.S. participants have been most often studied (7 studies), with 4 studies from Germany and 3 from Japan and Taiwan. One study has been performed in each; Australia, Canada, the Faroe Islands, Slovakia, China, the Czech Republic, Sweden, Switzerland, and the U.K.

Most studies (85%; $n = 22$) measured PCB concentrations in blood (including plasma/serum); 3 studies included breast milk, and 2 used adipose tissue samples. Data from the literature search were obtained from individuals from a wide age range, including babies of 0 to older

adults (80+ yrs old). The fewest participants in a study was 1 participant (Ryan et al., 1993; Masuda, 2001), with many other studies containing several hundred to thousands of participants (S.I. 1a). Half-lives were reported for 43 different PCBs (S.I. 1c & d) and elimination rates reported for 145 different PCBs (S.I. 1e).

3.2. Reported half-lives

Half-lives have been reported for PCB Aroclors and individual congeners; however, only half-lives for individual congeners have been considered. Due to analytical limitations, it is impossible to separate all 209 PCBs in one analytical run; therefore, some co-elutions have been reported. These co-elutions were not consistent across the manuscripts included for review. Data for unique individual PCBs or combinations of co-eluting PCBs have been recorded. This resulted in the generation of reported half-lives for 43 unique PCBs (or PCB co-elutions), presented in Table 1.

It is important to note that an individual's PCB body burden is a product of multiple years of varying exposure and a lifetime of varying elimination rates. Different PCB congeners have different persistence in humans, reflected in their half-lives. This review identified considerable variability in reported half-lives within the scientific literature. This has been summarised in Table 1, which displays the lowest, highest, and average reported half-lives. For some PCBs, the reported half-lives were reasonably consistent (e.g., PCB 44 and PCB 66); however, in each of these cases, this is because these half-lives have only been reported a handful of times. For more widely studied PCBs (e.g., PCB 180), the half-lives reported can differ by nearly three orders of magnitude (e.g., 0.34 years–300 years).

3.3. Half-life terminology

Half-life is the time required to reduce or eliminate a toxicant to one-half its level at initial measurement (Hallare and Gerriets, 2020). The elimination is commonly predicted based on compound-related

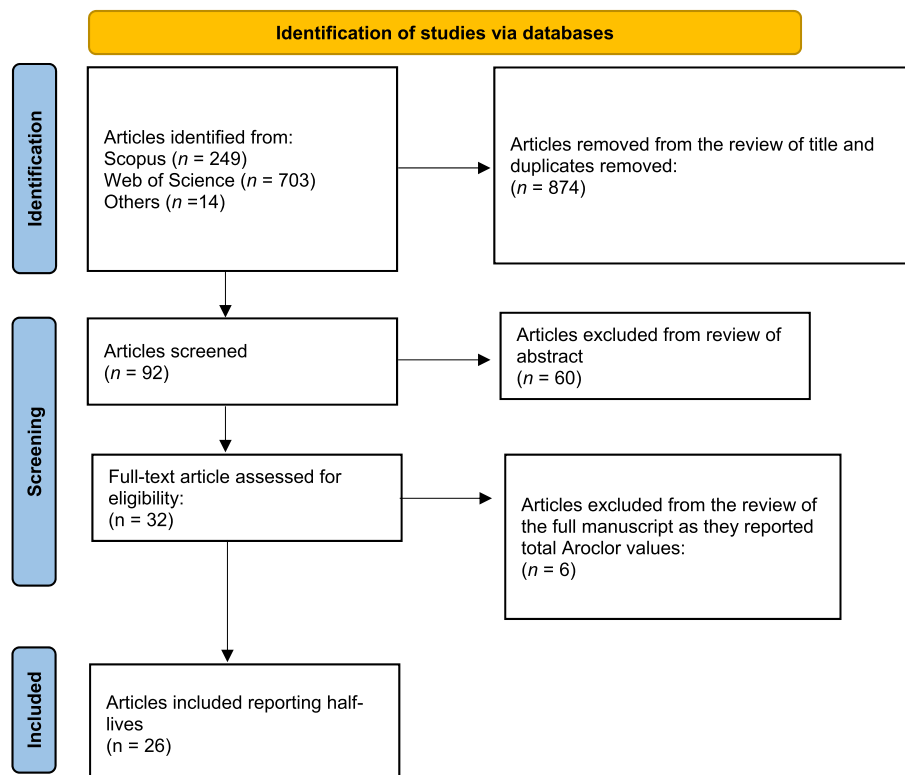


Fig. 1. Flow chart of manuscript identification, screening, and final selection process.

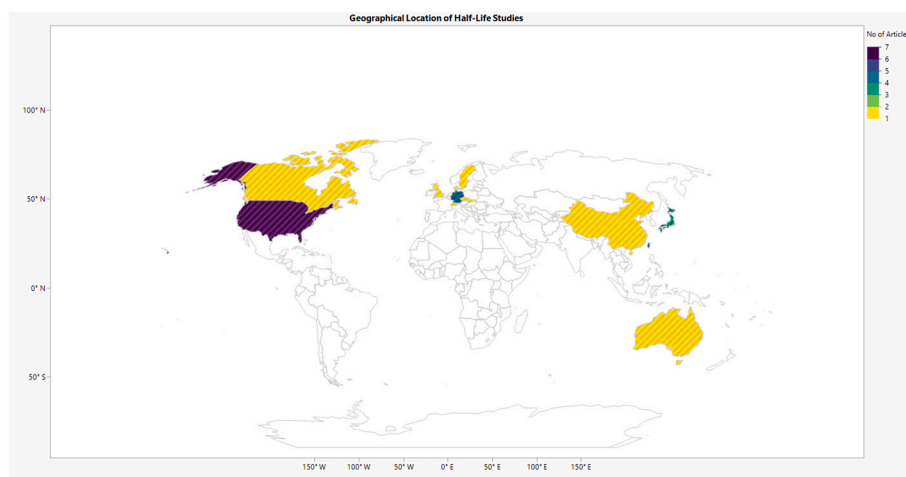


Fig. 2. The geographical location of half-life studies.

pharmacokinetics and host-related factors, which affects the rate of metabolism (Gallo et al., 2015). PCBs can be eliminated via metabolic transformation, respiratory elimination, fecal egestion, renal excretion, and reproductive losses. Growth dilution is also a factor that affects the elimination of PCBs in the body. However, this factor is usually observed more when comparing the PCB concentrations in infants and adolescents. It is a pseudo-elimination process, as the PCB body burden obtained in the follow-up measurement is not eliminated (Gascon et al., 2015). Still, the difference is a function of biomass/body weight changes (Arnot et al., 2014).

Manuscripts included in this review have reported half-lives from two main data categories: measurements from the same individual (longitudinal data) and population biomonitoring data from many individuals at a point in time (cross-sectional data). In longitudinal or cross-sectional human biomonitoring, PCB half-lives are estimated by analyzing PCBs in biological matrices: blood/serum/plasma, adipose tissue, and breast milk. Initially, half-lives of PCB Aroclors were estimated from individuals with a high workplace or accidental exposure (Chen et al., 1982; Yakushiji et al., 1984; Steele et al., 1986). In this situation, ongoing exposure to PCB from the environment (background level exposure) was considered to have a negligible impact on that group. A negative correlation has been observed between the estimated half-life and initial PCB blood concentration (Shirai and Kissel, 1996). High initial blood concentration due to high exposure results in a shorter half-life due to rapid elimination rates, while lower concentrations are associated with longer half-lives. Hence, it can be said that elimination rates of PCBs from the human body are highly concentration dependent. Liver enzymes increase the elimination rate of PCB congeners because they are induced (upregulated) in high-exposure scenarios. Therefore, there are significant differences in the elimination rates observed in a highly exposed individual compared to background-level exposure. For example, PCB 153 half-life values were lower in an exposed cohort reported by Esser et al. (2021a) and Grandjean et al. (2008) (9 years and 8.40 years, respectively) than those reported for low background exposed cohorts reported by Ritter et al. (2011) and Bu et al. (2015) (13.8 years and 17 years respectively). The liver enzyme induction was higher in the exposed groups causing PCBs to be eliminated quicker, resulting in faster half-lives.

Terminologies referring to half-lives are used interchangeably in the literature. These include half-life, biological half-life, apparent half-life, relative half-life, true half-life, total/overall half-life, reduction half-life, biotransformation half-life, terminal half-life, intrinsic half-life, population half-life, and estimated half-life. The inconsistent reporting of half-life terminologies from the literature poses a challenge when comparing half-life values. Variations observed in half-life terminologies

stem from the understanding that some studies consider continuous/ongoing exposure and confounding factors between the initial and follow-up measurement. The influence of these factors affects the true elimination assumption as it pertains to half-life definition. Therefore, the half-life for this same PCB congener varies from one cohort to another when not corrected for these confounding factors. For this reason, we have re-classified half-lives from the literature and sorted them into two groups based on the following terms: “apparent” and “intrinsic” half-lives (S.I. 1c and S.I. 1d). Shirai and Kissel (1996) first attempted to define “apparent” and “true” half-lives because it was recognized that failure to account for continuing exposure could produce high half-life estimates. However, Ritter et al. (2011) introduced the term “intrinsic” half-life rather than “true” half-life, as used in Shirai and Kissel (1996). An apparent half-life estimates reflect observed changes in PCB blood concentrations in one individual over time. The changes in concentration, from the initial to the follow-up measurement, do not account for ongoing exposure or other factors that could have increased or reduced the observed concentration at the follow-up measurement. Therefore, the combined effect of ongoing exposure (environmental, dietary), body composition changes (weight, height, BMI), and additional factors such as smoking status or parity are all included in the estimated half-life. Because these factors vary from one individual or group to another, the half-life estimate obtained for each PCB congener does not represent the ‘true’ half-life value for the congener. This accounts for the considerable variation in reported apparent half-lives from different studies.

According to Ritter et al. (2011), intrinsic half-lives represent half-life estimates with methods that account for effects of ongoing exposure and changes in body weight. Effects of ongoing exposure and different factors e.g., diet, smoking, or lactation, could lead to preferential elimination or persistence of some PCB congeners, which leads to inaccurate estimation of half-life. When these are accounted for, the precise half-life estimate for such PCB congener is obtained.

Based on this definition, most half-lives reported in the literature are regarded as apparent, especially when the half-life for the analyte is long in a low background or general population exposed group. Apparent half-life estimates have been widely reported and may either over- or under-estimate the intrinsic elimination rates for such compounds. The concern over the effect of continuous exposure and varying elimination that is dependent on individual’s lifestyle has led to some beliefs that it is difficult to present a reliable half-life estimation from longitudinal data, hence a preferred estimate from cross-sectional data. However, it is challenging to also estimate half-life values from background or general exposure using cross sectional data. The background levels of lower chlorinated PCBs are usually not detected in plasma samples in general

Table 1

Summary of estimated half-lives in the scientific literature.

PCB Congeners	Lowest reported half-life	Highest reported half-life	Average of reported half-lives	Factor the difference between the lowest and highest estimate	Number of times reported
PCB28	0.5	6.7	3.6	13	26
PCB44	1.6	1.7	1.6	1	3
PCB47 + 48+52	2.9	15.5	8.0	5	3
PCB47	0.3	0.3	0.3	1	1
PCB52	0.8	12.51	3.6	16	16
PCB66	2	3.1	2.6	2	9
PCB72	0.98	1.3	1.2	1	4
PCB74 + 66	∞	∞	∞	NA	4
PCB74	0.74	124.9	19.7	169	13
PCB 77	NA	0.74	0.2	NA	6
PCB81	NA	1.7	1.0	NA	7
PCB95 + 56+60	1.9	4.3	2.9	2	4
PCB95	0.4	0.4	0.4	NA	1
PCB99 + 101	3.9	8.1	6.1	2	4
PCB99	2.8	15	8.7	5	9
PCB101	1.2	1.3	1.2	1	4
PCB105	0.1	46.5	6.1	465	33
PCB114	0.5	25	13.8	50	15
PCB108/ 118	0.27	0.82	NA	3	2
PCB118	0.2	33.7	7.7	169	57
PCB122	4.6	4.6	4.6	NA	1
PCB123	0.4	12	6.5	30	11
PCB126	0.1	4.5	2.8	45	9
PCB128	5.2	5.4	5.3	1	2
PCB128 + 183	7.9	65	37.6	8	3
PCB138	0.88	40	12.2	45	38
PCB138 & 158	9.6	9.6	9.6	NA	1
PCB138 & 163 & 164	22.32	22.32	22.3	NA	1
PCB 138 & 163	5.82	27.75	13.6	5	7
PCB146	21	21	21.0	NA	1
PCB153 + 105	∞	∞	∞	NA	4
PCB153	0.93	47	12.4	51	43
PCB156	0.9	90.1	15.4	100	36
PCB 156 & 171	5.15	6.46	5.8	1	2
PCB157	1	27	14.7	27	15
PCB167	0.7	14.5	8.4	21	15
PCB169	0.4	13	8.5	33	9
PCB170	3.4	443.7	40.0	131	25
PCB171	7.4	24	15.7	3	2
PCB171 + 156	4.41	4.41	4.4	NA	1
PCB180	0.34	300	26.8	882	36
PCB187	5.9	15	9.3	3	6
PCB189	1.2	41	17.2	34	15

population (Esser et al., 2021b), especially as new cross-sectional dataset emerges in human biomonitoring studies. Low detection challenges were initially attributed to limitation in analytical techniques in the past, however, with advancement in analytical instrumentation, the low detection observed is now largely due to reduction in environmental emission of PCBs.

Based on our reclassification of half-life literature values reported in all articles for this review, twenty-one (21) manuscripts reported apparent half-lives for a total of thirty-nine (39) PCBs, and eleven (11) manuscripts reported intrinsic half-lives for a total twenty-seven (27)

PCBs. It is to be noted that some literature, Ritter et al. (2011), Esser et al. (2021a) reported both apparent and intrinsic half-lives. Most commonly reported half-lives are from blood/plasma/serum; studies in each dataset were collated to compare these methods. When comparing the two datasets, apparent half-lives were generally lower than intrinsic half-lives (Fig. 3). However, a two-sample *t*-test showed no statistically significant difference between half-lives estimated by either method (at a 95% confidence level). It is possible that no significant differences could be established due to small sample sizes as only 1 or 2 intrinsic half-lives have been reported for several PCBs.

When reviewing the scientific literature, we identified some manuscripts that should be used cautiously when conducting human exposure assessments. Most manuscripts in this study reported PCB half-lives on a congener-specific basis. However, some manuscripts reported Aroclor half-lives, Yakushiji et al. (1984), Steele et al. (1986), Phillips et al. (1989), Taylor and Lawrence (1992), and Hopf et al. (2013). Caution is advised when using half-lives obtained from Aroclors to predict past exposure. Any exposure results from multiple sources or mixtures of PCBs, e.g., Aroclor mixtures, which include different arrays of PCB congeners. Caution is also advised when using half-lives estimated from the Finland study by Luotamo et al. (1991), as this study reported extremely low values for each congener in their exposed cohort. The blood samples in this cohort were taken shortly after exposure at the pulp mill (between days 1 and 30). According to Shirai and Kissel (1996), if blood/adipose equilibrium had not been reached at the time of first collection, the apparent rapid loss reported could simply result from redistribution. Half-lives of individual PCB congeners from participants in the Finland study are reported in Shirai and Kissel (1996). The values obtained from Brown (1994) were estimated from various sources, including data from rats, fish, and mice. While this manuscript provides excellent coverage of PCBs (145 out of the 209 PCB congeners), uncertainties in the reported elimination rates must be carefully considered before these values are adopted. The manuscript was essential for identifying broad structural activity relationships (SARs) in the 1990s, but its direct adoption to estimate human half-lives will have associated uncertainties.

3.4. Factors affecting half-lives

Biotransformation and elimination is a highly complex process that can be impacted by different factors that can alter the half-life of PCBs. Differences in the half-life terminology, e.g., intrinsic, apparent half-lives, and reported values of PCB congeners, have been attributed to several factors. It is clear that different PCB congeners will exhibit varying elimination or clearance rates due to their peculiar chemical properties, which differ from one congener to the other because of various substitutions on their biphenyl backbone ring. However, there are a large number of additional confounding factors that can affect the half-lives reported in different cohorts or individuals. These factors include total PCB concentration (body burden), gender, age, breast-feeding, BMI (correlated to body fat), and smoking status. Unfortunately, it was impossible to use our compilation of half-life data reported in the literature to undertake a robust statistical analysis to confirm the importance of each factor. This was because there were too many variables in each different study that were not always appropriately reported. Rather than perform statistical analysis, we have provided a commentary with key links to the scientific literature where each factor has been considered in detail.

Concentration/Body Burden: PCB elimination is known to be concentration dependent, commonly dependent on the duration of exposure. For example, in the case of accidental/incidental exposure to high concentrations (within a short time), the elimination rate is faster (Yakushiji et al., 1984; Ryan et al., 1993). Organochlorine compounds are known to up-regulate the cytochrome P450 enzymes responsible for their elimination in the body, and this has been shown in several studies (Shirai and Kissel, 1996; Milbrath et al., 2009; Ryan et al., 1993).

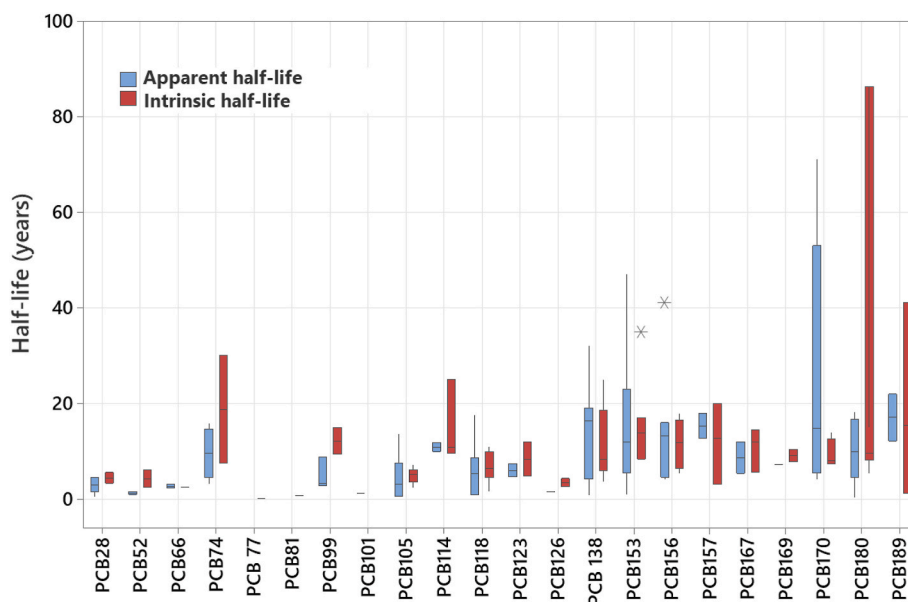


Fig. 3. Comparison of apparent and intrinsic half-lives.

Degree of chlorination and PCB structure: Prediction of the residence times of individual congeners based on the position of chlorine atoms on the biphenyl have been discussed by Brown (1994). Less chlorinated PCBs have shorter half-lives than more chlorinated PCBs (Seegal et al., 2011). PCB congeners with chlorine bonding in the 2,5- and 2,3,6- positions (and 2- in di- and tri-chlorinated congeners) are susceptible to biotransformation and elimination. They will likely have shorter half-lives (Hansen, 2001; Megson et al., 2013). PCBs with chlorine bonding in the 2,3,4-, 2,4,5-, 3,4,5-, and 2,3,4,5- positions are often more resistant to biotransformation and elimination and so are likely to have relatively longer half-lives (Hansen, 2001; Megson et al., 2013).

Gender: Several studies have shown that the concentration of PCBs in male participants in studies is higher than in female participants. There have not been many studies focusing on estimating the half-life of PCBs in gender, nor have there been clear explanations for gender-related differences when observed, although some have attributed PCB blood concentration difference in women to pregnancy and lactation. Two studies in our review, Hopf et al. (2013) and Seegal et al. (2011), reported gender-based half-life estimates. Although Hopf et al. (2013) reported half-life values based on Aroclor and not individual PCB congeners, half-life estimates for sera from female participants were generally longer than those from male participants. Seegal et al. (2011) half-lives were about 1.5 times longer in women than in men in former capacitor workers.

Age: The relationship between age and half-life is complex because age is strongly associated with other factors affecting PCB half-lives in humans, e.g., smoking status and percent body fat (Milbrath et al., 2009). In a background or general population exposure, a strong positive correlation has been observed in various studies between age and PCB serum concentration. A similar observation has been reported with half-lives too, PCB congeners tend to have longer half-lives in older individuals than younger individuals (Gao et al., 2019). This relationship has been previously assumed to reflect the role of age in bio-accumulation, however, this does not hold true. According to Ritter et al. (2011) and Quinn and Wania (2012), age-concentration dependencies are highly correlated to exposure during the PCB preban and the postban. Individuals who were adults during the PCB preban period experienced a high exposure without the mitigating effect of growth dilution. Their longer intrinsic half-life was attributed to the “memory effect” of past exposure. Although individuals in the postban period benefited

from the declining exposure trend, as the postban period becomes longer, the corresponding larger part of the adult population shows an increase when compared to the younger ones (Quinn and Wania, 2012; Malarvannan et al., 2009). Due to the declining exposure trend in the aging population, there is likely a decrease in enzyme activity compared to their initial high exposure period. The reduction in the elimination rate in adults can further be attributed to changes in organ sizes and redistribution of body fat, which results in the redistribution of lipophilic chemicals like PCB. In children, pseudo-elimination of PCB occurs due to growth; however, the effect of elimination on apparent half-life becomes more critical than that of dilution (Milbrath et al., 2009).

The differences in factors that influence PCB serum concentration and half-lives of the adult and younger population make it challenging to compare. Hence, accounting for these factors through the estimation of half-life using intrinsic calculation will likely make the half-lives of both populations comparable.

In this review, half-lives were reported for adolescents, young, and old adults, some reporting intrinsic half-lives with age as a co-factor. Caution is advised when comparing apparent half-lives obtained from the elimination rates of adolescents and young adults to older adults because a proportion of the reduction in PCB concentration observed in adolescents and young adults is due to growth dilution. Three studies presented half-lives for adolescents and young adults aged 4.5–21 (Grandjean et al., 2008; Gallo et al., 2015; Wimmerová et al., 2011). Grandjean et al. (2008) expressed half-life in two cohorts of Faroe Islands children exposed to high PCB concentration through their diet from whale blubber. The initial age of evaluation for the first cohort was 4.5 years with follow-up analysis carried out at 7.5 years while the initial sample for the second cohort was obtained when the children were age 7 with a follow-up at 14 years old. The younger cohort was observed to have shorter PCB half-lives compared to the older group. This can be explained based on the accumulation rate of PCBs in their respective age groups. Studies have suggested increased PCB concentration from birth, primarily due to maternal transfer (breastfeeding) to about four years in both exposed and background or general populations, and a decrease until teenage years attributed to growth dilution. However, the body burden remains high (Gascon et al., 2015). Gallo et al. (2015) estimated half-life from the Mohawk Adolescent Well-Being Study (MAWBS) (ages 10–17 years) and Young Adults Well-Being Study (YAWBS) (17–21 years). The intrinsic half-life reported for PCB 153 using linear regression was 13.18 years, but when respondents with increased levels were

eliminated, PCB 153 half-life was 5.5 years. In Slovak children environmentally exposed to PCB due to industrial production of PCBs in Michalovce, Wimmerová et al. (2011) estimated half-life using PCB serum concentration in children measured at the age of 8 and 12 years. This is a similar age range to the second cohort of the Faroe Islands children reported by Grandjean et al. (2008). The reported half-life for PCB 153 reported for both studies is similar for their respective age groups. Wimmerová et al. (2011) reported 9.37 years for Slovak children while Grandjean et al. (2008) stated that half-life is 8.90 years for Faroese children. Further comparing apparent half-life reported in children/young adults, PCB 153 has a higher half-life as reported by Gallo et al. (2015) estimated PCB 153 in their study as 14.13 years while Wimmerová et al. (2011) mean half-life value was 11.48 years. Using this data, the apparent half-life values reported in children are similar to the intrinsic values reported in the exposed adult population reported by Esser et al. (2021a). The same is observed for PCB 118. The intrinsic half-lives range from 3.63 to 5.70 years for young/adolescents, similar to the intrinsic half-life reported in exposed adults reported by Esser et al. (2021a). However, because intrinsic half-life considers different confounding factors, similarities between adolescent/young adult and adult is expected. Huge differences will occur when comparing apparent half-lives.

Breastfeeding: Breastmilk has a relatively high-fat content; hence, lipophilic compounds such as PCBs from the mother will be transferred to the milk. Lactation/breastfeeding is considered one of the elimination routes of PCBs in women due to its ability to transfer PCBs from the mother to the infant. Landrigan et al. (2002) estimated that up to twenty percent (20%) or more of the maternal body burden could be transferred. The transfer of PCBs from the mother's serum to breastmilk is influenced by several factors, including the congener, maternal body burden, molecular weight and diameter, lipophilicity, and duration of breastfeeding (Wittsiepe et al., 2007). Studies have shown that the half-life of PCB congeners in the serum of lactating women is shorter than that of non-lactating women. Although there is no standard method for determining a chemical's half-life as a function of breastfeeding, two studies in this review reported half-lives in breast milk. The half-lives of PCBs in breast milk show the preferential elimination of reported PCB congeners from the blood through lactation (Schectet et al., 1998). Norén and Meironyté (2000) indicated differences in the half-lives of specific congeners in breast milk. The half-life for PCB 153 was reported as 17 years, PCB 138 was 14 years, and PCB 118 was estimated at 11 years. Mikeš et al. (2012) reported a half-life of 11.4 years for PCB 118, which was approximately two-fold higher than the average half-life of 5.86 years reported by Ogura (2004).

BMI: Due to the lipophilic properties of PCBs, they are known to accumulate in fatty tissues such as the adipose layer or body fat in humans. The adipose tissue serves as a storage for lipophilic compounds due to limited transportation to excretory and metabolizing organs. Individuals with high BMIs are known to have more adipose tissue. This can result in a higher body burden for organic compounds like PCBs and a likely influence on the serum concentration and congener half-lives. Grandjean et al. (2008) show that increased BMI was associated with decreased serum congener concentrations, however, there has not been a defined relationship between BMI and PCB congener half-lives as a moderate correlation was reported. Wolff et al. (2000) found a strong correlation between BMI and half-life in their control group for their study while Seegal et al. (2011) did not observe a relationship in their study.

Smoking: Smoking status is a confounding factor; active smokers have lower PCB levels than non-smokers or passive smokers. Milbrath et al. (2009) attributed this observation to a preferential increased induction of degrading enzymes or through a combination of other physiological effects. Smoking has been shown to induce the activity of cytochrome P450 enzymes, which are responsible for the metabolism of lipophilic compounds such as PCBs. This increased metabolism can result in a shorter half-life of PCB congeners in individuals who smoke

than those who do not. In addition to influencing the metabolism of PCB congeners, smoking may also affect the elimination of these compounds from the serum. However, establishing a positive or negative relationship between smoking status and preferential elimination of PCBs is still challenging, results of smoking-related enzyme induction are not very clear (Moon et al., 2017).

Other substances that selectively up-regulate CYP1A1 and CYP1A2 isozymes on chronic ingestion and may lead to increased metabolism of those PCB congeners that are substrates for the induced P450 enzymes are cruciferous vegetables such as cabbage, broccoli, cauliflower, Brussels sprouts (James et al., 2008) and caffeine (Jain and Wang, 2011). Jain and Wang (2011) observed a marked difference based on caffeine consumption frequency for each PCB group in the general U.S. population, NHANES 2003–2004 data.

Sample Matrix: PCB congener half-lives can be estimated from different biological matrices. Half-lives have been estimated from plasma/serum, breast milk, and adipose tissue in humans. The estimation of half-lives for PCB congeners in different matrices may vary based on several factors. Due to their lipophilic nature, PCBs accumulate in adipose (fat) tissue. They are distributed to all body parts from adipose tissue according to the equilibrium mediated by blood transport. The partitioning from adipose tissue to blood serum is related to the lipid content of the blood because PCBs bound to blood lipids, phospholipids, albumin, and macromolecular components of blood serum (Waliszewski et al., 2000; Brown Jr and Lawton, 1984). Due to the relatively high-fat content, PCBs are also transferred into breast milk. Their levels in milk have been strongly correlated to the fat content of milk (Norén and Meironyté, 2000). Hence, adipose tissue, blood, or breast milk are appropriate surrogates to estimate half-lives of congeners in the human body (Ogura, 2004). Based on our review, most PCB half-lives (22 out of 26 studies) are estimated from blood serum samples (SI 1a – Characteristics). It was not possible to perform a robust comparison of half-lives estimates from the different sample matrices as only one study reported PCB congener half-lives in blood, adipose tissue, and breast milk (Ogura, 2004). However, some half-life estimates obtained from the adipose tissue were longer than the comparative values estimated from breast milk and blood. For example, the half-life of PCB 189 and 156 in adipose tissue is almost twice as high as the value obtained from blood. A comprehensive evaluation of the differences between half-lives from the difference matrices will be important while evaluating the factors responsible for disparities. Since most existing studies have shown the suitability of blood serum for half-life estimation, future studies would benefit from using serum as a matrix as there are more studies for comparison.

3.5. Methods of calculating half-lives

Different procedures have been employed to estimate half-lives of PCB in humans. These procedures rely on longitudinal or cross-sectional data obtained from exposure (Yakushiji et al., 1984; Seegal et al., 2011; Esser et al., 2021a) and general biomonitoring studies (Ritter et al., 2011; Bu et al., 2015). The most common methods are the one-compartment or two-compartment pharmacokinetic (P-K.) models. The one-compartment model assumes that a single compartment represents the distribution of PCBs in the body and that the elimination follows first-order kinetics. In contrast, the two-compartment pharmacokinetic model considers that PCBs can be distributed to different body tissues and organs and eliminated from central and peripheral compartments. Other approaches include the use of stable isotope-labeled PCBs, ^{13}C - and ^{12}C -PCB, as reported in Bühler et al. (1988), physiologically based pharmacokinetic (PBPK) models Karmaus et al. (2004), and the use of biomarkers of exposure, e.g., PCB congeners or their metabolites (Quinete et al., 2017).

There are limitations to the one- and two-compartment models. First, these models assume a linear relationship between the concentrations of PCBs in the serum, their elimination rate, and an assumption

of the homogenous distribution of the congeners in the body. However, it is commonly recognized that PCBs preferentially accumulate in lipophilic tissues in the body. Hence, they are not homogeneously distributed in the body. Also, it is essential to note that each PCB congener eliminates at different rates; therefore, they have differing half-lives. Thus, determining congener-specific half-lives is preferred in determining PCB half-life instead of an Aroclor determination.

The most common approach used by manuscripts in this review was to utilize longitudinal data to estimate the elimination rate constant under an assumed exponential decay model to describe the metabolism/excretion of PCBs in humans, as defined by Friedman (1979). C_t is the concentration at time t , C_0 is the initial concentration measured in the study, and k is the elimination/velocity of steady state adjustment constant. k , the elimination/decay constant, is determined as the slope of the linear regression.

$$C_t = C_0 \times e^{-kt} \quad (1)$$

The estimation of elimination is assumed to follow first-order kinetics. Earlier studies did not account for ongoing exposure or parity; hence, only the reported intake and first-order loss were considered as the case of the one-compartment pharmacokinetic model. It is well known that half-life estimates will be artificially high if they fail to account for ongoing exposure and the effect of host-related factors on elimination (Shirai and Kissel, 1996; Gallo et al., 2015). Equation (1) transforms into Equation (2), commonly used in cohort studies.

$$\ln C_0 - \ln C_t = k \times t \quad (2)$$

Different authors have different estimates of the concentration of PCBs, C_0 and C_t . These include the use of the mean (Chen et al., 1982; Wimmerova et al., 2011; Esser et al., 2021a), median (Sjödén et al., 2004; Schettgen et al., 2012a), and geometric mean (Wolff et al., 1992; Seegal et al., 2011; Quinete et al., 2017). According to Seegal et al. (2011), median and geometric mean are commonly recommended by authors because these two estimators are often very close in value.

The elimination constant/coefficient (k) is defined in different studies to include the linear regression slope (Esser et al., 2021a) or the linear regression without the intercept (Quinete et al., 2017). These are the approaches commonly adopted in estimating apparent half-life, as reported by Taylor and Lawrence (1992), Shirai and Kissel (1996), and Esser et al. (2021a). Aylward et al. (2014), in the estimation of the apparent half-life in their study, estimated elimination rates based on the concentration and mass of the body.

For intrinsic half-life, the Ritter population-based pharmacokinetic model is widely referenced in studies determining intrinsic half-life (Ritter et al., 2011). Some of these studies include Arnot et al. (2014), Bu et al. (2015), Gao et al. (2019), and Quinn and Wania (2012). The Ritter-based approach describes changes in body concentration of PCBs as a function of age and calendar time for multiple individuals representing different birth cohorts of the average population. Equation (3) defines the time course of PCB concentration in one representative individual born at a time.

$$\frac{dC(t_{age})}{dt_{age}} = - \left(k_{elim} + \frac{1}{M_{lip}(t_{age})} \times \frac{dM_{lip}(t_{age})}{dt_{age}} \right) \times C(t_{age}) + \frac{I(t_{age}, t_{birth=constant})}{M_{lip}(t_{age})} \quad (3)$$

where t_{age} (years) is the age of the individual, $C(t_{age})$ (nanogram per gram lipid) is the lipid-normalized concentration of a chemical in the body under the assumption that the chemical is present only in the lipid compartment of the body, $M_{lip}(t_{age})$ (kilograms lipid) is the mass of total body lipid as a function of age, k_{elim} (years⁻¹) is the first-order rate constant describing intrinsic elimination, and $I(t_{age}, t_{birth=constant})$ (ng \times year⁻¹ \times kg lipid \times g lipid⁻¹) is the exposure trend of the representative average individual born at t_{birth} which is described in terms of age-

and calendar-time-dependent daily intake of chemicals.

Gao et al. (2019) examined the function between the elimination rate and age using three models to estimate intrinsic: the constant, linear, and exponential models (Equations (4)–(6)). This is similar to Esser et al. (2021a), where exponential regression was applied to develop an equation for estimating the age-depended share of the plasma levels.

Constant model

$$k_{elim}(t_{age}) = k_1 \quad (4)$$

Linear model

$$k_{elim}(t_{age}) = k_1 - k_2 \times t_{age} \quad (5)$$

Exponential model

$$k_{elim}(t_{age}) = k_1 \times e^{-k_2 \times t_{age}} \quad (6)$$

The study of a toxicokinetic model of PCB elimination in people working in a contaminated building in Germany defined k as the constant for the velocity of steady state adjustment. The constant, k , was calculated to build a model for the mean concentration as a function of employment duration. Grandjean et al. (2008) adjusted for possible confounding effects caused by age-related differences in distribution volumes and the body mass index (BMI) (Equation (7)).

$$\ln Y_{t1} - \ln Y_{t2} = k(t_2 - t_1) + c[\ln(BMI)_{t2}] + \ln(BMI)_{t2} + \varepsilon_{t1} - \varepsilon_{t2} \quad (7)$$

where t_1 and t_2 is the age at the first and second examinations, respectively, k is the coefficient of the age increase in a simple regression model without an intercept, and ε is the variance of the error dependent on the cohort. Additional covariates, weight, and serum lipid concentration were added to Equation (7) to test if BMI provided an adequate description of the changes in distribution volume. As highlighted in Grandjean et al. (2008), this approach was used to estimate intrinsic half-life in Wimmerová et al. (2011). In the estimation of changes in PCBs from adolescence to young adulthood by Gallo et al. (2015), a censored normal regression model to account for ongoing exposure was proposed to offer a conceptual match to the problem of estimating intrinsic elimination rate. This procedure treated individuals with a non-positive difference in log-transformed concentrations between initial and follow-up individuals as censored observations using serum concentrations thought to follow an exponential decay.

After the consideration of different covariates to obtain that rate of elimination/rate constant, k , the half-life $t_{1/2}$ of individual PCB congener is estimated as:

$$t_{1/2} = \frac{\ln 2}{k} \quad (8)$$

3.6. Occupational versus non-occupational exposure

One factor affecting the half-life estimate of PCBs in humans is concentration/body burden (Milbrath et al., 2009), which varies on the degree and duration of exposure. Everybody is exposed to some level of PCBs in the environment, called background or general population exposure. However, some high levels of exposure can also occur due to accidental contamination of a food source or workplace exposure to PCBs, termed occupational exposure. Occupational PCB exposure can occur in various industries, including electrical equipment manufacturing, paper and pulp production, and waste management plants. Other occupational exposure includes exposure in contaminated offices or school buildings. In these settings, individuals are exposed through all exposure routes: inhalation, dermal contact, and likely ingestion. Individuals with occupational exposure to PCBs tend to have higher levels of PCB congeners in their serum than those without similar exposure (Seegal et al., 2011; Esser et al., 2021a; Schettgen et al., 2012a; Broding et al., 2007). We collated all commonly reported half-lives from blood/plasma/serum studies to assess this (see Table 2). We grouped

Table 2
Comparison of reported half-lives based on exposure source.

	Occupational exposure				General population				Accidental/environmental exposure				Dietary exposure			
	Lowest reported half-life	Highest reported half-life	Average reported half-life	number of times reported	Lowest reported half-life	Highest reported half-life	Average reported half-life	number of times reported	Lowest reported half-life	Highest reported half-life	Average reported half-life	number of times reported	Lowest reported half-life	Highest reported half-life	Average reported half live	number of times reported
PCB28	0.500	6.60	3.56	11	5.50	5.60	5.55	2	not measured				not measured			
PCB44	1.60	1.60	1.60	1	not measured				not measured				not measured			
PCB47 + 48+52	5.50	5.50	5.50	1	not measured				not measured				not measured			
PCB47	0.300	0.300	0.300	1	not measured				not measured				not measured			
PCB52	1.00	6.07	2.51	4	2.60	2.60	2.60	2	not measured				not measured			
PCB66	2.50	3.10	2.80	2	not measured				2.37	2.37	2.37	1	not measured			
PCB72	1.20	1.20	1.20	1	not measured				not measured				not measured			
PCB74	3.20	125	29.1	6	30.0	30.0	30.0	1	not measured				not measured			
PCB 77	not measured				0.100	0.100	0.100	1	not measured				not measured			
PCB81	not measured				0.730	0.730	0.730	1	not measured				not measured			
PCB95 + 56+60	3.00	3.00	3.00	1	not measured				not measured				not measured			
PCB95	0.40	0.40	0.40	1	not measured				not measured				not measured			
PCB99 + 101	5.70	5.70	5.70	1	not measured				not measured				not measured			
PCB99	2.80	9.40	6.08	4	15.0	15.0	15.0	1	not measured				not measured			
PCB101	1.20	1.20	1.20	1	not measured				not measured				not measured			
PCB105	3.90	46.50	14.17	6	2.40	5.79	3.96	5	0.510	0.580	0.550	3	5.40	8.43	7.01	3
PCB114	10.90	11.80	11.35	2	9.54	25.0	14.8	3	not measured				not measured			
PCB118	5.40	29.20	11.56	7	1.60	11.0	7.66	7	0.770	17.6	4.06	8	5.70	7.68	6.62	3
PCB123	4.70	4.70	4.70	1	4.83	12.0	8.08	3	not measured				not measured			
PCB126	not measured				1.60	4.36	289	3	not measured				not measured			
PCB128	not measured				not measured				5.20	5.40	5.30	2	not measured			
PCB128 + 183	7.90	7.90	7.90	1	not measured				not measured				not measured			
PCB138	8.20	18.10	14.33	3	8.40	25.0	14.05	4	3.87	32.0	14.6	5	3.70	3.70	3.70	1
PCB138 & 158	9.60	9.60	9.60	1	not measured				not measured				not measured			
PCB138 & 163 & 164	not measured				not measured				not measured				22.3	22.3	22.3	1
PCB138 & 163	7.80	7.80	7.80	1	not measured				7.70	11.6	9.69	2	24.7	24.7	24.7	1
PCB146	not measured				21.0	21.0	21.0	1	not measured				not measured			
PCB153	8.40	14.2	11.7	3	11.0	35.0	18.2	5	4.20	47.0	15.9	7	8.40	16.3	13.0	3
PCB156	4.60	90.1	32.5	6	5.35	18.0	13.6	4	4.23	13.2	7.58	3	7.50	7.50	7.50	1
PCB156 & 171	not measured				not measured				6.46	6.46	6.46	1	not measured			
PCB157	12.7	12.7	12.7	2	3.16	20.0	13.7	3	not measured				not measured			
PCB167	5.40	5.60	5.50	2	12.0	14.5	12.8	3	not measured				not measured			
PCB169	not measured				7.30	10.4	851	3	not measured				not measured			
PCB170	not measured				7.40	15.5	1230	3	4.10	71.0	23.7	7	7.60	7.60	7.60	1
PCB171	24.0	24.0	24.0	1	not measured				not measured				not measured			
PCB171 + 156	not measured				not measured				4.41	441	4.41	1	not measured			
PCB180	9.90	18.2	12.7	3	5.50	300	83.0	4	4.57	16.7	9.47	5	9.10	9.10	9.10	1
PCB187	not measured				7.80	15.0	11.1	3	not measured				8.00	8.00	8.00	1
PCB189	12.2	15.5	13.8	2	1.30	41.0	21.4	3	not measured				not measured			

them into studies that estimated half-lives from occupational exposure (Brown et al., 1989; Seegal et al., 2011; Esser et al., 2021a) and those where half-lives were estimated from a general population (Gao et al., 2019; Bu et al., 2015; Ritter et al., 2011). This data is presented in Fig. 4 and was processed using a 2-sample *t*-Test. Reported PCB half-lives were generally longer in general population studies, with statistically significant differences (at the 95% confidence level) identified for PCBs 28 and 167. Exposure to PCBs from contaminated buildings and furnishings is an emerging concern (Johansson et al., 2003; Frederiksen et al., 2020; Herkert et al., 2018). Unfortunately, no article reported PCB congener half-lives in occupants of contaminated buildings.

Non-occupational exposure to PCBs, such as those reported in the background or accidental exposure, could occur through consuming contaminated food, such as fish and dairy products, and inhalation (Ritter et al., 2011; Ogura, 2004; Xue et al., 2014), Masuda et al. (1995). Although these exposures may be categorized together, PCB concentrations differ. For example, an accidental exposure in the Yusho and Yucheng incidents to PCBs in rice oil resulted in high dietary exposure (Masuda et al., 1985) compared to exposure via a similar route in the Akwesasne people of the Mohawk Nation (Gallo et al., 2015) and environmental exposure to background level PCBs.

An important observation with exposure to PCB, whether categorized as high or low, is that PCB blood levels in exposed individuals are higher than the general population/background level exposure, popularly referred to as an unexposed group. It has been reported that these levels remain higher in exposed cohorts years after exposure. Seegal et al. (2011) reported PCB levels in former capacitor workers 28 years after occupational exposure. Fitzgerald et al. (2007) presented levels in similarly aged individuals who resided in the same towns as the factories but were not occupationally exposed. It was observed that after 28 years, PCB blood levels of exposed workers are approximately twofold higher than those of the same town who were not exposed. Also, PCB congeners' half-life is shorter due to up-regulation by P450 enzymes, especially when exposed to high-level ends. In the general population, where exposure to PCBs is typically lower, the half-life of PCBs is longer. Half-lives from manuscripts reviewed presented half-lives from primarily occupational exposure. To assess if these trends were observed in the scientific literature, we collated all commonly reported half-lives from studies in blood/plasma/serum and grouped them into four groups; occupational exposure studies (capacitor/waste recycling plant workers), accidental/environmental exposure, dietary exposure, and general population studies. It is challenging to have an overall

comparison done due to the report of apparent and intrinsic half-life in the exposed/general population level exposed groups. For intrinsic half-lives for PCB 118, an average value of 5.5 was reported for the exposed population (Esser et al., 2021a; Grandjean et al., 2008; Gallo et al., 2015) compared to the average of 10.3 for the general population/background level exposed group (Ritter et al., 2011; Bu et al., 2015; Gao et al., 2019). A similar trend was observed for PCB 153, although intrinsic half-life values reported for PCB 105 in exposed and general population/background level exposed individuals are alike. The apparent half-lives reported for these three congeners in an exposed population are difficult to compare.

4. Conclusions, knowledge gaps, and uncertainty in the literature

Despite the relatively large number of studies on PCB half-lives, there are still several knowledge gaps. Many uncertainties in reported half-lives of PCB congeners mean this literature should be treated with caution. There is a poor consistency of reported half-lives; the reported half-life value for just one individual PCB was shown to vary by nearly 3 orders of magnitude (0.34 years–300 years for PCB 180). This highlights that this is a highly complex issue, and many factors impact PCB half-lives in humans. Half-lives from the scientific literature are often selected to perform modeling experiments to predict future or historic PCB concentrations. There is no one set of half-life values that are “the best”, so we cannot suggest a set of specific values that we recommend for use in future studies. Instead, we suggest that appropriate consideration should be placed on reviewing the associated demographic data with each reported half-life to ensure selecting the most appropriate half-life data for the specific cohort in question.

Comparison of half-life data from different studies proved a challenge due to inconsistent analytical methods and reporting statistics. Future studies should document what types of samples formed the basis of the study, accurately provide a detailed list of associated demographic details, and detail analytical methods used, including the potential for co-eluting congeners. These issues appeared less well documented in the older literature, making adopting some of the more historic half-life estimates challenging. In addition, many studies did not benefit from advanced analytical instrumentation such as HRGC-HRMS (High-resolution gas chromatography, high-resolution mass spectrometry) but instead relied heavily on GC-ECD (gas chromatography-electron capture detector) and so the underlying data may not be as robust as more recent

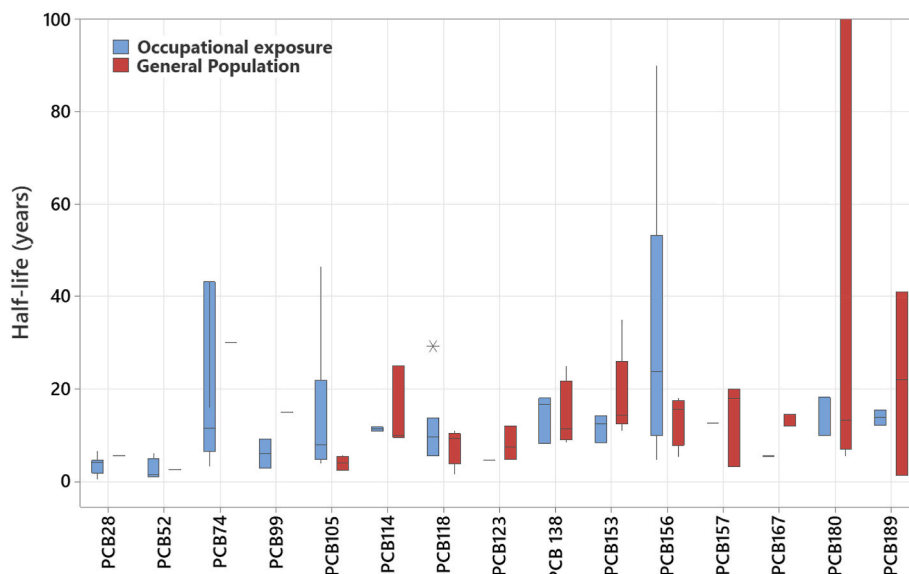


Fig. 4. Comparison of half-lives for occupational exposure studies and general population studies.

studies. Another challenge observed from the data is the different methods used to obtain half-life estimates. While Esser et al. (2021a) and Broding et al. (2007) reported half-life values estimated from mean values, Seegal et al. (2011) and Quinete et al. (2017) used geometric mean. The age group of participants in most studies was broad, thereby obscuring the importance of age-related half-lives. These disparities can make direct comparisons of datasets challenging as the numbers reported can all represent slightly different characteristics of participants in studies. The authors of this review have identified a dataset that likely addresses the data gap challenges, the National Health and Nutrition Examination Survey (NHANES) (US CDC, 2001). The NHANES is one of the world's oldest, most comprehensive, and on-going biomonitoring surveys monitoring the levels of chemical exposure assessments in the general population in the US. The NHANES study design, through the use of a complex, stratified procedure select a representative sample of the millions of non-institutionalized civilian populations living in the 50 states and the District of Columbia (DC). The sampling design consisted of selecting the PSUs. The primary sampling units (PSUs) for NHANES are typically defined as individual counties or a combination of adjacent counties. The PSUs are selected using multistage sampling design that considers demographic factors such as age, race/ethnicity, Hispanic origin, and income. Based on the comprehensive data available for the US population, obtaining values from these datasets may provide more reliable estimates, especially for demographics. Another parameter that can be used to evaluate the trend in PCB concentrations in the population is the percent decline. This was reported in the Norwegian population by Nost et al. (2019) using longitudinal data reported over 30 years. In their study, they reported an average annual decrease of 4% in medians of evaluated PCB congener concentrations for both women and men.

One current challenge in comparing the scientific literature is the wide range of terminologies used when reporting half-lives. We have attempted to consolidate the terminology and recommend using one of the two terms, "apparent" or "intrinsic", to report half-lives. An apparent half-life estimate reflects the observed changes in concentration in one individual over time with the combined effect of ongoing exposures and confounding factors. In contrast, an intrinsic half-life is a half-life estimate that accounts for the effects of ongoing exposure and changes in body weight.

A lingering question based on this review, considering various confounding factors evaluated when estimating half-life values, is the possibility of a back-estimation of PCB concentration at the initial exposure time. Is using half-life values or percent decline obtained from individuals or cohorts appropriate in back-estimating PCB congener concentrations from previous exposure? Three (3) have published procedures on back-extrapolating organochlorine contaminants, i.e., Karmaus et al. (2004), Axmon and Rignell-Hydbom (2006), and Verner et al. (2015). These procedures and results obtained are not without their limitations. However, understanding the variation of elimination of contaminants and its dependency on many factors, does back-estimation give precise or accurate concentration?

One important knowledge gap is that all studies undertaken to date focus on estimating half-lives of PCBs originating from technical PCB mixtures. Inadvertent sources of PCBs are an emerging area of concern. They can contain unique individual congeners and PCBs commonly detected in technical mixtures. Exposure sources can be occupational and linked to specific industries such as paint and silicone rubber manufacturing, but these PCBs are also regularly detected in background environmental samples.

CRediT authorship contribution statement

Ifeoluwa Grace Idowu: Resources, Conceptualization, Writing – original draft, Writing – review & editing. **David Megson:** Conceptualization, Writing – review & editing, Visualization, Supervision. **Guuske Tiktak:** Resources, Writing – original draft, Methodology. **Mike**

Dereviankin: Visualization. **Courtney D. Sandau:** Conceptualization, Writing – review & editing, Supervision.

Declaration of competing interest

Court Sandau reports a relationship with Monsanto Co. that includes: consulting or advisory and paid expert testimony. Ifeoluwa Grace Idowu, Mike Dereviankin, and Dave Megson, as paid consultants to Chemistry Matters Inc., are also therefore associated with these litigation matters. Guuske Tiktak declares no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

All data used is provided in the Supplemental Information

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.chemosphere.2023.140359>.

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