Effects of global treaty on commercial chemicals widely used as additives: meta-analysis of historical measurements of PBDEs

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**Summary**

**Background**

Commercial organic additives, many of which possess persistent, bioaccumulative, and toxic (PBT) features, are widely used in various products. Although some PBT chemicals have been restricted, the risks associated with long-term exposure remain. Polybrominated diphenyl ethers (PBDEs) are flame retardants in electronics, textiles, and many every-day products. They are a typical class of ubiquitous additive chemicals with PBT characteristics. PBDEs include three commercial formulations: penta-, octa-, and deca-BDE. Penta- and octa-BDE were banned in most countries in the early 2000s and listed under the Stockholm Convention in 2009 with recycling exemptions. Deca-BDE was banned later, with the US starting to phase it out in 2009, and was added to the Convention in 2017 without any exemptions. We conducted a meta-analysis and systematic regression analysis to explore the impact of global policies and treaties on both internal (human) and external (environmental) exposure to PBDEs.

**Methods**

On January 4, 2023, we conducted a search of electronic databases including Web of Science, Scopus, Embase, and PubMed, along with grey literature. The search results were updated on March 21, 2025. The inclusion criteria focused on studies reporting PBDE concentrations in indoor dust (a major source of external exposure) and in the human body (internal exposure). We collated concentration data of major PBDE congeners, which are present in different formulations of flame retardants used in different products, including BDE-47, BDE-99, BDE-153, BDE-183, and BDE-209. We used a breakpoint regression model to analyze the temporal trends of PBDEs and compared these trends with the timeline of national/regional policies.

**Findings**

We identified 9782 studies, of which 343 were included, covering data from 94 countries worldwide. Significant differences were observed in PBDE internal and external exposure across countries. Using the European Union (EU), China, and the United States (US) as examples, we summarized the general temporal patterns of large-scale indoor emissions (which dominate exposures of the general population) of different PBDE congeners and their effects on human exposure, correlating with treaty, production, and usage schedules. The results indicate that PBDE emissions in indoor environments have decreased following policy interventions, but reductions in human PBDE levels have been delayed and slow. Using breakpoint regression modeling, we identified a significant turning point in the concentrations of low-brominated PBDEs (BDE-47 and BDE-99) in human milk in the EU. Similar decreases were observed in China and the US. However, no decreasing trend over time was evident for BDE-153, nor for the higher-brominated BDE-183 and BDE-209. In adult serum, PBDE concentrations showed minimal decreases.

**Interpretation**

Long-term emissions from treated products with large stocks of these chemicals after bans, along with the bioaccumulation of PBDEs (especially BDE-153), significantly delay the effectiveness of treaties in decreasing human exposure and health risks. Moreover, regionally varied policy enforcement and consumption patterns further reduced effectiveness of these treaties on a global scale. The chemical diversity of different PBDE congeners also affects the effectiveness of the bans. Currently, there is a lack of systematic longitudinal studies to evaluate the effectiveness of monitoring at both global and national levels. This study highlights the need for more cautious and stringent chemical regulations and unified global monitoring and management framework in the future, to better regulate commercial additives.

**Funding**

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**Introduction**

Numerous organic additives are extensively added to diverse products, to enhance their functionality and convenience.1-3 Except for some reactive flame retardants that chemically bond with the product, additives are normally physically incorporated and can be continuously released from product materials into surrounding environments throughout products' life cycles.2,4 Many organic additives exhibit persistent, bioaccumulative, and toxic (PBT) features, potentially posing risks to human health.5-7 The Stockholm Convention on Persistent Organic Pollutants (POPs) Annex A includes a total of 30 categories of organic substances, with nearly half being used as additives.8 However, despite being restricted, exposure to additives can continue over long timescales, due to their persistent nature and prevalence in old every-day products or materials in homes and workplaces.9,10 There are often long delays between initial concerns being raised about a chemical and the introduction/enforcement of bans/restrictions on their manufacture and use. Large stocks of chemicals can potentially build up in products and environments, which can become an ongoing source of exposure. Concerns also apply to substitutes of restricted chemicals; they often have very similar properties, while chemical assessment and management frameworks are insufficient to predict the safety of new chemicals.11-15

To address this issue and learn lessons for the future, we take a well-studied group of typical legacy flame retardants, the polybrominated diphenyl ethers (PBDEs), as case chemical additives. Specifically, we examine how global time trends in their use, emissions, external exposure, and internal human exposure relate to the period before and after their ban. PBDEs are a common class of chemical additives extensively used in a wide range of consumer and industrial products.16-18 As PBT chemicals, a body of evidence has linked PBDE exposure to adverse health effects, including endocrine-disrupting effects, negative impacts on reproductive health and intellectual development.7,19,20 Therefore, different commercial formulations of PBDEs were listed in the Stockholm Convention, and regulated in various countries and regions, providing useful comparisons from which to elucidate mechanisms and processes of environmental and human exposure responses to chemical management/restrictions.21,22

Previous studies on local or regional scales have shown different results regarding impact of restriction policies on human PBDEs exposure. For example, Zota et al. and Parry et al. have observed significant reductions in PBDE concentrations in humans living in California after the phase-out of penta-BDE and octa-BDE by the US Environmental Protection Agency (EPA), while Hurley et al. have reported increasing trends for BDE-100 and BDE-153 in middle-aged and older California women.23-25 Van der Schyff et al. conducted a global meta-analysis of PBDE concentrations in human milk to assess temporal trends and the impact of regulatory measures.26 However, their analysis grouped data by continents (e.g., North America, Asia, Europe), which did not align with the jurisdictions where PBDEs regulations are implemented (e.g., national policies or supranational frameworks like the EU’s REACH). Moreover, all these studies did not investigate the temporal trend of emission and external exposure levels, which failed to discern whether observed trends in humans arise from ongoing exposure or historical accumulation. Therefore, additional investigations are essential to gain a comprehensive understanding of the efficiency of chemical management policies with assessment of changes in source emissions at the global scale. In this study, we therefore collated PBDE measurements in indoor dust, human serum, and human milk on a global scale through a comprehensive literature survey. Indoor dust is a crucial medium that plays two key roles in environmental health. It serves as an indicator of source emissions, due to its origin from volatilization and subsequent deposition, physical wear and tear/contact with indoor products containing chemical additives, particularly for highly hydrophobic chemicals.27-29 Meanwhile, it generally constitutes a primary source of human exposure to most PBDE congeners, especially for children.30 This is driven by two key factors: (1) people typically spend over 90% of their time indoors, at home and at work; and (2) although another important source, dietary exposure poorly predicts human internal exposure due to complex dietary patterns and limited foodstuffs correlating with internal exposure.27,31-36 PBDEs in human milk and serum, especially lower brominated congeners with long half-lives, can be used as reliable markers of long-term exposure, assuming equilibrium between PBDEs in serum/human milk and fat in humans.37-39 We aim to elucidate the effectiveness of the global treaty on chemical additives by analyzing long-term exposure patterns in indoor dust and humans relative to the policy timeline. This provides critical insights to refine chemical management, particularly with respect to optimizing regulations through advanced pre-risk assessment and strategically timing policy enforcement.

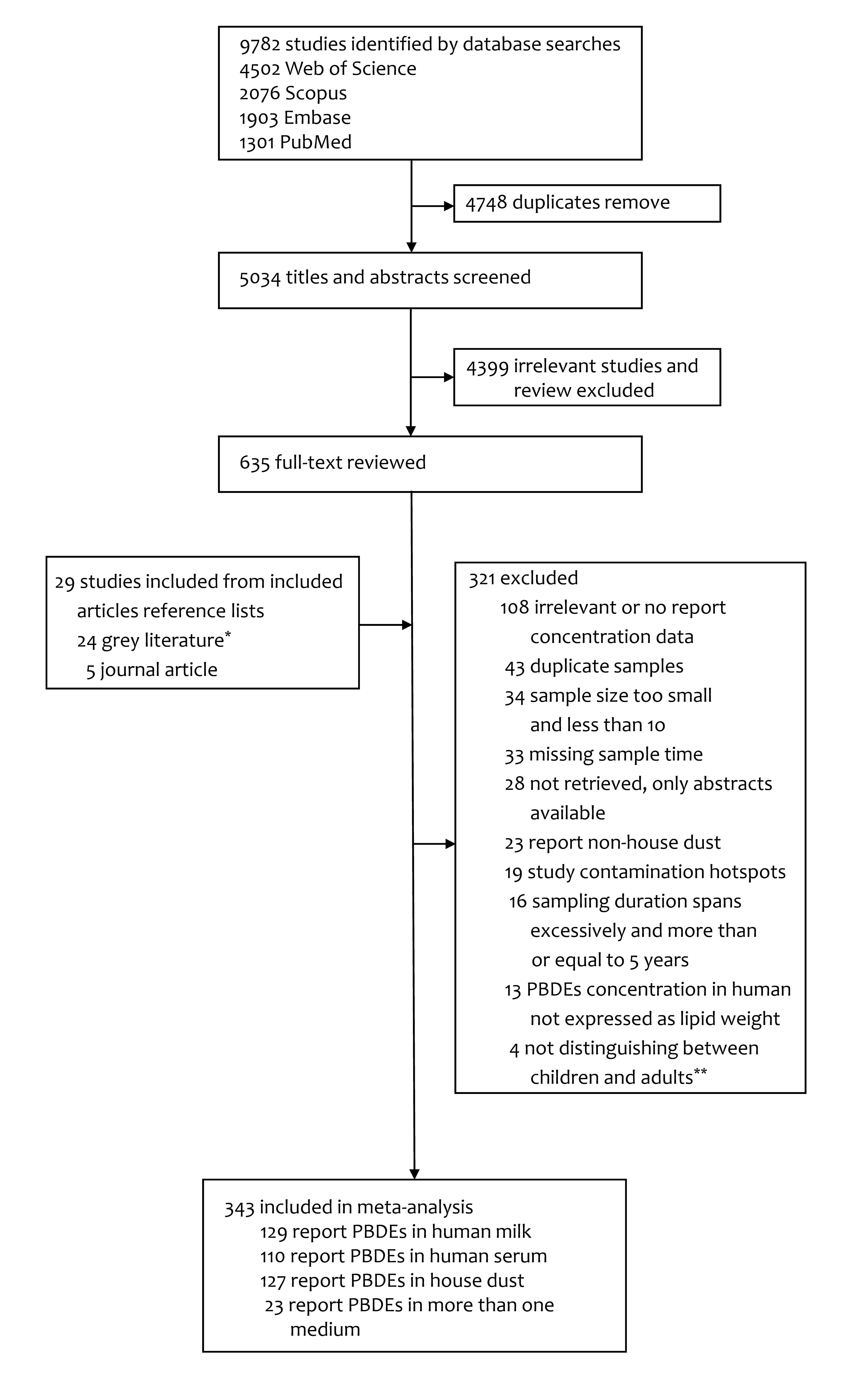
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| --- | --- |
| **Research in context**  **Evidence before this study**  The typical case chemical additives, Polybrominated diphenyl ethers (PBDEs), are widely used as chemical additives in consumer and industrial products, but have been linked to detrimental health effects such as endocrine disruption, reproductive issues, and impaired child cognitive development. They have been restricted in most countries and regions since around 2000. Existing studies have assessed the impact of restriction policies on local or regional PBDEs exposure, but the findings have been inconsistent. Previous studies have examined global trends of PBDEs in human breast milk to assess the effectiveness of regulatory interventions. Declines in certain low-brominated congeners across most regions suggest that these measures have had a positive impact. Notably, no research at the global scale has directly linked the timelines of PBDE production and usage regulations with temporal trends in major external exposure sources and internal exposure levels. As a result, the effectiveness of these policies remains largely unexplored. We conducted a global systematic review to comprehensively summarize external environmental exposure and internal human exposure levels, linking both to the timeline of PBDE production, usage, and regulation. By March 21, 2025, we searched Web of Science, Scopus, Embase, and PubMed for studies reporting PBDE concentrations in humans and indoor dust. The search used the following keywords: (halogenated flame retardant OR legacy flame retardant OR "polybrominated diphenyl ether\*" OR PBDE\*) AND (indoor dust OR indoor environment OR home dust OR house dust OR body burden OR "human milk" OR "breast milk" OR serum), including the search to both English and non-English language publications. Indoor dust, as a key medium, reflects both source emissions and human external exposure. We identified several reviews that discussed regional and global variations in PBDE exposure levels and associated health risks, but their findings were inconsistent. | **Add value of this study**  We screened 343 eligible studies, along with human milk data from the Stockholm Convention's Global Monitoring Plan. Our findings indicate that after PBDEs came under regulatory control, PBDE concentrations in both indoor dust and humans showed varying temporal change patterns across different countries/regions, media, and congeners. Insignificant decrease was found in many occasions, and BDE-209 in adult serum even increased.  **Implications of all available evidence**  These findings hold significance for the evolution of chemical management strategies. The existing approach to handling chemicals in products seems to follow a concerning cycle: chemicals are introduced, usage increases, environmental and health risks emerge, and then bans are implemented. Then, often, similar chemicals are introduced as substitutes. However, our results indicate that for numerous persistent chemical additives like PBDEs, the time required for bans to take full effects can be lengthy, due to their large in-use stock and bioaccumulation, which would yield hardly controlled enduring impacts on human exposure once introduced to the market. Currently, there is a lack of systematic longitudinal studies assessing the effectiveness of monitoring efforts at both global and national levels, limiting assessment of policy effectiveness. The prevailing chemical management paradigm requires reevaluation, calling for deliberate consideration of pre-assessment before chemical additives enter any markets. Meanwhile, strategies on systematic monitoring of exposure to used chemicals need to be established on the global scale under a unified management framework. |

**Methods**

**Search strategy and selection criteria**

A systematic review and meta-analysis were conducted on concentrations of PBDEs in house dust, human milk, and serum. We focused on house dust rather than workplace dust due to greater data availability and the predominance of home indoor exposure in the general population.9,17 In January 2023, we searched for peer-reviewed articles in the Web of Science, Scopus, PubMed, and Embase databases using the following keywords: (halogenated flame retardant OR legacy flame retardant OR "polybrominated diphenyl ether\*" OR PBDE\*) AND (indoor dust OR indoor environment OR home dust OR house dust OR body burden OR "human milk" OR "breast milk" OR serum). The literature search included publications in both English and non-English languages and was updated on March 21, 2025.

Title and abstract screening was conducted to include studies on our case additives – PBDEs, and exclude those on occupational exposure. Subsequently, a full-text review was performed to identify studies reporting PBDE concentrations in house dust, serum, or human milk. Additional studies were identified by screening the reference lists of selected papers. GZ and ZL independently screened the titles, abstracts and full texts for potential relevance. Study design was not used as an inclusion or exclusion criterion, except for studies targeting PBDE hotspot regions or occupational exposure. The review appropriately followed PRISMA guidelines and inclusion/exclusion criteria appear appropriate, with two people screening (appendix pp 1–4). We assessed the risk of bias to evaluate the methodological rigor and data reporting quality of the included studies, focusing on two key domains: selection bias and measurement bias (see appendix pp 5–27 for detailed criteria and results). Two authors (GZ and ZL) independently rated each study as having a low, moderate, or high risk. Discrepancies were resolved through discussion until consensus was reached. To test the robustness of our model estimates, we also conducted sensitivity analyses by excluding studies deemed high risk for either selection or measurement bias.

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**Figure 1. Study selection.** \*Conference papers can be found on this website: <https://dioxin20xx.org/>. \*\*Serum data not distinguishing between children and adults, considering the different time periods of exposure, bioaccumulation, and behaviors between these age groups.

**Data analysis**

Five major components of three commercial formulations, namely BDE-47 and BDE-99 (penta-BDE), BDE-153 and BDE-183 (octa-BDE), and BDE-209 (deca-BDE), were investigated in this study. They are the most commonly used and detected congeners in the environment and humans.17

We collected key information from each eligible study, including the first author, publication year, country, sampling years, sample size, and concentration measures including arithmetic mean, geometric mean, median, and maximum. Missing details were obtained by contacting authors. For sampling periods spanning multiple years without annual data, the midpoint year was considered the sampling year. Median concentrations were prioritized to minimize the influence of extremes, with geometric or arithmetic means used if medians were unavailable. As individual-level data were not available, summary concentrations were used for subsequent analysis. Measurements below detection limits were assigned half the detection limit.

We analyzed PBDE temporal patterns using weighted linear mixed-effects regression model with log-transformed response variable, implemented via the R package “lme4”. Weights were assigned between 0.1 and 1.0 for studies with sample sizes ranging from 10 to 100, and were fixed at 1.0 for studies with sample sizes exceeding 100.26,40-42

The model uses an identity link function, where *Y*i represents PBDE concentration, *t*i represents sampling year. The study is modeled as a random effect (1|studyi) to account for variability, which may be omitted if the number of studies equals the observations. *ϵ*i represents the random error, assumed to follow a normal distribution *N* (0, σ2). The coefficient *b* represents the annual rate of change in the log-transformed PBDE concentration, with exponentiate of *b* representing the yearly geometric mean ratio. We assessed the normality of the log-transformed response variable and the residuals using the Shapiro-Wilk test, and found departure from normality only in a small number of cases, which would not impact the overall validity of the model.43 The linearity assumption of the model was validated using the Ramsey RESET test.

Due to policies aimed at reducing human exposure to PBDEs, PBDE concentrations in humans are expected to initially increase and then decrease over time. A weighted breakpoint regression model was employed to identify the specific year when the concentration trend shifts from upward to downward.

Where *t*0 represents the time point of the trend change (if no change point, *t*0 = 0), *a*0 is the expected value of ln(*Yi*) at *t*0, and *b*1 and *b*2 represent the slopes before and after *t*0, respectively. The R package “segmented” was used to identify the change points, and their existence was examined using Davies test (if *p* < 0·05).44 Trends in PBDE concentrations were deemed significant if *p* < 0·05. All data analysis and visualization were performed in R (version 4.2.2).

**Role of the funding source**

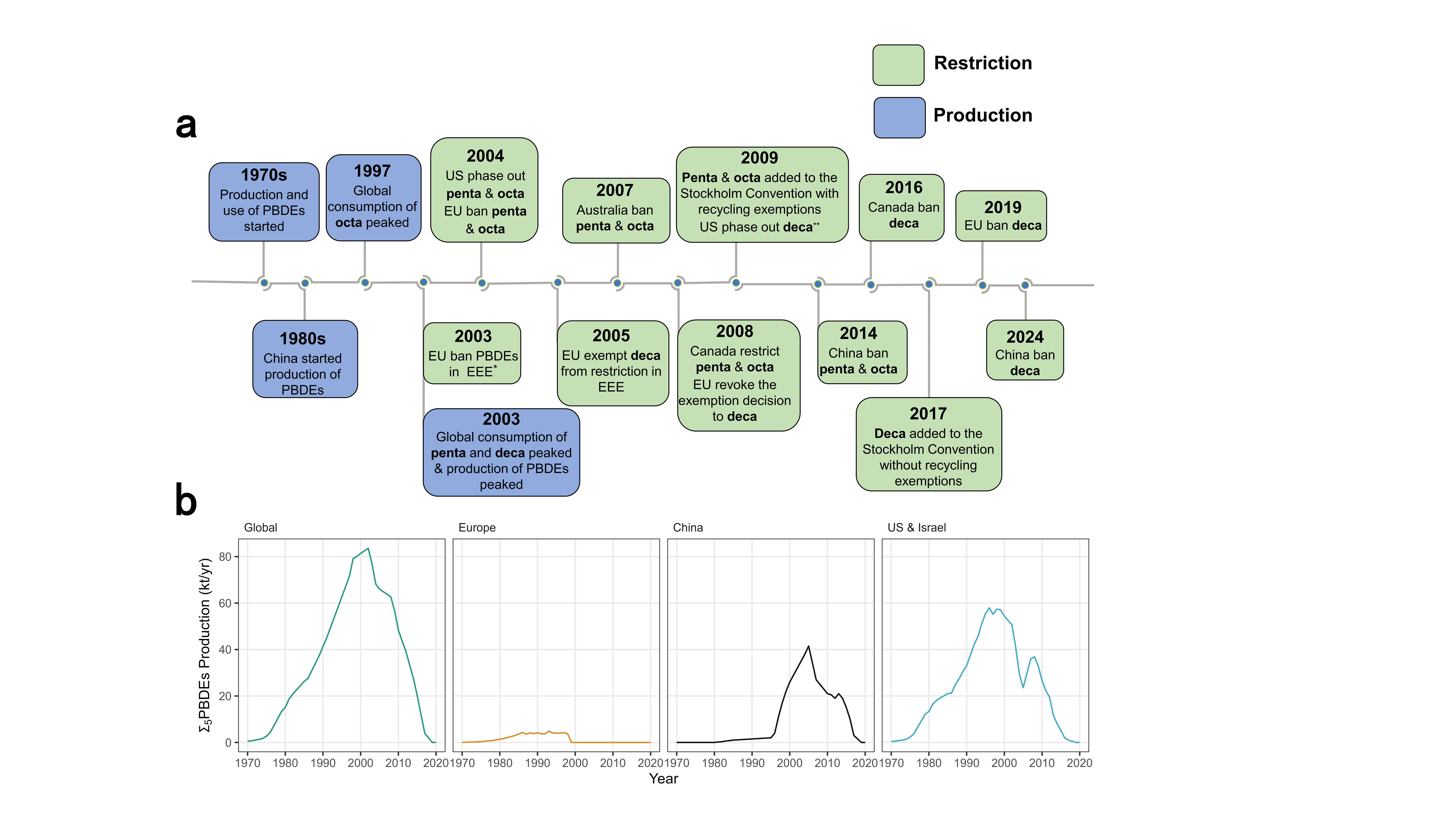
The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

**Results**

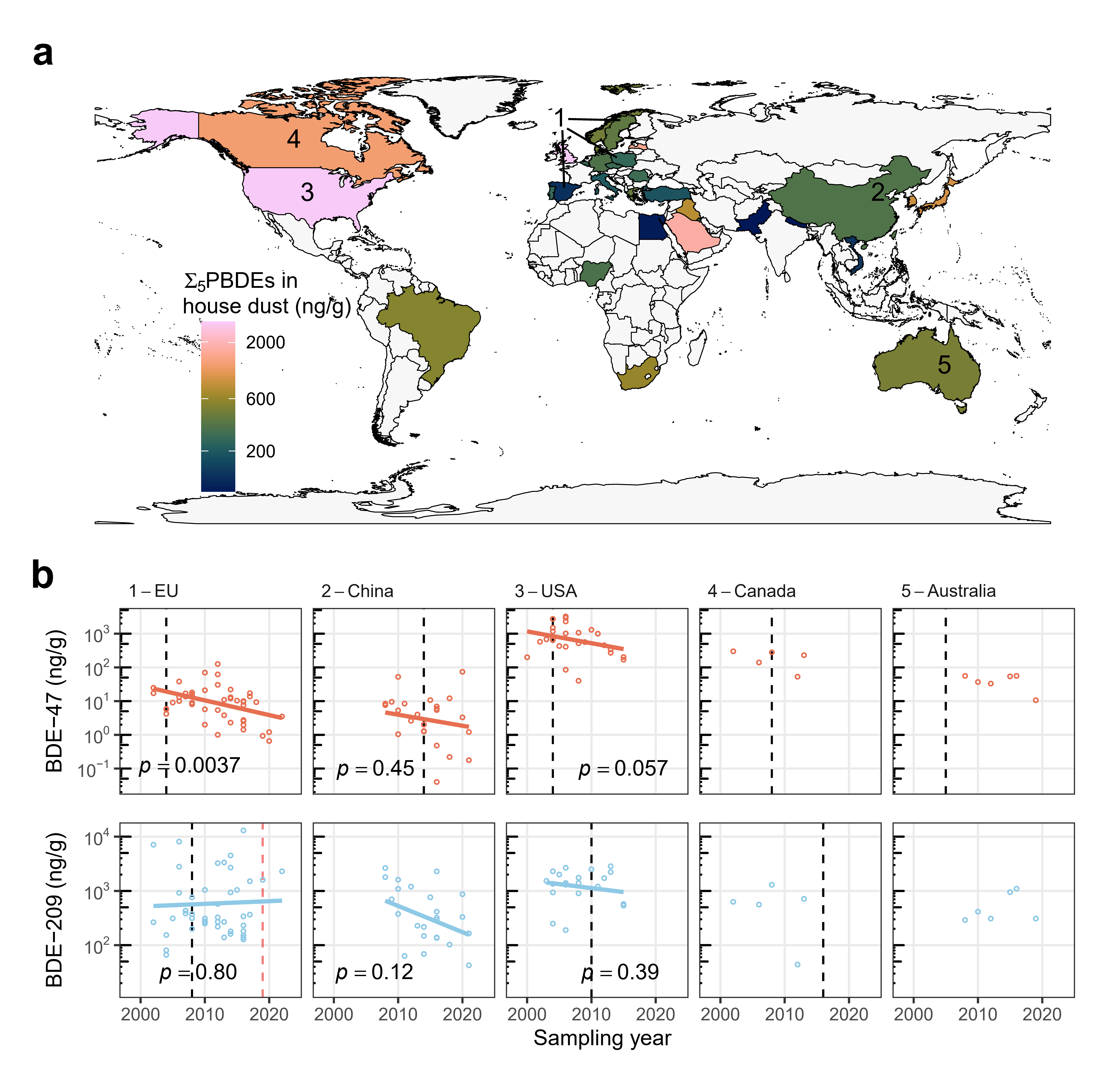
After removing duplicates, the database search identified 5034 studies. Title and abstract screening excluded 4399 studies, leaving 635 studies for full-text review. During the review, 321 studies were excluded for various reasons, including 43 that were removed due to the use of duplicate samples. Additionally, 29 studies were identified through reference list searches, resulting in 343 studies included (Figure 1). Of these, 129 and 110 studies reported PBDE concentrations in human milk and serum, respectively, while 127 studies reported PBDE concentrations in house dust. We also included data from the Stockholm Convention Global Monitoring Plan (https://data.pops-gmp.org/2020/all/#/gmp3/summary-statistics) on PBDE concentrations in human milk. In total, we gathered 630 records for PBDE concentrations in house dust, 622 in serum, and 1064 in human milk.

Available PBDE measurements in house dust span 37 countries. Most studies came from the EU (n = 45), China (n = 25), and the US (n = 24), with additional data from Australia (n = 6), Canada (n = 5), and South Korea (n = 4). Other countries had no more than three studies. PBDE measurements in human milk and serum cover 94 countries, providing broader geographic coverage than house dust data, benefiting from the Stockholm Convention Global Monitoring Plan, although typically limited to one or two years. Key regions included the EU (n =77), the US (n = 55), and China (n = 44), with additions from South Korea (n = 11), Japan (n = 8), Mexico, Canada and Australia (n = 7 each). Sporadic studies were available from other countries. The included studies reflect exposure in the general population, with details provided in appendix (pp 28–47). We examined statistical significance of temporal trends in the three targeted matrices for regions or countries with sufficient data and clear restrictions on PBDE use, specifically the EU, China, and the US. The risk of bias assessment revealed that the majority of included studies (n = 260, 76%) had a moderate risk of selection bias, as most samples were collected in large cities or specific regions. In terms of measurement bias, most studies (n = 324, 94%) were rated as low risk, indicating generally reliable quality control in reported analytical methods (appendix pp 6–27). Sensitivity analyses excluding studies with a high risk of selection or measurement bias showed minimal changes in the model estimates, supporting the robustness of our findings (appendix pp 52).

The timeline of PBDE production and regulatory interventions spans several decades (Figure 2), starting with the production and use in the 1970s. Global PBDE production was estimated to peak around 2003 at approximately 85 kt/yr, with usage reaching around 75 kt/yr.10 Initially, the US, together with Israel, was the primary producer, contributing 90% of global production, which peaked at 58 kt/yr in 1996 (86% of global production).10,45 North America, especially the US, dominated global consumption, using up to 95% of global penta-BDE.10,17,45 China began producing PBDEs in the 1980s and surpassed the US and Israel, becoming the leading producer in 2004 (38 kt/yr vs 29 kt/yr).10 This shift coincided with the 2004 ban on penta- and octa-BDE in the US and EU, driven by growing concerns over PBDE-related health risks.17,46 Australia and Canada implemented the ban in 2007 and 2008, respectively.47,48 The EU initially prohibited the addition of PBDEs in new electrical and electronic equipment (EEE) in 2003, with an exemption for deca-BDE in 2005. This exemption was overturned by the European Court in 2008, leading to a final ban in 2019.49-52 The US began phasing out deca-BDE in 2009, and Canada imposed a ban in 2016.17,53 China was the last to restrict penta- and octa-BDE in 2014, and deca-BDE in 2024.54,55 By 2007, new penta- and octa-BDE use had nearly ceased in most regions, with deca-BDE use following by 2019. Given the typical 20-year lifespan of most products (appendix pp 48), the remaining in-use stock is expected to be largely eliminated by the end of 2030s.10



**Figure 2. (a) Timeline of production and major** **regulatory policy for PBDEs****; (b). Estimated temporal trends in global and regional production of PBDEs by Abbasi et al.10** \* This directive came into effect in 2003, but it applied to EEE placed on the market after 2006. EEE represents electrical and electronic equipment. \*\* The phase-out began in 2009 and was gradually completed by the end of 2013.



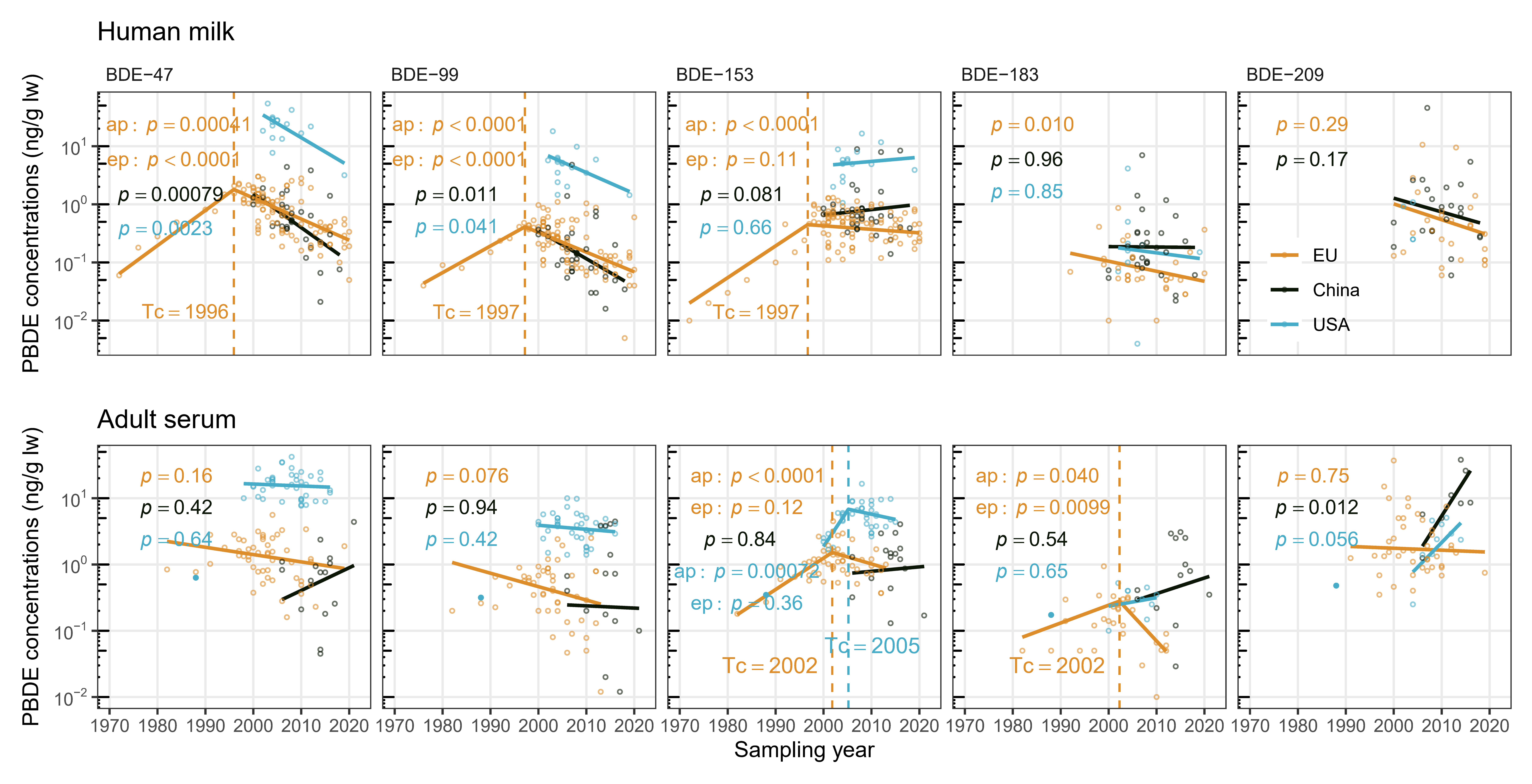
**Figure 3. (a) Global distribution of median house dust concentration of Σ5PBDEs (BDE-47, BDE-99, BDE-153, BDE-183, and BDE-209); (b) temporal trends of BDE-47 and BDE-209 concentrations in typical countries and regions.** Each open circle represents the median concentration from a literature report. The vertical dashed line marks the year when the policy regulating PBDEs was implemented in the country or region. For BDE-209 in the EU, two dashed vertical lines are shown: the black line marks the 2008 ban on its use in electrical and electronic equipment, and the red line marks the 2019 ban on all uses. Additional BDE congener concentrations in dust from typical countries and regions are provided in appendix pp 54. The trend (exponentiate of beta coefficient) estimates with 95% confidence intervals are provided in appendix pp 49–51.

Only seven longitudinal studies (two on house dust and five on human serum) have investigated temporal trends of PBDEs over periods exceeding one year at a local scale, reporting specific measurements. The decrease in PBDE congeners in house dust ranged from 6% to 56%. In serum, some studies reported declines of 4% to 39%, while others observed increases ranging from 8% to 190% (appendix pp 53).

Globally, PBDEs have been measured in human serum and milk over a longer period (1972 – 2021) compared to house dust (2000 – 2023) (appendix pp 28–47). Among the three major regions, only the EU has early measurements in humans, dating back to the 1970s and 1980s. In contrast, measurements in humans for the US and China began around 2000, apart from a single US data in 1988. This pattern is similar for house dust measurements. For BDE-209, human milk measurements are available after 2000 across all three regions. Most studies measuring PBDEs in house dust emerged after the EU and US implemented their earliest restrictions in 2004.17,46 House dust measurements in China began later, starting in 2008.

Figure 3 and S2 (appendix pp 54) depict the temporal trends of PBDE concentrations in house dust across different countries and regions. Significant declines have been observed for BDE-47, BDE-99, and BDE-153 in the EU, BDE-153 and BDE-183 in the US. Although noticeable decreases are evident for several other congeners and regions, statistical significance is not always achieved. In the EU, concentration of BDE-183 in house dust dropped by 62% from 2·6 ng/g (2002 – 2004) to 1·0 ng/g (2019 – 2022). In contrast, BDE-209 increased from 154 ng/g (2002 – 2004) to 1600 ng/g (2017 – 2022). In the US, BDE-47 and BDE-99 decreased by 59% and 38% from 580 and 520 ng/g (2000 – 2003) to 240 and 320 ng/g (2013 – 2015), while BDE-209 remained stable (1350 ng/g in 2003 – 2004 and 1400 ng/g in 2013 – 2015). The lack of statistical significance, probably stemming from a few data points diverging from the overall trend, might be the result of variability in data sources and sampling locations. Although statistical testing for Canada and Australia was not feasible due to insufficient data, a clear declining trend was observed for penta-BDE and octa-BDE, with reductions exceeding 50% in both countries. Notably, no significant temporal trend was found for BDE-209 in house dust, possibly due to later restrictions on this congener compared to others.





**Figure 4 Temporal trends of PBDEs in humans in the EU, China, and the US, encompassing human milk and adult serum.** Each open circle represents the median concentration of a literature report, while a solid circle indicates the exclusion of that particular data point from the time trend analysis. The vertical dashed line represents the time of change, Tc = changing time point, ap = accumulation phase, ep = elimination phase. The trend (exponentiate of beta coefficient) estimates with 95% confidence intervals are provided in appendix pp 49–51.

Given the extended timeline of PBDE measurements in serum and human milk, particularly in the EU, we applied breakpoint analysis and the Davies test to identify significant temporal shifts in concentrations across the two media. In the EU, the turning points for BDE-47, -99, and -153 in human milk occurred in 1996 (95% confidence interval, CI: 1991 – 2001), 1997 (CI: 1992 – 2003), and 1997 (CI: 1992 – 2002), respectively, aligning with Van der Schyff et al. for BDE-47 and BDE-99, but occurring later for BDE-153.26 While in adult serum, it occurred slightly later in 2002 for BDE-153 (CI: 1998 – 2005) and -183 (CI: 1999 – 2006). Significant increases and decreases in BDE-47 and -99 in human milk, as well as BDE-183 in adult serum, were observed before or after their respective turning points (Figure 4). These turning points generally preceded the 2004 EU prohibition of penta- and octa-BDE.46 In contrast, the turning points for BDE-99 and BDE-153 in Japanese human milk occurred later than their phase-out dates, but limited data hindered robust analysis (appendix pp 55). Despite an early turning point, BDE-47 and BDE-99 remained elevated in EU human milk, averaging 1·1 and 0·3 ng/g lipid weight (lw), respectively, from 2000 to 2010 before declining to 0·2 and 0·08 ng/g lw by 2020. BDE-153 in human milk increased significantly before 1997 but remain stable at an average of 0·5 ± 0·3 ng/g lw afterward. In adult serum, BDE-153 and -183 peaked at 4·5 and 0·9 ng/g lw, respectively, around their turning points and decreased to 1·0 ng/g lw by 2013 (BDE-153) and 0·1 ng/g lw by 2012 (BDE-183).

Although the US also phased out penta- and octa-BDE in 2004 (Figure 2), a significant declining trend only appeared for BDE-47 and BDE-99 in human milk, and a significant turning point only appeared for BDE-153 in adult serum in 2005 (CI: 2003 – 2007), one year post-restriction. The serum BDE-153 increased significantly from 2·4 to 7·9 ng/g lw during 2000 – 2005, stabilizing at 6·4 ± 3·0 ng/g lw thereafter. The decline in other congeners in serum and human milk in the US was less pronounced compared to the EU and China. Notably, China demonstrated a significant decline in BDE-47 and -99 (from 1·1 to 0·08 ng/g lw and from 0·3 to 0·03 ng/g lw, respectively) in human milk, and a significant increase in BDE-209 in adult serum (from 3·5 to 8·6 ng/g lw).

Data from 21 studies on serum PBDE concentrations in children, mostly from the US and Australia, spanning from 2002 to 2016, were analyzed (appendix pp 56). Statistical analysis of time trends was conducted for congeners with sufficient data from both countries, revealing significant declines in BDE-47, -99, and -153. Although data for BDE-183 were insufficient for robust statistical analysis, its serum levels in children generally declined over time. Serum levels in children depicted clearer declining patterns than those in adults. The limited data suggested stable levels of BDE-209 in children after 2005, though comparisons with adult trends were inconclusive due to insufficient data.

The US exhibited the highest PBDE concentrations in house dust and in adult serum and human milk (excluding BDE-183 and -209), typically 1 – 2 orders of magnitude higher than those in non-North American regions (appendix pp 33–45). This trend was similar for children’s serum, though the disparity between US children and those from other regions was less pronounced than in adults. PBDE levels in house dust in China were lower than in the US, but comparable to mid-range EU countries (Table 1). From 2008 to 2021, no significant temporal trends were observed in house dust in China. Serum and human milk concentrations of BDE-47, BDE-99, and BDE-153 in China were comparable to EU levels, while BDE-183 levels were higher.

A total of 113 studies investigating all five congeners for the three major regions with substantial measurements were analyzed to explore PBDE composition in different matrices (appendix pp 57). Deca-BDE consistently dominated house dust in China and the EU over time. Contrarily, both penta- and deca-BDE were the major components in house dust in the US, with the proportion of deca-BDE steadily rising after 2010. PBDE profiles in human samples differed markedly from those in house dust. Low-brominated PBDEs were the primary, often predominant, components in humans, particularly in human milk. Percentages of penta- and octa-BDE in human milk were higher than those in serum, particularly for BDE-153, which accounted for on average 15% (range: 3 – 38%) in serum while 22% (range: 2 – 46%) in human milk. The high percentage of BDE-209 of adult serum in China is another noteworthy characteristic, with averages of 74%, surpassing the proportions observed in the EU (54%) and the US (17%).

**Table 1 The concentrations of Σ5PBDE in various media worldwide (ng/g or ng/g lw).**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Country** | **Sample type** | **Sampling year** | **Median** | **Mean** |
| **Europe** |  |  |  |  |
| UK | House dust | 2002 – 2022 | 3070 | 3720 |
| Latvia | House dust | 2017 | 1560 | 1560 |
| Sweden | House dust | 2006 – 2016 | 390 | 590 |
| Norway | House dust | 2012 – 2014 | 460 | 640 |
| Denmark | House dust | 2007 | 450 | 450 |
| Greece | House dust | 2017 | 410 | 410 |
| Turkey | House dust | 2012 – 2016 | 190 | 350 |
| Germany | House dust | 2002 – 2005 | 330 | 330 |
| Romania | House dust | 2010 | 280 | 280 |
| Czech | House dust | 2008 – 2013 | 270 | 270 |
| Portugal | House dust | 2008 – 2010 | 260 | 260 |
| Poland | House dust | 2012 | 250 | 250 |
| Belgium | House dust | 2004 – 2016 | 260 | 240 |
| Italy | House dust | 2004 – 2016 | 210 | 210 |
| Spain | House dust | 2004 – 2016 | 120 | 120 |
| **Asia** |  |  |  |  |
| Saudi Arabia | House dust | 2014 – 2019 | 1750 | 1750 |
| South Korea | House dust | 2007 – 2015 | 880 | 940 |
| Japan | House dust | 2005 – 2010 | 930 | 930 |
| China | House dust | 2008 – 2021 | 340 | 690 |
| Iraq | House dust | 2013 | 760 | 760 |
| Kuwait | House dust | 2012 – 2018 | 340 | 340 |
| Vietnam | House dust | 2008 – 2018 | 130 | 130 |
| Pakistan | House dust | 2011 – 2012 | 84 | 84 |
| Nepal | House dust | 2015 | 1·4 | 1·4 |
| **Americas** |  |  |  |  |
| US | House dust | 2000 – 2015 | 3020 | 4070 |
| Canada | House dust | 2002 – 2013 | 1240 | 1170 |
| Brazil | House dust | 2023 | 540 | 540 |
| **Africa** |  |  |  |  |
| South Africa | House dust | 2010 – 2018 | 610 | 680 |
| Nigeria | House dust | 2012 – 2019 | 320 | 330 |
| Egypt | House dust | 2013 – 2014 | 88 | 88 |
| **Oceania** |  |  |  |  |
| Australia | House dust | 2008 – 2019 | 480 | 670 |
| **Europe** |  |  |  |  |
| Austria | Human milk | 2013 – 2016 | 6·3 | 6·2 |
| Belgium | Human milk | 2000 – 2015 | 6·9 | 7·0 |
| Czech Repubic | Human milk | 2001 – 2020 | 1·0 | 1·1 |
| Spain | Human milk | 2001 – 2018 | 5·0 | 5·0 |
| UK | Human milk | 2002 – 2014 | 4·5 | 4·5 |
| Ireland | Human milk | 2001 – 2019 | 2·7 | 3·4 |
| France | Human milk | 2005 – 2012 | 2·8 | 2·8 |
| Norway | Human milk | 2000 – 2004 | 2·2 | 2·3 |
| Sweden | Human milk | 1972 – 2019 | 2·3 | 2·2 |
| Slovakia | Human milk | 2001 – 2019 | 0·8 | 0·8 |
| Germany | Human milk | 1992 – 2019 | 1·4 | 1·6 |
| Denmark  Serbia  **Asia** | Human milk  Human milk | 1998 – 2007  2015 | 2·6  3·7 | 2·6  3·7 |
| South Korea | Human milk | 2007 – 2011 | 11 | 17 |
| China | Human milk | 2000 – 2018 | 2·2 | 6·2 |
| Philippines | Human milk | 2002 – 2008 | 2·6 | 2·7 |
| Japan | Human milk | 1973 – 2008 | 1·2 | 1·2 |
| **Americas** |  |  |  |  |
| US | Human milk | 2002 – 2019 | 35 | 37 |
| Canada | Human milk | 1990 – 2010 | 12 | 14 |
| Colombia | Human milk | 2014 – 2019 | 0·7 | 0·7 |
| **Africa** |  |  |  |  |
| Uganda | Human milk | 2009 – 2018 | 1·3 | 1·4 |
| Ghana | Human milk | 2004 – 2019 | 2·2 | 2·1 |
| Morocco | Human milk | 2018 – 2019 | 0·7 | 0·7 |
| Tunisia | Human milk | 2010 – 2019 | 6·2 | 6·2 |
| **Oceania** |  |  |  |  |
| Australia | Human milk | 1993 – 2013 | 8·0 | 8·4 |
| **Europe** |  |  |  |  |
| Denmark | Adult serum | 2003 – 2011 | 14 | 14 |
| Norway | Adult serum | 1982 – 2013 | 8·4 | 13 |
| France | Adult serum | 2003 – 2011 | 10 | 10 |
| Spain | Adult serum | 2002 – 2008 | 8·8 | 8·2 |
| UK | Adult serum | 2003 – 2012 | 4·7 | 6·0 |
| Sweden | Adult serum | 1991 – 2010 | 3·6 | 4·2 |
| Greece | Adult serum | 2007 | 2·0 | 2·0 |
| **Asia** |  |  |  |  |
| China | Adult serum | 2006 – 2021 | 12 | 18 |
| Japan | Adult serum | 2003 – 2008 | 2·2 | 2·5 |
| South Korea | Adult serum | 2002 – 2013 | 21 | 21 |
| Iran  **America** | Adult serum | 2014 | 1·0 | 1·0 |
| US | Adult serum | 1988 – 2015 | 27 | 29 |
| **Africa** |  |  |  |  |
| Ghana | Adult serum | 2004 – 2009 | 2·0 | 2·0 |
| **Oceania** |  |  |  |  |
| Australia | Adult serum | 2002 – 2004 | 8·9 | 8·9 |
| New Zealand | Adult serum | 2001 – 2012 | 7·9 | 7·9 |
| **Asia**  China  **America** | Children’s serum | 2014 – 2016 | 13 | 13 |
| US | Children’s serum | 2006 – 2015 | 54 | 55 |
| **Oceania** |  |  |  |  |
| Australia | Children’s serum | 2002 – 2014 | 21 | 21 |

Note: As not all the five PBDE congeners were consistently reported across studies, total Σ­5PBDE concentrations represent the sum of congener-specific aggregated medians or means. For each congener, the median (or mean) was calculated from literature-reported was calculated medians (or means), and then were summed to obtain the media (or mean) of Σ5PBDEs. The measure of dispersion for each congener refers to appendix 28–47.

**Discussion**

Based on the observed data patterns, we highlight the following key findings and concerns. The first major finding is that while bans have slowed the increase in human exposure to PBDEs, the long-lasting emission after bans, combined with the bioaccumulative nature of chemical additives (especially those with long half-lives), significantly delays the effectiveness of regulatory policies in reducing human exposure and associated health risks**.** High concentrations of most PBDE congeners persist in house dust, declining only gradually 18 years post-ban, suggesting delayed global reduction and sustained regional emissions (Figure 3 and appendix pp 54). Reasons include in-use stock, local manufacture due to lax enforcement, transnational trade in finished products, and emissions from waste stream (e.g. from landfills/waste tips), which can also involve trans-boundary movements as legal/illicit waste.10,45

Due to extensive past application, in-use stock will remain the predominant source of banned chemicals for a long time into the future. Many consumer products, including electronic equipment, long-lived furniture, as well as interior decorations and building materials, could have lifespans ranging from 3 to over 100 years.9,10,56,57 Replacing these items with PBDE-free alternatives is a slow process, through renovations or new constructions.45,58 Moreover, plastic recycling, not fully covered by bans, extends PBDE presence in new products, contributing to ongoing emission from in-use stock.59

Exemptions further complicate global phase-out. For example, despite the ban, the US permits new applications of penta- and octa-BDE with a 90-day prior notice to the US EPA.60 The US, together with Canada, has a historical use pattern of deca-BDE similar to China, where a ban hasn’t taken effect until 2024.10,55 This is because although the phase-out began in 2009 and was scheduled to finish by the end of 2013, the commitment in the US was only made by the major producers and importers, with smaller entities not being subject to the ban until 2021.60,61 Meanwhile, the high expense of measurement limits routine monitoring frequency and coverage of legacy additive producers, making it difficult to effectively enforce some chemical legislation. Furthermore, varying restriction timelines across countries or regions have caused relocation of major production to less regulated regions, e.g. shift from the US to China in the early 2000s.10,62,63 The trade of finished products encasing legacy chemicals is often not regulated, which exacerbates global emission issues. These factors have sustained elevated concentrations in house dust, which explains the slow decline or stability of PBDE levels in humans post-ban, as well as the significant increase of BDE-209in China adult serum, where deca-BDE is still used until 2024. Despite the above, voluntary bans or industry-led changes can yield faster results. In Germany, industrial users stopped using penta-BDE in 1986, well before the EU’s 2004 regulation.64 Sweden halted production by 1999 and soon banned imports, later advocating for a global ban.65 This also explains why the turning point in BDE-47 and -99 levels in EU human milk occurred before the official ban (Figure 4).

However, continuous exposure alone cannot explain why BDE-209 does not show a rising trend in Chinese human milk, while in contrast, BDE-153 - banned earlier, exhibits a rising trend in US human milk and remains stable in the EU and China. Variations in chemical properties across PBDE congeners contribute to these patterns, with different bioaccumulative potentials affecting their accumulation in adipose tissue, which can be proxied by human milk in biomonitoring.66 After exposure, contaminants enter serum first and then adipose tissue, approaching equilibrium between the two matrices quickly. However, at the time a sample is taken, equilibrium is not necessarily attained because of possible recent exposure. So, human milk concentrations could better reflect a long-term historical exposure than serum, especially for highly bioaccumulative chemicals, while serum concentrations could be more influenced by recent exposure. BDE-153, with the longest half-lives (3 – 21.7 years in different human tissues) and the highest bioaccumulation potential, is more likely to show stable or rising trends in human milk post-ban, reflecting the accumulation of historical exposure.26,30,37,38 In contrast, BDE-209 is less bioaccessible with a shorter half-life (4 – 15 days) in humans, making it indicative of recent exposure.17,67,68 Therefore, its stable trend in human milk and rising trend in serum over two decades probably reflects ongoing emissions. BDE-183 also has low bioaccessibility and shorter half-lives in humans (68 – 120 days) compared to BDE-153, but exhibits more obvious decreasing trends in human milk as a result of early bans.67 However, being less bioaccumulative does not necessarily indicate that BDE-209 and -183 are safer than other congeners. Studies indicate their instability can lead to biotransformation into lower-brominated congeners through debromination, which exhibit higher bioaccumulative potential.69,70 This makes it difficult to differentiate whether the low-brominated congeners originated from external exposure, or partially from debromination processes. Meanwhile, the debromination of BDE-209 resulting from more recent exposure may help explain why, despite the decreasing trend in concentrations of lower-brominated PBDEs in dust due to earlier bans, these congeners continue to persist in biological samples, as stated above. BDE-47 and BDE-99, with smaller molecular sizes, higher bioaccessibility and moderate half-lives (1 – 2.9 years in different tissues), show a moderate accumulation capacity, between BDE-153 and BDE-183, -209.17,37,38,68,69 This also results in the increasing proportion of BDE-47, -99, and -153 from house dust to adult serum, and then to human milk (appendix pp 57).

An additional finding is that children’s serum and human milk may be the most suitable media for monitoring trend changes in human exposure to organic additives, as indicated by the significant differences in data patterns of PBDEs between adult and children’s samples. Van der Schyff et al. similarly demonstrated the utility of human milk in capturing long-term exposure trends.26 In contrast to adult serum samples, which span a broader age range and exhibit more scattered concentrations without clear patterns, human milk samples represent women of similar ages born in different periods with comparable exposure durations.26 Thus, more PBDE congeners show significant turning points in human milk than in adult serum, reflecting the impact of the PBDE ban. Children, exposed to PBDEs for a shorter period, are more affected by house dust concentrations than adults due to frequent hand-to-mouth behaviors.70,71 Their serum concentrations respond more quickly to changes in emissions and external exposure compared to adults. This explains the more obvious decreasing trend of penta- and octa-BDE in children’s serum than adult serum, with statistical significance for BDE-47, -99, and -153 in the US and Australia after 2005. The significantly declining BDE-183 and relatively stable BDE-209 in children’s serum further confirms recent exposure, aligning with temporal patterns in house dust (Figure 3, appendix pp 54 and 56). Adult serum samples are also significant for monitoring human internal exposure levels, as they represent a broader range of ages and genders within the general population. If age stratification of adult serum samples is provided, it could offer more detailed and nuanced insights into exposure patterns.72Therefore, selecting proper sample matrices can improve the efficiency of time trend monitoring.

Thirdly, regional differences in chemical use, flammability standards, phase-out timelines, product lifespans, and interior decoration practices significantly affect human exposure levels and temporal trends. The elevated concentrations in the US compared to other regions probably result from its longer and more extensive use of PBDEs, as well as the higher incorporation levels of PBDEs in consumer products. This trend is driven by historically more stringent flammability standards in the US relative to other regions, such as California’s former furniture flammability Technical Bulletin 117 (TB117).10,17,26,45 This aligns with the perspective presented by van der Schyff et al.26 Following the shift from the stringent TB117 standard to the more relaxed TB117-2013 standard, an 87% decline of BDE-47 and BDE-99 in indoor dust in New England, the US, reported by Rodgers et al., confirms the influence of flammability standards from another aspect.73 In contrast to the US, the EU only accounted for less than 10% of global historical production, and both China and the EU had shorter application periods and lower additive levels of penta- and octa-BDE than the US due to the absence or looser flammability standards for consumer products.17,45,74,75 Consequently, the US experienced higher emissions before the ban, and continues to generate higher post-ban emissions from extensive in-use stock. China has become a major chemical producer and consumer in recent decades, leading to high recent chemical emission and exposure.10 China’s later regulation of all PBDE congeners, particularly BDE-209 - which remains actively produced and used until 2024, is reflected in the predominance of BDE-209 in house dust and its increasing trend in adult serum. This suggests that it is still far from reaching steady-state in the Chinese population. The significant decreasing penta-BDE in human milk in China since early 2000s, similar to the EU but much earlier than the China’s national ban, may be influenced by international markets. The EU, closely following early regulations, shows more scattered data points for BDE-209 across various matrices, possibly due to the oscillation between bans and exemptions for deca-BDE in EEE during 2003 and 2008.

Additionally, interior decoration practices may compound regional variations in exposure, as a result of different product lifespans, material features and inclusion levels of individual congeners in decoration materials. For example, the US and the UK etc. have widespread use of carpets, which trap dust longer and extend exposure times due to their rougher surface compared to the smoother hard-surface floors that are more common in China and the other countries in the EU.76 In China, wallpaper, with higher BDE-209 contents than paint, has been a prevalent interior material over the past decade, contributing to indoor exposure, while it is seldom used in the US and much of the EU.77 The frequency of renovations or new housing construction may be higher in China than in the EU and the US at present, due to rapid economic growth and urbanization, which could expedite the effect of PBDE bans in China, with PBDEs replaced by alternative flame retardants in building materials or furniture due to bans.78,79 Thus, different countries may confront different contamination issues due to the regional variation in use patterns and dwelling style, which leads to variable effectiveness of bans across countries or regions.

Fourthly, the global data collected from independent literature and databases is highly fragmented and heterogeneous, lacking systematic longitudinal monitoring of humans and environmental media associated with major exposure routes at both global and national scales. This hinders a more accurate understanding of the temporal trends in exposure for both scientists and policymakers. Specifically, most available data are snapshots in time, compiled from diverse geographical regions and populations, with analyses conducted in different laboratories worldwide. Inter-laboratory variability and data incomparability may obscure true temporal trends, complicating result interpretation. The scattered data pattern for certain congeners and the contradictory trends across different matrices could be attributed to the inconsistency. Moreover, data integration from such fragmented spot samples usually lacks contextual information about sampling sites – such as the age of indoor items/furnishings or renovation history – which limits the ability to assess potential contamination sources (e.g., whether materials contain restricted additives like legacy PBDEs and per- and polyfluoroalkyl substances (PFAS) etc.). This gap critically constrains the interpretation of temporal trends in the dataset, the robust assessment of policy efficacy, and therefore the future decision-making by policymakers.

This is a limitation of analysis in this study owing to the deficiency in global monitoring framework and insufficient data availability, which also result in several additional limitations. Firstly, since individual sample-level concentration is typically not reported in publications, modeling relies on aggregated summary statistics (e.g., mean or median values). Although we employed a sample-size-adjusted weighting approach to reduce data heterogeneity, information regarding inter-study exposure distribution patterns and variance may remain unaddressed, which could inherently obscure intra-study variability and increase the risk of model misspecification bias. Secondly, additional potential change points – indicating multiple temporal trend shifts - may exist for some congeners for regions having experienced chemical policy reversals. The breakpoint regression model with one knot currently adopted is proved to be more robust than the model with 3-5 knots, e.g., restricted cubic splines. However, the statistical power to detect multiple trend shifts may be compromised by data paucity Finally, systematic measurement of PBDEs in food can help elucidate bioaccumulation in humans, especially for congeners like BDE-153, for which dietary exposure is relatively important, particularly for adults.30,35 However, existing data is excessively scattered across different food categories, each with varying bioconcentration factors due to diverse organism biology.25,34,80 Dietary habits vary geographically, impacting far-field exposure through transboundary food trade and local production and processing.30,81 The lack of comprehensive monitoring of regional diets and food traceability prevents a clear understanding of dietary exposure’s contribution on regional scales. Dietary exposure may be less important for PBDEs, but vital for other persistent chemical additives such as perfluorooctanoic acid (PFOA), and perfluorooctane sulfonic acid (PFOS).82

The current study design and analysis approaches have been the optimal based on the best available data. As indicated previously, above limitations are primarily induced by the absence of systematic longitudinal monitoring of external and internal exposure levels, as well as transparent data reporting and aggregation protocols.

To date, only seven longitudinal studies on dust and serum have been conducted, all on a local scale. Most countries lack systematic long-term monitoring and research programs for PBDEs and other POPs in both humans and environments. The Global Monitoring Plan assesses effectiveness of the Stockholm Convention by collecting and analyzing POPs concentrations, primarily atmospheric and human samples (mainly human milk, from the UNEP/WHO survey) from over 80 countries and regions, covering all POPs listed in the convention.83 The project ensures reliable data through strict regulation of analytical methods and quality control. However, limited human POPs data, typically spanning only 1 – 2 years in most countries, hinders tracking long-term trends (https://data.pops-gmp.org/2020/all/#/gmp3/summary-statistics). While atmospheric POPs data is more complete, it overlooks indoor exposure to additives. Some developed countries have implemented long-term human monitoring, such as health-related environmental monitoring in Sweden,84 and the National Health and Nutrition Examination Survey in the US,72,74 but broader and more sustained global human monitoring efforts remain insufficient. The approach of the mothers’ milk center in Stockholm, Sweden, is worth emulating for establishing a unified global framework for long-term monitoring. They collect human milk samples annually from healthy Swedish mothers. These preserved samples have helped observe the trends of BDE-47, BDE-99, and BDE-100, which rapidly increased since 1980, peaked in the late 1990s, and then gradually declined. Meanwhile, BDE-153 continued to increase, peaking in 2001 and remaining stable thereafter.85,86

The effectiveness of bans on organic chemical additives varies regionally and depends on chemical properties and existing stocks in products and populations. Tracking emission changes for widely used additives, such as PBDEs primarily exposed through indoor dust, may require 5 – 15 years, given product lifespans. Changes in body burdens of adults may necessitate even longer periods, 10 – 20 years or longer for more persistent chemicals. Estimating exposure alterations for chemical additives more reliant on far-field exposure, such as PFOA and PFOS, is complex due to more complicated emission sources and chemical accumulation in food during its production, process, and distribution. The global trade dynamics today and policy loopholes allowing banned chemicals to enter regions through finished products, makes it more challenging to observe the effectiveness of ban policies. Nevertheless, systematic monitoring of both human samples and external exposure levels, such as indoor dust and food, is essential for evaluating policy effectiveness.

However, ban policies represent post-application chemical management. We stress the importance of rigorous pre-assessment of chemical risk and the necessity to address this before market entry. Current chemical management and registration systems only require limited chemical information on rough production volumes and toxicity classification, which is far from a complete knowledge of chemical behaviors in humans and environments.87,88 Because of low-cost rough chemical pre-risk assessment and substantial commercial profits, newly developed chemicals are easily introduced by industry. However, some of them may have doubtful necessity, e.g. the extensive employment of flame retardants, particularly with elevated frequencies and concentrations across various products. Evidence has shown that although California has the strictest fire safety regulations (TB117, now replaced TB117-2013) and markedly elevated human exposure compared to other parts of the US, , it has death and injury rates from structural fires which are only slightly lower than the national average.74,89,90 Some other states in the US which do not have furniture flammability standards have achieved a similar decline in fire-related fatality rates as California, implying that there are effective alternative measures to using flame retardants in products.89,91 The loose pre-assessment leads to the iterative cycle of chemical use, hazard discovery, substitution, and repeated replacement. Lessons from history regarding polychlorinated biphenyls (PCBs) and dichlorodiphenyltrichloroethane (DDT) have demonstrated the long-term effects of post-application management, with great costs to environmental health.6,92 Therefore, in addition to a proactive and stringent chemical management, it is essential for policy makers to re-evaluate the current chemicals management model, rather than hastily replacing chemicals with regrettable alternatives under pressure.11

**Contributors**

GZ was involved in literature search, data collection, data analysis and interpretation, visualization of charts, writing and revising the manuscript. ZL contributed to the literature search and data collection. KJ was involved in data interpretation, visualization of charts, and manuscript revision. YZ led the conception and design of the study, participated in data analysis and interpretation, chart visualization, and the writing and revising of the manuscript. YZ and GZ accessed the raw data. All authors had full access to all data and have read and approved the final manuscript.

**Declaration of interests**

All authors declare no competing interests.

**Data sharing**

This manuscript used data from published studies and public databases, and therefore, no original data are available for sharing.

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