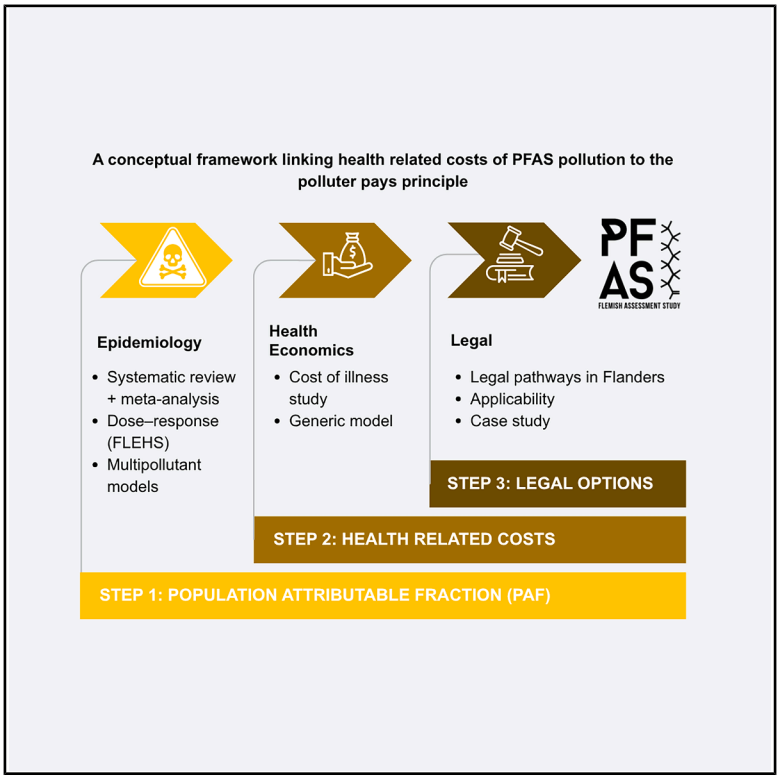
iScience

Article

A conceptual framework linking health related costs of PFAS pollution to the polluter pays principle

Graphical abstract



Highlights

- Interdisciplinary framework linking epidemiology, health economics and law
- PAF-based estimation of PFAS-attributable disease burden
- Cost-of-illness modeling of healthcare and societal costs
- Legal framework using hypothetical cases and compensation fund evaluation

Authors

Zoë Vandamme, Brigitte Reimann, Bo Vandenbulcke, ..., Britt Weyts, Michelle Plusquin, Koen Putman

Correspondence

zoe.vandamme@vub.be (Z.V.), bo.vandenbulcke@vub.be (B.V.)

In brief

Medical economics; Pollution; Exposure assessment

Vandamme et al., 2026, iScience *29*, 116748
August 21, 2026
https://doi.org/10.1016/j.isci.2026.116748

CellPress

iScience

CellPress
OPEN ACCESS

Article

A conceptual framework linking health related costs of PFAS pollution to the polluter pays principle

Zoë Vandamme,[1,4,6,*] Brigitte Reimann,[2] Bo Vandenbulcke,[1,4,*] Nick Portugaels,[3] Larissa Vanhooff,[3] Freek Louckx,[3] Britt Weyts,[3] Michelle Plusquin,[2] and Koen Putman[1,5]

[1]Interuniversity Centre for Health Economics Research (i-CHER), Vrije Universiteit Brussel, Brussels, Belgium
[2]Centre for Environmental Sciences, Hasselt University, Diepenbeek, Belgium
[3]University of Antwerp, Antwerp, Belgium
[4]Present address: Laarbeeklaan 103, 1090 Jette, Belgium
[5]Senior author
[6]Lead contact
*Correspondence: zoe.vandamme@vub.be (Z.V.), bo.vandenbulcke@vub.be (B.V.)
https://doi.org/10.1016/j.isci.2026.116748

SUMMARY

Exposure to per- and poly-fluoroalkyl substances is associated with adverse health outcomes and may generate substantial healthcare and societal costs. This concept study presents an interdisciplinary framework that links epidemiological evidence, health economic modeling, and legal analysis to estimate the health-related costs of PFAS pollution and explore compensation under the polluter pays principle. The framework combines systematic evidence synthesis, pooled effect estimates, and population attributable fractions to quantify the disease burden attributable to PFAS exposure. These estimates are integrated into cost-of-illness analyses to assess preventive and curative healthcare costs, productivity losses, and wider societal impacts. Legal analysis, including hypothetical cases and existing compensation fund mechanisms, is used to examine how quantified health-related costs can inform liability and compensation approaches. By connecting scientific evidence, economic valuation, and legal reasoning, the framework supports evidence-informed policymaking and adaptable compensation mechanisms as knowledge on PFAS-related health effects develops.

INTRODUCTION

Per- and poly-fluoroalkyl substances (PFASs) are a large class of man-made chemicals that share strong carbon-fluorine bonds but differ in chain length, functional groups, and polymeric forms. This chemical diversity produces wide variation in persistence, mobility, and bioaccumulation, making PFAS a moving target for exposure assessment and risk evaluation. Human exposure arises through multiple, intersecting pathways (contaminated drinking water and food, indoor dust and air from treated products, direct contact with consumer materials, and occupational settings) with transfer also occurring during pregnancy and breastfeeding.[1,2] Once in the body, PFAS bind to proteins and distribute unevenly across tissues, and different molecules can follow different kinetic patterns. As a result, PFAS are linked to effects across several organ systems through distinct mechanisms: immune dysregulation (altered vaccine responses), hepatic effects (lipid metabolism and enzyme changes), endocrine and thyroid signaling disruption, kidney and metabolic outcomes, and reproductive and developmental impacts.[1,3]

Research on the health impacts of PFAS pollution is a rapidly growing area of interest, with new findings emerging at a regular pace. Numerous public and private organizations are actively studying the effects of PFAS on health.[4] As with any environmental hazard, mapping the pollution in the environment is the first step. There is a wide array of databases available, offering extensive data on PFAS pollution. Governmental databases exist that provide information on environmental pollution at the country-specific level, for example the US database[5] and the Flanders database[6] initiated by the government. Also journalists and action groups have set up databases.[7] The purpose of the databases depends on the initiative taker. Governments aim to use these to map out pollution in order to initiate remediation efforts or implement "no-regret" measures for the population. Private databases, on the other hand, are mainly driven by activist goals, seeking to confront authorities and companies with the pollution and push them into action.[5–7]

The pollution caused by PFAS in the environment and the use of PFAS containing products eventually leads to the presence of PFAS in human blood, which in turn has significant health impacts. These health impacts are investigated at various levels. Animal studies, as well as population research with blood analyses, provide insights into the odds ratio of disease outcomes related to PFAS.[3,8]

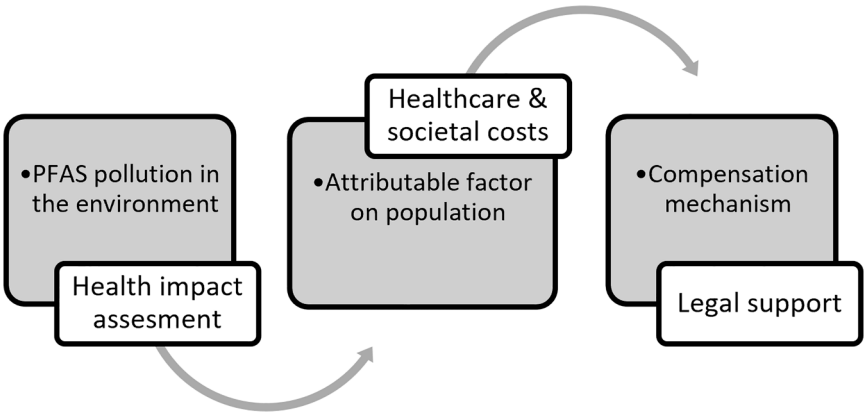


Figure 1. Conceptual framework for the study

The health effects of PFAS exposure result in a wide range of costs, encompassing not only healthcare expenses such as medical treatments, diagnostics, and hospitalizations but also indirect costs. These indirect costs include productivity losses due to illness, long-term informal care and the emotional burden placed on individuals and communities.[9,10] A comprehensive analysis is needed to give an overview of the costs of preventive and curative healthcare interventions linked to the burden caused by PFAS exposure. While cost estimates of PFAS-related health effects have already been developed at the European level and in several other countries, a comparable assessment is still lacking for Flanders. Following growing concerns about PFAS contamination and population exposure in the region, the Flemish government requested the development of a structured framework to estimate the associated health-related costs.[11] This project aims to fill that gap and provide the necessary evidence base to support policy evaluation and the potential application of the polluter pays principle.

In this context, legal support plays a critical role in ensuring that scientific research and the estimation of costs are properly integrated into policymaking. Legal expertise helps to bridge the gap between scientific research and regulatory action. Key questions arise in this domain, such as how to delineate the scope of the damage caused by PFAS pollution (both in terms of geographic regions and affected populations) and how to establish a fair and effective compensation system. Such a system must balance the needs of affected individuals with the principle of holding polluters accountable. Addressing these questions requires collaboration between legal, economic, and epidemiological disciplines to create a framework that is both equitable and feasible.

Arising from the comprehensive character of this study, three main objectives have been established, shown in Figure 1. The first is to map the health-related consequences of PFAS pollution in Flanders. Next, the costs associated with these health impacts are assessed. Lastly, a range of options for compensation frameworks are included.

As previously mentioned, the research on the health impacts is still ongoing. Therefore, a limited number of diseases are initially selected. Our aim is to provide an up-to-date cost of illness analysis and develop a framework that allows for the inclusion of future diseases and their associated costs. This approach will ensure that cost estimates and the compensation mechanism can be updated as new developments and data emerge.

To our knowledge, this is the first study to integrate three components (epidemiological, health-economic, and legal) within a single framework. This section offers a concise overview of the existing literature on the health economic burden of PFAS pollution. Its purpose is not to be exhaustive, but to identify key research gaps and to clarify the methodological basis for our work. Internationally, several studies have estimated the health related costs from PFAS pollution and in this section we describe three representative examples. These studies can be grouped into three categories based on their cost-calculation methods: those that rely on burden-of-disease metrics, those that use monetary values derived from systematic reviews, and those that adopt a mixed approach in which direct costs are monetized while indirect costs are estimated through burden-of-disease measures. Notably, we did not identify any study that calculates the costs of PFAS exposure solely on the basis of monetary values.

An example of a study using burden of disease metrics namely value-of-statistical-life is the Nordic Study by Goldenman et al. called ”the cost of inaction.” This study has been utilized by European organizations addressing PFAS pollution to guide decisions on eradicating PFAS from the environment through health economic analysis. The study describes the costs associated with PFAS in the European Economic Area (EEA), calculating health costs and non-health costs due to environmental contamination.[9,12] Exposure levels are stratified using NHANES data (low/medium/high) supplemented with values from the literature, and impacts are quantified from epidemiological studies reporting standardized mortality ratios, odds ratios or relative risks (RRs). By applying the cost per life lost as defined by the European Chemicals Agency (ECHA) and utilizing case studies that track the life cycle of PFAS, the number of lives lost can be estimated for a limited set of health endpoints. This approach focuses on endpoints where risk ratios are available for affected populations.

Although the study methodology is interesting, the research has some limitations especially with regard to the outcomes. The Nordic Study takes into account several cases of contamination in the EEA, for example contamination of the environment around Schiphol Airport due to fire-fighting foam. Derived from these sites and linked studies, it calculates the health related costs of exposure for a few health endpoints. For occupational exposure (people working in and around PFAS producing sites) only the health endpoint kidney cancer was considered (with only deaths due to kidney cancer and value of life lost taken into account). As noted by the authors at the beginning of the report, the primary goal is to raise awareness of the costs and

provide an estimate of the socioeconomic impact caused by PFAS pollution.[12]

An example of cost calculation using mixed method of monetary values and burden of disease metrics is the study by Obsekov et al., calculating the costs of PFAS pollution in the United States via a systematic review.[10] The calculation of the attributable fraction of disease is methodologically similar to Goldenman et al., and this study likewise uses NHANES data to characterize exposure distributions, while deriving exposure-outcome associations from the literature (via meta-analysis or an individual study).[12] Obsekov et al. extracts costs for 13 PFAS-linked conditions but apply a limited cost analysis. For example, direct costs of low birth weight are extracted from an existing study in the USA, only using the hospitals billing systems while non-admission costs are significant. For the indirect costs a mixed method was used to calculate costs. For example burden of disease metrics were used to calculate the costs for the indirect costs of obesity, while for low birth weight, lost lifetime economic productivity costs due to lost IQ points were taken into account. But only a limited number of clinical endpoints were used for indirect cost calculation. An extrapolation to a broader context is therefore impossible due to a lack of quantifiable health care utilization data and a lack of identification and valuation of all indirect costs.[10]

Another example of cost calculations using burden of disease metrics based on systematic reviews is the study conducted by the European Environment Agency. They used odds ratios and population-based exposure estimates to calculate an attributable factor that represents the share of disease burden that can be attributed to PFAS. The costs were determined using burden of disease metrics, specifically Disability-Adjusted Life Years (DALYs), which include both years lived with disability (YLD) and years of life lost. These existing data for the diseases studied were then used to calculate the associated costs. By applying the attributable factor for PFAS-related health impacts, an attributable cost was calculated from the burden of disease data.[13]

RESULTS

The study comprises three components. First, we estimate health impacts for predefined endpoints using dose-response relationships for the environmental health priority area (Flanders). Second, we perform cost-of-illness analyses and attributable budget impact assessments. Third, we carry out a legal analysis to identify and evaluate potential legal actions.

Epidemiological section

We conduct a systematic review and meta-analysis of epidemiological studies on PFAS and the selected health outcomes. Reporting follows the preferred reporting items for systematic reviews and meta-analysis (PRISMA 2020).[14] We search PubMed and Scopus using search strings covering PFAS (e.g., PFOS, PFOA, and "per- and poly-fluoroalkyl") and the targeted outcomes. For the appraisal of included observational studies, we use elements aligned with STROBE to guide data abstraction of study characteristics,[15] while risk of bias is evaluated with the OHAT risk-of-bias tool (NTP/OHAT, 2015; 2019 update). Eligible studies comprise original epidemiological studies conducted in human populations, primarily observational research (e.g., cohort, case-control, and cross-sectional studies), that provide quantitative data on the associations between PFAS exposure and the predefined health outcomes.

After bias assessment, we harmonize the extracted data to enable direct comparison between studies. To ensure comparability across studies that used different log-transformations or scales, we convert regression coefficients and CIs by published conversion methods to obtain a common scale, representing the association per 1 ng/mL increase in PFAS.[16,17] When necessary, standard errors (SEs) were computed from reported CIs or *p* values using standard formulas.[18]

Pooled estimates are calculated using both fixed- and random-effects models with the generic inverse-variance method.[19] In this approach, studies with more precise effect estimates receive greater weight. Statistical heterogeneity is assessed using the I^2 statistic, and between-study variance in the random-effects models is estimated using restricted maximum likelihood (τ^2).[20,21] Publication bias is explored using funnel plots and Egger's test. All analyses and visualizations are performed in R using published code from Frigerio et al. and the CRAN package metaforest.[22]

The population attributable fraction (PAF) is calculated to estimate the proportion of disease cases in the population that could be prevented if the exposure was eliminated. The pooled results of the meta-analysis are first transformed into a RR, as recommended when the disease prevalence is non-negligible.[23] This transformation used the formula as follows:

$$RR = \frac{OR}{1 - Pd + (Pd \times OR)}$$

where P_d is the prevalence of the disease in the population. The RR is then applied in Levin's formula for calculating the PAF, which incorporates the exposure prevalence (P_e):

$$PAF = \frac{(P_d \times (RR - 1))}{(Pd \times (RR - 1) + 1)}$$

Levin et al.[24] Here, P_e represents the prevalence of exposure in the population and is derived from the third cycle of the Flemish Human Biomonitoring Program (FLEHS III).[25] To estimate the absolute number of cases attributable to the exposure, the PAF is multiplied by the total number of disease cases in the population. The total number of cases is calculated using the total population size (*N*) and the disease prevalence (P_d): *total disease cases* = $N \times P_d$. The attributable number of cases is then calculated as: *attributable cases* = $PAF \times (N \times P_d)$. This approach allows for the integration of meta-analytic evidence with regional prevalence data to estimate the public health impact of a specific exposure.

In addition, we conduct a health impact assessment based on dose-response relationships derived from the Flemish human biomonitoring (FLEHS) datasets.[25] Specifically, we estimate dose-response relationships between PFAS and selected health outcomes within FLEHS cycles. The biobank of the Limburg birth cohort (representative of Flanders by maternal age and education) is additionally used to assess dose-response relationships in a sensitive population of newborns, linking PFAS metabolite

Table 1. Categorization of costs

Categories of costs	Subcategories
C1 Health sector	C1.1. Costs due to screening for illness Outpatient costs Inpatient costs C1.2. Costs due to illness Outpatient costs Inpatient costs C1.3. Survivorship costs
C2 Other sectors	
C3 Patient/family	C3.1. Out of pocket expenses Out of pocket expenses patient Out of pocket expenses family C3.2. Transportation costs
C4 Productivity losses	C4.1. Productivity loss patient Increased mortality before retirement Increased absenteeism C4.2. Productivity loss family

levels in cord blood to relevant health outcomes. In parallel, we develop a multipollutant model to account for co-exposures and potential confounding among correlated pollutants in the health impact assessment.

Health economic section

This study adopts a purely monetary approach and does not include burden-of-disease metrics. This choice reflects the legal objective of the project, which requires the estimation of attributable financial costs rather than broader societal burden measures. The analysis begins with a description of the selected pathologies and their associated costs. Cost classification follows Drummond's framework (Table 1), which provides an overview of the categories considered in the analysis. Not all categories are applied to every disease; inclusion depends on the specific pathology and the associated healthcare pathway.

For cost categories C1, C2, and C3, healthcare utilization matrices and unit costs are applied. The healthcare-related costs are calculated by determining the number of healthcare services used for each state and multiplying this by the corresponding unit cost. Productivity losses are estimated using the Human Capital Approach, in accordance with the Belgian guidelines for economic evaluations and budget impact analyses developed by the Belgian Health Care Knowledge Centre (KCE). This method estimates the economic impact of absenteeism by multiplying the total number of days an employee is absent from work by the national average labor cost per day, thereby reflecting the monetary value of lost productivity due to employee absence.[26]

The cost-of-illness models are developed following the transparent modeling framework described by Alarid-Escudero et al. and applied in related work.[10,27] In line with this framework, model development consists of two stages: a development phase and an analysis phase.

During the development phase, an appropriate modeling approach is selected and all required input parameters are specified. Following ISPOR recommendations and standard guidance on health economic modeling, model structure is tailored to the characteristics of each disease and target population.[28–31] This includes defining the start states, transition probabilities, cycle- or age-related corrections, and expert-informed assumptions where empirical data are limited. The starting population corresponds to the Flemish population for whom cost estimates are generated, allowing both total and per-patient-year costs to be calculated across disease-specific states.

Once the model structure and inputs are established, the analysis phase ensured that the model produced credible and conform to the literature outputs. This includes validation to assess internal consistency and alignment with external evidence, as well as a probabilistic sensitivity analysis (PSA) to quantify uncertainty by assigning probability distributions to key parameters and propagating that uncertainty through repeated simulations. Together, these steps form a systematic process to build robust models and evaluate their reliability.

Finally, all cost estimates are adjusted using the PAF associated with PFAS exposure, which is embedded within the PSA to generate a distribution of costs reflecting uncertainty.

Legal section

The legal component of this study examines how the financial responsibility for PFAS-related health damage is allocated under Belgian law and how this allocation may shift depending on possible legal actions taken by citizens suffering from PFAS-related health issues or other persons concerned.[32]

A central challenge is translating empirical scientific evidence, including its uncertainties, into a legal framework that allows systematic analysis of how Belgian law allocates financial responsibility across different PFAS-related situations. To support this analysis, we developed a framework based on three key variables: (α) exposure to PFAS emission sources, (β) evidence of internal contamination through measured blood concentrations, and (γ) the presence of medically recognized PFAS-associated health conditions.

Using this framework, the analysis considers three hypothetical individuals who satisfy all three variable sets.

- Marc, a resident living near a PFAS-producing facility who develops metabolic dysfunction associated fatty liver disease (MAFLD);
- Maria, an employee of such a facility diagnosed with kidney cancer;
- Anna, a consumer exposed through contaminated drinking water who develops PFAS-associated chronic anxiety.

For each model person, two distinct scenarios are examined. Scenario 1 assumes that neither the individual nor third parties recognize or assert a link between PFAS exposure and the health condition. Scenario 2 assumes that such a link is alleged, investigated or established, and compensation is sought.

In Scenario 1, the financial burden of PFAS-related harm may fall largely on existing collective mechanisms.[33] Belgium's compulsory health insurance covers, for example, the majority of medical costs, including some of the cost of psychological support. Furthermore Belgian social security protects workers incapable to work for medical reasons against loss of income. Residual expenses, co-payments, uninsured care, informal care costs, fall,

in principle, on the individual. But some employers may bear guaranteed-salary obligations during early periods of incapacity, while private insurance may absorb additional losses.

Scenario 1 will thus probably show a hybrid model of cost socialization combined with partial individualization.

Scenario 2 assesses whether Belgian liability law enables a legally enforceable shift of these costs toward polluters, operators of emission sources, water suppliers, employers or the government. Several legal regimes may be relevant, like the following.[34]

- Fault-based liability requires proof of a breach of statutory or general safety duties in the production, handling or release of PFAS.
- Neighbor-nuisance liability may apply where environmental burdens exceed normal neighborhood risks, even in the absence of fault.
- Product liability becomes relevant if contaminated water or PFAS-enriched consumer goods are considered defective.
- For employees such as Maria, occupational-disease insurance may intervene if recognition criteria are met, thereby shifting part of the burden from compulsory health insurance to the workers' compensation system.

Scenario 2 might show that the application of those regimes leads to a redistribution of the collectively baren costs and a prevalence of individualized financial responsibility. But we also expect to find that, across all these regimes the proof of causation between a source of exposure to PFAS-pollution and the occurrence of PFAS-related health issues in an individual case, might constitute a central bottleneck. PFAS exposure is typically chronic, low-dose and multi-source, and Belgian courts traditionally require convincing causal evidence. The α-β-γ modeling framework allows us to identify when causal reconstruction becomes legally plausible: exposure must be established, internal contamination must be objectively documented, and a PFAS-associated condition must be medically diagnosed. Even then, courts may require historical environmental measurements, source attribution, or exposure-pathway reconstruction-requirements that create substantial evidentiary obstacles. These constraints significantly limit the practical implementation of the polluter-pays principle.

The analysis also considers the recourse rights of compulsory health insurance and occupational-disease insurers. When liability is established, these institutions may recover some expenditures from responsible actors, creating a theoretical mechanism for shifting costs.

The study also evaluates compensation funds as an alternative mechanism. Belgian and international examples—including the Asbestos Fund, the Walloon PFAS-water initiative, and foreign PFAS compensation schemes—illustrate that such funds may lower evidentiary thresholds, provide predictable compensation and align compensation more closely with epidemiological evidence. Based on these examples, the analysis identifies key design parameters for a potential PFAS-specific fund.[35]

Sustainability/scalability

As highlighted earlier, research on the topic of health related costs of PFAS pollution is still ongoing. Ensuring the flexibility of the developed framework to incorporate new insights into diseases linked to PFAS pollution is therefore essential for the long-term applicability of the model. If we were to limit our framework to today's knowledge, the framework would be quickly deficient. The objective is to create an interactive application that allows users to input data, enabling cost calculations and the application of attributable factors. This approach ensures a user-friendly and efficient way to estimate costs.

DISCUSSION

This concept study outlines the development of a comprehensive framework aimed at addressing the healthcare related costs of PFAS pollution through an interdisciplinary approach. First, an epidemiological framework is developed to estimate the burden of disease specifically attributable to PFAS exposure. Next, a health economic model is designed to calculate the healthcare and societal costs of these diseases. Finally, a legal framework is proposed to apply the polluter pays principle, ensuring that polluters bear the financial responsibility for the health damage caused by PFAS pollution.

The methodology combines epidemiological data with health economic analysis and legal principles to create an integrated approach to PFAS-related pollution. By bridging these three domains, the project seeks to provide policymakers with a robust tool for addressing the health impacts of PFAS pollution while ensuring that those responsible for the contamination are held accountable.

Limitations of the study

In our project, we will focus solely on health-related costs. The costs of remediation will not be included. While we aim to create a generalizable application, it is important to exercise caution when assuming that the application and framework can be applied to other countries. Health care systems and sources of pollution vary significantly across regions, which may limit the direct applicability of the findings.

In addition, the epidemiological evidence base linking PFAS exposure to health outcomes largely consists of observational studies. While these studies provide essential information for estimating associations between exposure and disease, they inherently limit causal inference. Furthermore, exposure assessment in PFAS research remains challenging due to variability in exposure pathways, timing of measurements, and differences between study populations. These uncertainties may affect the strength of the estimated exposure-outcome relationships and therefore represent an important limitation of the proposed methodology.

Finally, the legal component of the framework is primarily developed for application within the Flemish context. Legal mechanisms related to liability, compensation, and the implementation of the polluter pays principle differ across jurisdictions, which may limit the direct transferability of this component of the framework to other countries. Nevertheless, the general structure of the approach may still provide useful guidance for adaptation in other legal settings.

RESOURCE AVAILABILITY

Lead contact

Requests for further information and resources should be directed to and will be fulfilled by the lead contact, Zoë Vandamme (zoe.vandamme@vub.be).

Materials availability

This study did not generate new unique reagents.

Data and code availability

- This study does not report original study data.
- This study does not report original code.
- Any additional information required to reanalyze the data reported in this study is available from the lead contact upon request.

ACKNOWLEDGMENTS

This research was funded by the Flemish Government. Grant number: VR 2022 2312 DOC.1505.

AUTHOR CONTRIBUTIONS

Conceptualization, Z.V., B.R., N.P., L.V., F.L., B.W., M.P., and K.P.; methodology, Z.V., B.R., B.V., N.P., F.L., and K.P.; visualization, Z.V.; writing – original draft, Z.V., B.R., and N.P.; writing – review and editing, B.V., L.V., F.L., B.W., M.P., and K.P.; funding acquisition, F.L., B.W., M.P., and K.P.; supervision, K.P.

DECLARATION OF INTERESTS

The authors declare no competing interests.

DECLARATION OF GENERATIVE AI AND AI-ASSISTED TECHNOLOGIES IN THE WRITING PROCESS

During the preparation of this work, the authors used ChatGPT in order to format and structure the references according to the journals style. After using this tool or service, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

STAR★METHODS

Detailed methods are provided in the online version of this paper and include the following:

- KEY RESOURCES TABLE
- EXPERIMENTAL MODEL AND STUDY PARTICIPANT DETAILS
- METHOD DETAILS
- QUANTIFICATION AND STATISTICAL ANALYSIS

Received: February 11, 2026
Revised: April 29, 2026
Accepted: June 24, 2026

REFERENCES

1. Arnesdotter, E., Stoffels, C.B.A., Alker, W., Gutleb, A.C., and Serchi, T. (2025). Per- and Polyfluoroalkyl Substances (PFAS): Immunotoxicity at the Primary Sites of Exposure (Taylor and Francis Ltd). https://doi.org/10.1080/10408444.2025.2501420.
2. United States Environmental Protection Agency (EPA) (2026). Our current understanding of the human health and environmental risks of PFAS. https://www.epa.gov/pfas/our-current-understanding-human-health-and-environmental-risks-pfas.
3. Pelch, K.E., Reade, A., Kwiatkowski, C.F., Merced-Nieves, F.M., Cavalier, H., Schultz, K., Wolffe, T., and Varshavsky, J. (2022). The PFAS-Tox Database: A systematic evidence map of health studies on 29 per- and polyfluoroalkyl substances. Environ. Int. *167*, 107408. https://doi.org/10.1016/J.ENVINT.2022.107408.
4. National Science and Technology Council (2023). Per- and polyfluoroalkyl substances (PFAS) report (White House Office of Science and Technology Policy). https://bidenwhitehouse.archives.gov/wp-content/uploads/2023/03/OSTP-March-2023-PFAS-Report.pdf.
5. Environmental Working Group (2024). PFAS contamination in the U.S. https://www.ewg.org/interactive-maps/pfas_contamination/.
6. Vlaamse Milieumaatschappij (2024). PFAS-verkenner. Databank Ondergrond Vlaanderen (Vlaamse Milieumaatschappij (VMM)). https://vmm.vlaanderen.be/feiten-cijfers/catalogus-feiten-cijfers/pfas-verkenner.
7. Arena for Journalism in Europe (2024). The Forever Pollution Project. https://foreverpollution.eu/about/.
8. De Decker, A., Gabaret, I., Den Hond, E., and De Brouwere, K. (2024). Proof-of-concept study on the coupling of PFAS results from human biomonitoring studies to health endpoints in the INTEGO-database. Department Care of the Flemish Government. https://assets.vlaanderen.be/image/upload/v1709886845/PFAS_-_Studie_-_Coupling_of_PFAS_results_from_human_biomonitoring_to_health_effects_m1tna1.pdf.
9. Cordner, A., Goldenman, G., Birnbaum, L.S., Brown, P., Miller, M.F., Mueller, R., Patton, S., Salvatore, D.H., and Trasande, L. (2021). The True Cost of PFAS and the Benefits of Acting Now. Environ. Sci. Technol. *55*, 9630–9633. https://doi.org/10.1021/acs.est.1c03565.
10. Obsekov, V., Kahn, L.G., and Trasande, L. (2023). Leveraging Systematic Reviews to Explore Disease Burden and Costs of Per- and Polyfluoroalkyl Substance Exposures in the United States. Expo. Health *15*, 373–394. https://doi.org/10.1007/s12403-022-00496-y.
11. PFAS Commissioner (2023). Final Report of the PFAS Commissioner (Government of Flanders).
12. Goldenman, G., Fernandes, M., Holland, M., Tugran, T., Nordin, A., Schoumacher, C., and McNeill, A. (2019). The Cost of Inaction (Nordic Council of Ministers). https://doi.org/10.6027/TN2019-516.
13. Plass, D., Beloconi, A., Bessems, J., Buekers, J., Kienzler, S., Martinez, G.S., Purece, A., and Vounatsou, P. (2025). Estimating the environmental burden of disease resulting from exposure to chemicals in European countries – Potentials and challenges revealed in selected case studies. Environ. Res. *269*, 120828. https://doi.org/10.1016/j.envres.2025.120828.
14. Page, M.J., McKenzie, J.E., Bossuyt, P.M., Boutron, I., Hoffmann, T.C., Mulrow, C.D., Shamseer, L., Tetzlaff, J.M., Akl, E.A., Brennan, S.E., et al. (2021). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ *372*, n71. https://doi.org/10.1136/bmj.n71.
15. von Elm, E., Altman, D.G., Egger, M., Pocock, S.J., Gøtzsche, P.C., and Vandenbroucke, J.P.; STROBE Initiative (2007). Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. BMJ *335*, 806–808. https://doi.org/10.1136/bmj.39335.541782.AD.
16. Frigerio, G., Ferrari, C.M., and Fustinoni, S. (2023). Prenatal and childhood exposure to per-/polyfluoroalkyl substances (PFASs) and its associations with childhood overweight and/or obesity: a systematic review with meta-analyses. Environ. Health. *22*, 56. https://doi.org/10.1186/s12940-023-01006-6.
17. Rodríguez-Barranco, M., Tobías, A., Redondo, D., Molina-Portillo, E., and Sánchez, M.J. (2017). Standardizing effect size from linear regression models with log-transformed variables for meta-analysis. BMC Med. Res. Methodol. *17*, 44. https://doi.org/10.1186/s12874-017-0322-8.
18. Borenstein, M., Hedges, L.V., Higgins, J.P.T., and Rothstein, H.R. (2009). Introduction to Meta-Analysis (Wiley). https://doi.org/10.1002/9780470743386.
19. Cochran, W.G. (1954). The Combination of Estimates from Different Experiments, First edition (International Biometric Society).

20. Higgins, J.P., and Thompson, S.G. (2002). Quantifying heterogeneity in a meta-analysis. Stat. Med. *21*, 1539–1558.

21. Viechtbauer, W. (2005). Bias and Efficiency of Meta-Analytic Variance Estimators in the Random-Effects Model. J. Educ. Behav. Stat. *30*, 261–293. https://doi.org/10.3102/10769986030003261.

22. van de Schoot, R., and Miočević, M. (2020). Small Sample Size Solutions (Routledge). https://doi.org/10.4324/9780429273872.

23. Zhang, J., and Yu, K.F. (1998). What's the Relative Risk? JAMA *280*, 1690. https://doi.org/10.1001/jama.280.19.1690.

24. Levin, M. (1953). Symposium on endemiology of cancer of lung: Occurrence of lung cancer in man. Acta Unio Int. Contra Cancrum *9*, 531–541.

25. Schoeters, G., Govarts, E., Bruckers, L., Den Hond, E., Nelen, V., De Henauw, S., Sioen, I., Nawrot, T.S., Plusquin, M., Vriens, A., et al. (2017). Three cycles of human biomonitoring in Flanders – Time trends observed in the Flemish Environment and Health Study. Int. J. Hyg Environ. Health *220*, 36–45. https://doi.org/10.1016/j.ijheh.2016.11.006.

26. Cleemput, I., Neyt, M., Van De Sande, S., and Nancy, T. (2015). Belgian guidelines for economic evaluations and budget impact analyses. In Health Technology Assessment (HTA), Second edition (Belgian Health Care Knowledge Centre (KCE)), KCE Reports 183C. https://doi.org/10.57598/R183C.

27. Alarid-Escudero, F., Krijkamp, E.M., Pechlivanoglou, P., Jalal, H., Kao, S.-Y.Z., Yang, A., and Enns, E.A. (2019). A Need for Change! A Coding Framework for Improving Transparency in Decision Modeling. Pharmacoeconomics *37*, 1329–1339. https://doi.org/10.1007/s40273-019-00837-x.

28. Briggs, A., and Sculpher, M. (1998). An introduction to Markov modelling for economic evaluation. Pharmacoeconomics *13*, 397–409. https://doi.org/10.2165/00019053-199813040-00003.

29. Briggs, A., Claxton, K., and Sculpher, M. (2011). Decision Modelling for Health Economic Evaluation (Oxford University Press).

30. Drummond, M.F., Sculpher, M.J., Claxton, K., Stoddart, G.L., and Torrance, G.W. (2015). Methods for the Economic Evaluation of Health Care Programmes, Fourth edition (Oxford University Press).

31. Siebert, U., Alagoz, O., Bayoumi, A.M., Jahn, B., Owens, D.K., Cohen, D.J., and Kuntz, K.M.; ISPOR-SMDM Modeling Good Research Practices Task Force. (2012). State-Transition Modeling: A Report of the ISPOR-SMDM Modeling Good Research Practices Task Force-3. Value Health *15*, 812–820. https://doi.org/10.1016/j.jval.2012.06.014.

32. Portugaels, N. (2018). De Vaststellingsovereenkomst (Intersentia).

33. Van Langendonck, J., Jorens, Y., and Louckx, F. (2023). Handboek Sociale zekerheidsrecht, Eleventh edition (Intersentia).

34. Vansweevelt, T., and Weyts, B. (2025). Handboek Buitencontractueel Aansprakelijkheidsrecht, Second edition (Intersentia).

35. Vanhooff, L. (2024). Vergoedingsfondsen. Aard, werking en wettigheid (Intersentia).

STAR★METHODS

KEY RESOURCES TABLE

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Software and algorithms		
RStudio	Posit	RRID:SCR_000432
Shiny	R package	RRID:SCR_001626

EXPERIMENTAL MODEL AND STUDY PARTICIPANT DETAILS

This study did not involve experimental models, biological samples, animals, cell lines, or human participants. The paper presents a conceptual methodological framework and therefore no participant-level data were collected or analyzed.

METHOD DETAILS

This paper presents a conceptual framework for estimating the health-related economic burden attributable to PFAS exposure. The proposed approach combines epidemiological evidence, population attributable fractions, disease-specific burden estimates, healthcare costs, productivity losses, and health-related quality-of-life losses.

The paper does not report a primary empirical study or experimental procedures. Instead, it describes the methodological steps required to identify relevant PFAS-related health outcomes, select exposure-response evidence, estimate attributable fractions, and combine these with disease-specific economic and health-utility inputs.

QUANTIFICATION AND STATISTICAL ANALYSIS

No original statistical analysis of primary data was conducted. Any calculations presented in this concept paper are illustrative and are used to demonstrate the proposed methodological framework.