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Review

Review

A Scoping Review of Technologies and Their Applicability for Exposome-Based Risk Assessment in the Oil and Gas Industry

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Abstract

Introduction: Oil and gas workers have been shown to be at increased risk of chronic diseases including cancer, asthma, chronic obstructive pulmonary disease, and hearing loss, among others. Technological advances may be used to assess the external (e.g. personal sensors, smartphone apps and online platforms, exposure models) and internal exposome (e.g. physiologically based kinetic modeling (PBK), biomonitoring, omics), offering numerous possibilities for chronic disease prevention strategies and risk management measures. The objective of this study was to review the literature on these technologies, by focusing on: (i) evaluating their applicability for exposome research in the oil and gas industry, and (ii) identifying key challenges that may hamper the successful application of such technologies in the oil and gas industry.

Method: A scoping review was conducted by identifying peer-reviewed literature with searches in MEDLINE/PubMed and SciVerse Scopus. Two assessors trained on the search strategy screened retrieved articles on title and abstract. The inclusion criteria used for this review were: application of the aforementioned technologies at a workplace in the oil and gas industry or, application of these technologies for an exposure relevant to the oil and gas industry but in another occupational sector, English language and publication period 2005—end of 2019.

Results: In total, 72 articles were included in this scoping review with most articles focused on omics and bioinformatics ($N = 22$), followed by biomonitoring and biomarkers ($N = 20$), external exposure modeling ($N = 11$), PBK modeling ($N = 10$), and personal sensors ($N = 9$). Several studies were identified in the oil and gas industry on the application of PBK models and biomarkers, mainly focusing on workers exposed to benzene. The application of personal sensors, new types of exposure models,

What's Important About This Paper?

Oil and gas workers have been shown to be at increased risk of chronic diseases including cancer, asthma, chronic obstructive pulmonary disease, and hearing loss, among others. New exposome technologies like sensors and omics offer great promise for personal monitoring of workers in the oil and gas industry, and subsequently will help to better prevent workers from developing diseases. In this scoping review, we explore the current application of these technologies in this industry and identify challenges and barriers for future application. Results will help in reducing occupational diseases.

and omics technology are still in their infancy with respect to the oil and gas industry. Nevertheless, applications of these technologies in other occupational sectors showed the potential for application in this sector.

Discussion and conclusion: New exposome technologies offer great promise for personal monitoring of workers in the oil and gas industry, but more applied research is needed in collaboration with the industry. Current challenges hindering a successful application of such technologies include (i) the technological readiness of sensors, (ii) the availability of data, (iii) the absence of standardized and validated methods, and (iv) the need for new study designs to study the development of disease during working life.

Keywords: biomonitoring and biomarkers; exposome; external exposure modeling; oil and gas industry; omics and bioinformatics; personalized sensors; physiologically-based kinetic (PBK) modeling; technologies and tools

Introduction

Although there have been many successful efforts worldwide to seek for new sources of cleaner energy, oil and gas still remain among the most important raw materials, with products based on these materials being widely used in modern society (Pickl, 2019). Oil and gas workers have been shown to be at increased risk of various types of diseases, including several types of cancers, asthma, chronic obstructive pulmonary disease, and hearing loss (Lim et al., 2012). It is therefore imperative that measures continue to be put in place in order to minimize the impacts of petrochemical industry related exposures. However, there is still limited available knowledge on the association between the complex exposures in the oil and gas industry and health (Bamber et al., 2019).

Traditionally, occupational health research is based on the single-exposure-to-disease concept. With the introduction of the exposome paradigm defined as 'the totality of exposures a person experiences during a lifetime' (Wild, 2005), and subsequently the occupational exposome concept (Faisandier et al., 2011; Pronk et al., 2020), a more holistic view was introduced and research started to investigate the integrated effect of multiple exposures in relation to human health across the (working) life course. Applying an exposome approach in the oil and gas industry will help to better understand the associations between complex exposures and effects, and subsequently will help to better prevent workers from developing diseases. However, it is not straightforward to translate this concept into practice. Three large challenges, which hamper the practical application of the exposome approach, are (i) the assessment of most external exposures (the external exposome) need to be improved, (ii) measuring and relating biological effect responses to the external exposome is in its infancy, and (iii) dealing with the spatiotemporal nature of the life course continuum of the exposome is complex, including the unraveling of the contribution of the occupational and nonoccupational exposome components (Vrijheid, 2014).

Exposome studies make use of a combination of targeted and untargeted technologies to overcome these aforementioned challenges and to more holistically assess external and internal exposures (Buck Louis et al., 2017). Current technologies (further explained in the method section) often used in exposome studies include: (i) personal sensors, (ii) external exposure modeling, (iii) physiologically based kinetic (PBK) modeling, (iv) omics and bioinformatics, which involves the analysis of thousands of biomolecules (at DNA, mRNA, protein, metabolite level) and computer-assisted interpretation of the biological meaning in relation to exposure or health effects, and (v) biomonitoring and biomarkers (DeBord

et al., 2016; Haddad et al., 2019). Presently, no review is available to verify if well-designed exposome studies, involving the (partial or full) integration and application of the aforementioned technologies to document the external and internal exposome, have been executed within the oil and gas industry. However, we expect that some of these more common and established technologies may have been applied to assess (oil and gas) industry exposures.

In this scoping review, we aimed to address the following two questions: (i) What relevant technologies for exposome research have been used in the oil and gas industry and other relevant industrial settings, to monitor and manage external and internal exposures? (ii) What are the key challenges for a successful application of these technologies for future exposome studies in the oil and gas industry?

Methods

Scope

Within this scoping review, we focused on the oil and gas industry and the aforementioned five groups of technologies, these being personal sensors, external exposure modeling, PBK modeling, omics and bioinformatics, and biomonitoring and biomarkers. However, due to the potential absence of literature describing the application of some of these technologies in the oil and gas industry we also considered the application of such technologies in industries where exposures relevant to the oil and gas industry were present. The methodology used is described in more detail below.

Definitions

The following definitions were used to focus the review:

- *Oil and gas industry* (or petrochemical industry): is concerned with the production and trade of petrochemicals and is further divided in (i) the upstream sector (production and exploration of crude oil and natural gas), (ii) the midstream sector (processing, storing, and transport), and (iii) the downstream sector (refining, selling, and distribution) (Lu et al., 2019).
- Technologies considered:
    - *Personal sensor*: a wearable device, which detects or measures a physical property and records, indicates, or otherwise responds to it. Such sensors can be used more widely over traditional methods because of lower costs, to capture exposure variability over longer periods of time, e.g. to identify exposure hotspots and activities or behavior resulting in high exposures (Goede et al., 2020). Personal sensors for this review include both low-cost sensors (<500 euro) detecting exposures and sensors capable of detecting contextual information (e.g. location using GPS, activities using video) that may be used to predict exposures.
    - *External exposure modeling*: an in silico system trying to estimate representative exposure levels in a simplified way. External exposure models can be e.g. mathematic (using mathematical concepts), deterministic (using data for a single estimate), or probabilistic (using data to give a distribution of possible outcomes) (Goede et al., 2020). Traditional occupational exposure models are often calibrated with time-integrated measurements and are capable of predicting task-based or shift-based personal exposure estimates. However, these models are by definition a simplification of a realistic work environment, which is characterized by exposure fluctuations in place and time (Goede et al., 2020). For exposome studies, more dynamic models, which take into account spatial and temporal resolution, may be more informative (Vineis et al., 2020). External exposure models included within the scope of this review were based on three key modeling approaches that were previously identified as being essential in the context of new types of (sensor) high resolution data. These are (i) enrichment of existing time-integrated exposure models with high resolution data, (ii) an extension of existing models to data-driven (empirical) models with a higher temporal resolution (time resolved models), and (iii) dispersion models modeling occupational exposures with more spatial resolution, similar to the approach for environmental exposome modeling (Goede et al., 2020). More conventional exposure assessment models often used for regulatory purposes were excluded in this review but could be used to underpin newer models.
    - *PBK modeling*: a mathematical modeling technique for predicting the absorption, distribution, metabolism, and excretion (ADME) of synthetic or natural chemical substances in humans (and other animal species). In the exposome context, there is a growing interest in PBK modeling and more specific physiologically based toxicokinetic (PBTK) and physiologically based toxicodynamics (PBTD) modeling for the interpretation of internal

exposome data as well as exposure reconstruction (Martínez et al., 2018).

- *Biomonitoring and biomarkers*: targeted approach (using modern analytical technology) to detect (known) markers of exposure (e.g. chemical residues, metabolites), markers of (early) effect (e.g. DNA adducts, changes in methylation status of selected genes, expression of selected mRNAs and proteins) or single markers of susceptibility (e.g. genetic polymorphism, metabolic phenotype).
- *Omics and bioinformatics*: high throughput analytical technologies, emerging from the human genome sequencing efforts (Lander et al., 2001; Venter et al., 2001). Recent developments of omics technologies make it possible to more broadly study the effect(s) of exposure(s) by using an untargeted strategy to look at the biological system as a whole. For exposome research, data driven bioinformatics approaches can be used to distinguish exposed from non-exposed individuals. In addition, pathway or network biology-based bioinformatics approaches can be used to infer changes in biological mechanisms. These can be reflective of primary exposure (e.g. uptake, transport, metabolism), early biological (reversible) change and, depending upon the study design and time window between initial exposure and sampling, also reflect possible persistent biological changes that occur later in time and underlie development of disease (Vinken, 2013). In this review, we focused on omics technologies that aim to detect exposure-related changes in genes (genomics), mRNA (transcriptomics), proteins (proteomics), and metabolites (metabolomics) in biological samples. Genomics is further divided into technologies focusing on variability in DNA sequences in the genome (genotyping) and identifying factors influencing the gene expression (epigenomics) (Thomas et al., 2002; Sellers and Yates, 2003; Callinan and Feinberg, 2006; Claudino et al., 2007). Importantly, these genomics technologies (and specially genotyping) were only included once applied to study in relation to the exposome.

Search strategy

For the development of the search strategy, the PRISMA guidelines were considered (Liberati et al., 2009; Moher et al., 2009). Keywords were defined and a preliminary search was conducted per technology in the oil and gas industry, to ensure the identified peer-reviewed articles were within the scope of this review and assess the number of articles of interest. When we identified less than five articles specific for the oil and gas industry (for a specific technology), the search was broadened to other industries with exposures also relevant for the oil and gas industry. The exposures of most relevance included volatile organic compounds (VOCs), benzene, toluene, polycyclic aromatic hydrocarbons (PAHs), mercury, noise, (respirable crystalline) silica, and particulate matter (Witter et al., 2014). Based on the preliminary searches, a broader search was needed for the final search, for all technologies except for the technology category 'biomonitoring and biomarkers'. Structured per technology, the exact search queries and the number of articles identified per search are available in the Supplementary Information SI1 in both MEDLINE/PubMed (https://pubmed.ncbi.nlm.nih.gov/) and SciVerse Scopus (https://www.scopus.com).

The inclusion criteria for articles identified in the final searches were as follows: published in a peer reviewed journal, English language, studies describing application of a technology in the oil and gas industry or based upon broader search terms application in the occupational settings of relevance to oil and gas, research published between 2005 (which is the start of exposome era) and end of December 2019 and research on exposures relevant for the oil and gas industry. The enumeration of exposures in the previous paragraph is not an exclusive list, so other exposures identified during the searches with relevance for the oil and gas industry were also included in this review.

Articles were initially screened in the following sequence: (i) combining Medline and Scopus, (ii) removal of duplicates, (iii) title screening, (iv) abstract screening. This initial screening was undertaken by two assessors independently who had been trained on the search strategy and were fully familiar with the scope and inclusion/exclusion criteria. The results of the screening process were compared and any disagreements discussed before finalizing the list of articles for which full copies were to be obtained. In the event of any uncertainty during the abstract screening process, the full article was obtained and screened. RefWorks (https://www.refworks.com/) was used to store the included references. Data from the included articles were manually extracted into a data extraction file, storing among others information on the industry, the type of technology, the exposure(s) of interest, the number of workers involved. Quality of the articles was not individually assessed since the scoping review was focused on establishing the breadth of the application of exposome technologies in

(the oil and gas) industry, rather than any formal review off the study quality or possible bias. For each article, the data extraction was completed independently by two separate assessors. The results were compared and any major discrepancies were discussed and a consensus agreement was made.

Results

A total of 178 peer-reviewed articles were identified as potentially relevant. From these, only 72 (40%) articles were included in this review after application of the inclusion criteria (Fig. 1). Most articles were included on omics and bioinformatics (N = 22) and biomonitoring and biomarkers (N = 20), followed by external exposure modeling (N = 11), PBK modeling (N = 10), and personal sensors (N = 9). Only for biomonitoring and biomarkers was the initial search focused exclusively on the oil and gas industry. For the other four technologies broader searches were conducted to also include occupational settings and exposures of possible relevance to the oil and gas industry, since only a limited number of studies were identified with application in the oil and gas industry. The applied technologies at the workplace in the oil and gas industry and other sectors are summarized in more detail in the following sections.

Personal sensors

In total, nine peer reviewed articles on personal sensors were included in this scoping review (Edwards et al., 2005; Huang et al., 2010; Negi et al., 2011; Pancardo et al., 2015; Brown et al., 2016; Fathallah et al., 2016; Uejio et al., 2018; Zuidema et al., 2019b). None of the selected articles described an application of personal sensors in the oil and gas industry. Measured chemical exposures with sensors were diverse, including particulate matter (PM), carbon monoxide (CO), hydrocarbons and acids, formaldehyde, VOCs, nitrogen oxides (NOx), and ozone (O_3) (Edwards et al., 2005; Negi et al., 2011; Fathallah et al., 2016; Zuidema et al., 2019b) (Table 1). In general, the number of workers involved was relatively low [1–5 worker(s)], as these studies focused on either demonstrating or testing the feasibility of using low-cost sensors to collect personal exposure data.

In addition to the studies that focused on chemical exposure, two studies applied the Thermochron iButton sensor to measure occupational heat exposure among municipal workers (Sugg et al., 2018; Uejio et al., 2018). The number of workers included in these two studies were relatively high (50 and 66), with the results showing the promise of applying a relatively large number of personal low-cost sensors, by developing local temperature maps for the study area. In addition, several low cost sensors, including an accelerometer and a heart rate monitor, were used to estimate occupational heat stress for outdoor workers (Pancardo et al., 2015).

Lastly, a feasibility study was conducted on the use of active radio frequency identification (RFID) technology for collecting time location data of indoor workers which can be used when linked with exposure data for identification of presence in e.g. exposure hotspots (Huang et al., 2010). These techniques were further developed in recent years (but not yet applied and described in literature) and are promising to replace more time consuming methods in exposure assessment (e.g. observations, time/activity diaries) to collect time location data (Mendoza-Silva et al., 2019).

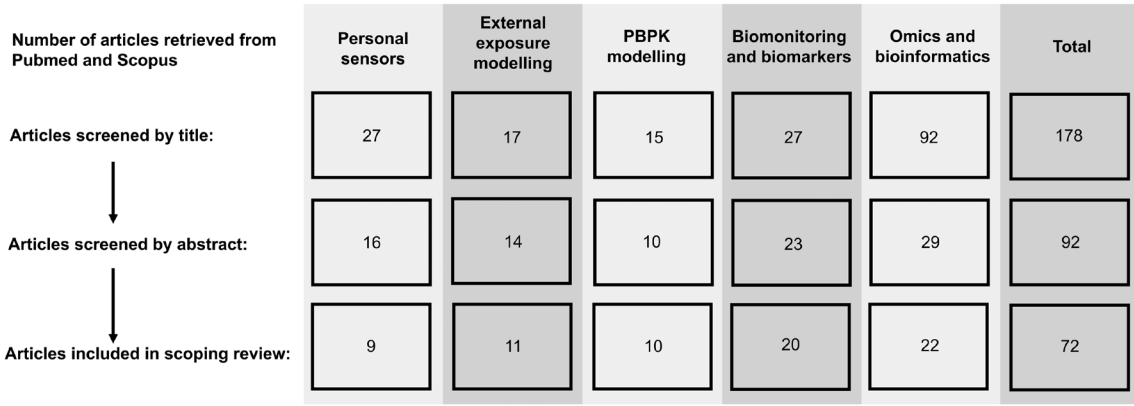

Figure 1. Overview results scoping review per technology. *Note:* one included article falls within two technology groups and was registered in both groups.

Table 1. Overview of applied personal sensor technologies.

Exposure, contextual info or health outcome	Industry/population	Technology (only real time readings)	References
Exposure			
CO	Firefighters (*N* = 4)	Draeger Pac III CO monitors	Edwards et al., 2005
	Indoor/office workers (*N* = 5)	CO-B4, Alphasense	Zuidema et al., 2019b
CO_2	Copy room worker (*N* = 1)	Multi-pollutant sensor node (not specified)	Fathallah et al., 2016
Formaldehyde	Copy room worker (*N* = 1)	Multi-pollutant sensor node (not specified)	Fathallah et al., 2016
Hydrocarbons and acids	Cleaning workers, firefighters, and waste management workers (*N* = 4)	Sensor cartridge (not specified)	Negi et al., 2011
NOx	Indoor/office workers (*N* = 5)	OX-B431, Alphasense	Zuidema et al., 2019b
O_3	Indoor/office workers (*N* = 5)	OX-B431, Alphasense	Zuidema et al., 2019b
$PM_{2.5}$	Firefighters (*N* = 4)	UCB particle monitor	Edwards et al., 2005
	Indoor/office workers (*N* = 5)	GP2Y1010AU0F, Sharp Electronics	Zuidema et al., 2019b
Temperature	Outdoor cleaning workers (*N* = 20)	Sensirion SHTC1	Pancardo et al., 2015
	Outdoor municipal workers (*N* = 50)	Thermochron iButton	Uejio et al., 2018
	Outdoor municipal workers (*N* = 66)	Thermochron iButton	Sugg et al., 2018
	Indoor/office workers (*N* = 5)	AM2302, Adafruit	Zuidema et al., 2019b
VOCs	Lab workers (*N* = 4)	PID sensor	Brown et al., 2016
Contextual information			
Location	Steel industry (*N* = 5)	Radio-frequency identification (RFID) technology	Huang et al., 2010
	Copy room worker (*N* = 1)	Wifi tags	Fathallah et al., 2016
	Lab workers (*N* = 4)	Ubisense UWB	Brown et al., 2016
Movement	Outdoor cleaning workers (*N* = 20)	Gene Activ accelerometer wristband	Pancardo et al., 2015

External exposure modeling

In total, 11 peer-reviewed articles on external occupational exposure modeling incorporating high resolution data were included in this scoping review (Table 2) (Davies et al., 2008; Davis et al., 2009; Sarigiannis et al., 2009; Flynn and Susi, 2010; Davis, 2012; Schaffernicht et al., 2017; Berman et al., 2018; Kuo et al., 2018; LeBlanc et al., 2018; Thomas et al., 2018). Only one of the selected articles described an application of external exposure modeling for the downstream oil and gas industry. For the first key modeling approach (enrichment of current models), one application was identified (LeBlanc et al., 2018). In this study, the outcomes of two conventional exposure assessment models [Near Field/Far Field (NF/FF) exposure model (Nicas, 1996) and the Advanced Reach Tool V1.5 (ART) (Fransman et al., 2011)] were compared to the ART model with Bayesian adjustment (which is considered as an example of a relatively new approach). Models were tested for exposures to vapors emitted from low concentrations of a contaminant in a common solvent, e.g. benzene in mineral spirits, and revealed better performance after Bayesian adjustment with high resolution exposure measurements.

More applications described in literature were found for the second key modeling approach as described by Goede et al. (2020), which includes data-driven models at higher temporal resolution than traditional models predicting time-weighted average (TWA) exposures (Davies et al., 2008; Davis et al., 2009; Sarigiannis et al., 2009; Flynn and Susi, 2010; Davis, 2012; Kuo et al., 2018). Exposures of interest included respirable PM, elemental carbon (EC), (respirable crystalline) silica, welding fumes, noise and benzene, with models developed for a variety of workplaces including milling industry, trucking terminals, construction industry, oil and gas filling stations, and foundries (Table 2). Model development was often based on a relatively large number of personal high-resolution measurements (15–547 workers). The modeling technologies used were mainly regression models, but other techniques such as artificial neural networks and structural equation modeling

Table 2. Overview of applied external exposure modeling technologies.

Exposure	Industry/population	Technology	References
Enrichment of existing time-integrated exposure model			
Benzene	Washing fluid (N = 2)	Advanced REACH tool and Bayesian adjustment	LeBlanc et al., 2018
Data-driven (empirical) model with a higher temporal resolution			
Benzene	Filling station employees (N = 15)	Bayesian algorithm, artificial neural networks	Sarigiannis et al., 2009
Elemental carbon	Trucking terminals (N = 114)	Structural equation model (SEM)	Davis et al., 2009
	Trucking terminals (N = 547)	Structural equation model (SEM)	Davis et al., 2012
Noise	Mill workers (N = 286)	Regression model	Davies et al., 2008
(Respirable) PM	Foundry (N = 236)	Predictive models, multiple linear regression	Kuo et al., 2018
(Respirable) Silica	Foundry (N = 236)	Predictive models, multiple linear regression	Kuo et al., 2018
Welding fumes	Construction (N = 58)	Johnson system of multivariate probability distributions	Flynn et al., 2010
Occupational dispersion model with more spatial resolution			
CO, NOx, O_3	Heavy vehicle manufacturing facility (N = 30)	Kriging-based hazard mapping	Thomas et al., 2018
	Heavy vehicle manufacturing facility (N = 40)	Kriging-based hazard mapping	Zuidema et al., 2019a
(Respirable) PM	Foundry (N = 1)	Echo state maps and Gaussian Processes	Schaffernicht et al., 2017
	Heavy vehicle manufacturing facility (N = 82)	Kriging-based hazard mapping	Berman et al., 2018
	Heavy vehicle manufacturing facility (N = 30)	Kriging-based hazard mapping	Thomas et al., 2018
	Heavy vehicle manufacturing facility (N = 40)	Kriging-based hazard mapping	Zuidema et al., 2019a

were also used to predict personal exposure. Most of these studies describe the development of a model and subsequently explore the goodness-of-fit (accuracy) with other (independent) high resolution or TWA data. In general, the accuracy of the developed models was considered adequate for estimating personal exposure, but the application of the model was only recommended by the authors for the scenarios captured in the training data.

Four peer-reviewed articles described dispersion models in an occupational setting with more spatial resolution (Schaffernicht et al., 2017; Berman et al., 2018; Thomas et al., 2018; Zuidema et al., 2019a), the third modeling approach which was considered in this review. Three of these publications were part of a larger research project in a heavy-vehicle manufacturing facility, implementing a (calibrated) sensor network and using the data for developing and optimizing kriging-based hazard mapping for several pollutants including PM and CO (Berman et al., 2018; Thomas et al., 2018; Zuidema et al., 2019a). The kriging method was used to interpolate data from measurement locations of the sensor network to unsampled locations, to be able to estimate personal exposures during e.g. a workday. Median biases ranged from 1% for noise exposure up to 41% for PM exposure, largely explained by sensor stability over time (Zuidema et al., 2019a). In addition, a combination of a continuously moving robot with sensors and stationary sensors in a foundry was used to apply the echo state map approach (a tool for time series analyses) (Schaffernicht et al., 2017). Spatial interpolation was used by applying the Gaussian method, which is comparable to the methodology used by the aforementioned articles, to develop dynamic exposure maps. In this explorative study, the model showed good results for low dust concentrations but the sensor-based interpolation was more difficult during peaks in dust concentrations.

PBK modeling

In total, 10 peer-reviewed articles on PBK modeling were included in this scoping review with some manuscripts specific for the oil and gas industry (Table 3) (Dennison et al., 2005; Sarigiannis et al., 2009; Wang et al., 2009; Hays et al., 2012; Jongeneelen and Ten Berge, 2012; Heredia Ortiz et al., 2014; Mork et al., 2014; Marchand et al., 2015; Majumdar et al., 2016; Marchand et al., 2016). Most of these studies focused on exposure to benzene (Sarigiannis et al., 2009; Wang et al., 2009; Hays et al., 2012; Majumdar et al., 2016) or on mixed exposure to toluene, ethylbenzene, and xylene (Dennison et al., 2005; Mork et al., 2014; Marchand et al., 2015, 2016), followed by exposure to PAHs (Jongeneelen and Ten Berge, 2012; Heredia Ortiz et al., 2014) and chloroform as a VOC (Marchand et al., 2016). Dennison et al. (2005), Marchand et al. (2015) and (2016) used (partly) a PBK model previously published by (Tardif et al., 1997). Dennison et al. (2005) used this model to evaluate the potential toxicity from mixtures taking into account kinetic interactions of specific chemicals in these mixtures. The same model was further developed for predictions of urinary biomarkers and evaluated based on experiments with volunteers (Marchand et al., 2015, 2016).

Two of the studies on exposure to benzene used data from subjects (N = 15 and 35) working in the downstream oil and gas industry at petrol filling stations (Sarigiannis et al., 2009; Majumdar et al., 2016). Most models available for benzene were six-compartment models including the liver, adipose tissue, richly perfused tissues, poorly perfused tissues, bone marrow (the main target organ for benzene toxicity), and the kidney. In one of the studies, a method was developed to calculate real time personal exposure to benzene using sensor data in artificial neural networks. This study assessed the association between exposure to benzene and cancer risks by using a benzene specific PBK model for employees at rural and urban filling stations (Sarigiannis et al., 2009). For a different working population (numbers not specified) exposed to benzene, a PBK model was used to convert external exposure threshold limit values (TLVs) for benzene into biomonitoring equivalents (BE) for risk assessment purposes (Hays et al., 2012). Lastly, to estimate cancer risks for workers in a foam production company exposed to benzene, a traditional PBK model was used

Table 3. Overview of applied PBK modeling technologies.

Exposure	Industry/population	Model description	References
Benzene	Filling station employees (N = 15)	Six compartment PBK model based on Medinsky et al. (1996); Yokley et al. (2006)	Sarigiannis et al., 2009
	Foam production company (N = 20)	Six compartment PBK model evolved from Bois et al. (1996)	Wang et al., 2009
	Workers (not specified)	PBK model from Brown et al. (1998)	Hays et al., 2012
	Petrol pump workers and car drivers (N = 35)	Four compartment PBK model from Bernillon and Bois (2000)	Majumdar et al., 2016
Chloroform	Volunteers with exposure relevant for workers (N = 14)	Four compartment PBK model partly based on Tardif et al. (1997)	Marchand et al., 2016
PAHs	Workers (data from literature)	Generic, cross-chemical predictive toxicokinetic model from Jongeneelen and Berge (2011)	Jongeneelen et al., 2012
	Workers (N = 14)	Four compartment PBK model constructed by the authors	Heredia Ortiz et al., 2014
Toluene, ethylbenzene, and xylene (mixtures)	Simulations with worker relevant exposures (N = 6)	Four compartment PBK model from Tardif et al. (1997)	Dennison et al., 2005
	Volunteers with exposure relevant for workers (N = 5)	Four compartment PBK model partly based on Tardif et al. (1997)	Marchand et al., 2015
	Volunteers with exposure relevant for workers (N = 14)	Four compartment PBK model partly based on Tardif et al. (1997)	Marchand et al., 2016
Toluene, styrene, and methyl chloride	Workers (not specified)	Population-based PBK models from Jonsson and Johanson (2001)	Mork et al., 2014

(Wang et al., 2009) with the model based on previous work (Bois et al., 1996).

The studies on exposure to PAHs focused on different metabolites (Jongeneelen and Ten Berge, 2012; Heredia Ortiz et al., 2014). Jongeneelen and Ten Berge (2012) studied the urinary excretion of 1-hydroxypyrene using a generic, cross-chemical PBTK model (IndusChemFate), while Ortiz et al. simulated the profiles of 3-hydroxybenzo(a)pyrene using a PBK model based on an animal study for benzo(a)pyrene.

Biomonitoring and biomarkers

In contrast to the other technologies reviewed, biomonitoring and biomarkers have been largely studied in the oil and gas industry, and no additional search terms spanning non-oil and gas industry settings were included. In total, 20 peer-reviewed articles on biomonitoring and biomarkers were included in this scoping review with application in the oil and gas industry (Table 4) (Farmer et al., 2005; Garte et al., 2005; Navasumrit et al., 2005; Roma-Torres et al., 2006; Hoet et al., 2009; Martins et al., 2009; Pesatori et al., 2009; Wickliffe et al., 2009; Carrieri et al., 2010, 2012; Basso et al., 2011; Fustinoni et al., 2012; Seow et al., 2012; Gonçalves et al., 2016; Kamal et al., 2016; Hajizadeh et al., 2018; Liang et al., 2018; Ayas et al., 2019; Federico et al., 2019; Kirkhus et al., 2019). Predominantly, these studies focused on workers in the midstream or downstream sectors, exposed to benzene. Only six articles described research on different exposures, which were petroleum derivatives, 1,3 butadiene, PAHs, VOCs and drilling fluids, xylene, respectively (Martins et al., 2009; Wickliffe et al., 2009; Kamal et al., 2016; Hajizadeh et al., 2018; Ayas et al., 2019; Kirkhus et al., 2019). The early relatively large studies on benzene (Number of workers: 110–623) used the urinary biomarkers of exposure S-phenylmercapturic acid (S-PMA), and trans,trans-muconic acid (t,t-MA), which are still commonly used for regulatory purposes via comparison with existing biological limit values (BLVs) (Farmer et al., 2005; Garte et al., 2005; Hoet et al., 2009; Carrieri et al., 2010). In addition, using markers of exposure but not for benzene, associations between exposure to VOCs and urinary metabolites were studied which included mandelic acid, phenol, and phenylglyoxylic acid (Hajizadeh et al., 2018).

Most of the peer-reviewed articles identified, used a combination of markers of exposure and markers of effect (Navasumrit et al., 2005; Roma-Torres et al., 2006; Martins et al., 2009; Wickliffe et al., 2009; Basso et al., 2011; Fustinoni et al., 2012; Seow et al., 2012; Gonçalves et al., 2016; Kamal et al., 2016; Liang et al., 2018; Ayas et al., 2019; Federico et al., 2019; Kirkhus et al., 2019). Three of these studies evaluated the effect of exposure and found exposure-induced effects on DNA strand breaks, cellular death, and repair capacity (Navasumrit et al., 2005; Roma-Torres et al., 2006; Martins et al., 2009). Three other studies reported the detrimental effect of exposure on functioning of lymphocytes (Wickliffe et al., 2009; Basso et al., 2011; Gonçalves et al., 2016). Additionally, serum proteins (plasminogen, platelet basic protein, and apolipoprotein B100) were identified as potential biomarkers of effects, associated with relatively low exposures of benzene (Liang et al., 2018), while three other pneumoproteins related to systemic inflammation (club cell protein 16, surfactant protein D, and C-reactive protein) were found to be significantly different in a population exposed to drilling fluids (Kirkhus et al., 2019). Furthermore, blood parameters were studied in petrochemical workers exposed to PAHs and benzene, respectively (Kamal et al., 2016; Federico et al., 2019). Also, (targeted) DNA methylation and the effect of benzene exposure was evaluated (Seow et al., 2012). In addition, the uptake of benzene and the effect of environmental and lifestyle factors on this uptake were evaluated (Fustinoni et al., 2012).

Finally on the intensity of the effect, the influence of (glutathione S-transferase) polymorphisms on biological effect monitoring for workers exposed to benzene was studied (Pesatori et al., 2009; Carrieri et al., 2012). Results showed that S-PMA, but not t,t-MA can be used to monitor exposure, with GSTT1 null genotype having a low but significant influence on the aforementioned metabolite excretion markers (Carrieri et al., 2012). In addition, no effect on benzene hematotoxicity was detected for CYP2E1 and NQO1 polymorphisms (Pesatori et al., 2009).

Omics and bioinformatics

In total, 22 peer-reviewed articles on omics and bioinformatics were included in this scoping review (Table 5) (Vermeulen et al., 2005; Lan et al., 2009; McHale et al., 2009, 2011; Broberg et al., 2010; Rihs et al., 2011; Alegría-Torres et al., 2013; Li et al., 2013; Pacheco et al., 2013; Thomas et al., 2013, 2014; Wei et al., 2013; Motts et al., 2014; Shen et al., 2014, 2016; Chuang et al., 2015; Walker et al., 2016; Zheng et al., 2017; Sun et al., 2018; Zhang et al., 2018; Alhamdow et al., 2019; Li et al., 2019).

Six of these studies addressed the influence of (a) single nucleotide polymorphism(s) (SNP), as detected by genotyping technologies, onto metabolism of chemicals or disease outcome, in relation to external

Table 4. Overview of applied biomonitoring technologies.

Exposure	Industry/population	Technology	References
1,3 Butadiene	Petrochemical workers (*N* = 30)	HPRT gene mutant lymphocytes	Wickliffe et al., 2009
Benzene	Gasoline filling station attendants (*N* = 623)	S-PMA	Farmer et al., 2005
	Petrochemical workers (*N* = 158)	S-PMA, t,t-MA, DNA-SSB	Garte et al., 2005
	Occupational gasoline and factory workers (*N* = 125)	Blood benzene t,t-MA, DNA-SSB, repair capacity	Navasumrit et al., 2005
	Petrochemical workers (*N* = 110)	t,t-MA, S-PMA en urinary benzene	Hoet et al., 2009
	Petrochemical workers (*N* = 203)	Hematological outcomes, t,t-MA, genetic polymorphisms	Pesatori et al., 2009
	Petrochemical workers (*N* = 145)	t,t-MA, S-PMA	Carrieri et al., 2010
	Petroleum refinery workers (*N* = 129)	Cytokinesis block micronucleus, PBL	Basso et al., 2011
	Petrochemical workers (*N* = 28)	t,t-MA, S-PMA, GST genotypes	Carrieri et al., 2012
	Petrochemical workers (*N* = 33)	Urinary benzene, cotinine, creatinine	Fustinoni et al., 2012
	Petrochemical workers (*N* = 208)	Urinary benzene, S-PMA, t,t-MA, DNA methylation (LINE-1, MAGE, p15)	Seow et al., 2012
	Petrochemical workers (*N* = 36)	Genotoxicity in lymphocytes (chromosomal gaps, breaks, and aneuploid)	Gonçalves et al., 2016
	Petrochemical workers (*N* = 532)	PLG, PBP, ApoB100 and blood cell counts	Liang et al., 2018
Benzene, toluene, and xylene (BTX)	Petroleum refinery workers (*N* = 78)	CA, MN, DNA damage, t,t-MA, HA, MHA	Roma-Torres et al., 2006
Drilling fluids, oil mist, oil vapor	Offshore drill floor workers (*N* = 65)	CC-16, SP-D, CRP	Kirkhus et al., 2019
PAHs	Petrochemical workers (*N* = 55)	1-OHP yr, α- and β-naphthols, blood parameters	Kamal et al., 2016
Petroleum derivatives	Petrol station attendants (*N* = 46)	DNA damage and cellular death	Martins et al., 2009
	Petroleum refinery workers (*N* = 50)	MN and ONA	Federico et al., 2019
VOCs (benzene, styrene, ethylbenzene, and phenol)	Petrochemical workers (*N* = 84)	Urinary metabolite (phenol, MA, and PGA)	Hajizadeh et al., 2018
Xylene	Petrochemical workers (*N* = 30)	MN, MHA	Ayas et al., 2019

1-OHPyr, 1-pyrenol; ApoB100, apolipoprotein B100; CA, chromosome aberrations; CC-16, club cell protein 16; CRP, C-reactive protein; DNA-SSB, DNA single strand breaks; GST, glutathione S-transferases; HA, hippuric acid; MA, mandelic acid; MHA, methylhippuric acid; MN, micronuclei; ONA, other nuclear anomalies; PBL, peripheral blood lymphocytes; PBP, platelet basic protein; PGA, phenylglyoxylic acid; PLG, plasminogen; S-PMA, S-phenylmercapturic acid; SP-D, surfactant protein D; t,t-MA, urinary t,t-muconic acid.

exposures (Lan et al., 2009; Broberg et al., 2010; Rihs et al., 2011; Li et al., 2013; Shen et al., 2014, 2016). Three of these studies were on workers (*N* = 340, 612, 613, respectively) exposed to noise and noise-induced hearing loss (NIHL) (Li et al., 2013; Shen et al., 2014, 2016). In these case–control cohorts, the associations between genetic variation (in GRHL2, Ser326Cys, and APE1) and NIHL were studied. From the genotyping

Table 5. Overview per type of omics technology and per exposure on applied technologies.

Exposure per type of omics technology	Industry/population	Technology	References
Epigenomics			
Benzene	Benzene-exposed workers (*N* = 76)	Methylation analysis focused on specific CpG sites of ERCC3	Zheng et al., 2017
PAHs	Brickmakers (*N* = 39)	Methylation analysis using pyrosequencing	Alegría-Torres et al., 2013
Genotyping, to address susceptibility toward external exposure			
Benzene	Workers in shoe factories (*N* = 250)	Analysis of 1536 SNPs in 411 genes	Lan et al., 2009
Bitumen	Workers exposed to bitumen (*N* = 218)	Analysis of 18 SNPs in genes involved in PAHs and amine metabolism	Rihs et al., 2011
Noise	Workers with NIHL (*N* = 340)	Analysis of polymorphisms in GRHL2 genes	Li et al., 2013
	Workers with NIHL (*N* = 612)	Analysis of polymorphisms in hOGG1 Ser326Cys	Shen et al., 2014
	Workers with NIHL (*N* = 613)	Analysis of polymorphisms in APE1	Shen et al., 2016
TDI	Workers involved in production of polyurethane foams and paints (*N* = 70)	Analysis of polymorphisms in several genes	Broberg et al., 2010
Metabolomics			
Benzene	Painting workers and workers in shoe factories (*N* = 30)	Global metabolite profiles using MS, pathway analyses	Sun et al., 2018
Metal fumes	Welders (*N* = 11)	Global metabolite profiles using MS, pathway analyses	Wei et al., 2013
TCE	TCE-exposed workers (*N* = 80)	Analysis using metabolome-wide association study framework	Walker et al., 2016
Proteomics			
Benzene	Workers in a shoe factory (*N* = 40)	Protein-expression pattern analysis using SELDI-TOF	Vermeulen et al., 2005
	Benzene-exposed workers (*N* = 165)	2D-DIGE and MALDI-TOF-MS	Zhang et al., 2018
	Benzene-exposed workers (*N* = 351)	2D-DIGE and MALDI-TOF-MS	Li et al., 2019
Mercury	Miners (*N* = 371)	ProtoArray analysis	Motts et al., 2014
Metal fumes	Welders (*N* = 66)	LC-MS/MS	Chuang et al., 2015
PAHs	Secondhand smoke (SHS) exposed workers in restaurants (*N* = 96)	2D-DIGE MS	Pacheco et al., 2013
	Chimney sweeps (*N* = 118)	Monoydroxylated metabolites of pyrene, phenanthrene, benzo[a] pyrene and benzo[a]anthracene, proximity extension assay	Alhamdow et al., 2019
Transcriptomics			
Benzene	Workers in shoe factories highly exposed (*N* = 8)	Affymetrix and illumine microarray analysis	McHale et al., 2009
	Workers in shoe factories (*N* = 125)	Illumine microarray analysis	McHale et al., 2011
	Workers in shoe factories (*N* = 83)	Illumine microarray analysis	Thomas et al., 2013
	Workers in shoe factories (*N* = 83)	Illumine microarray analysis	Thomas et al., 2014

2D-DIGE, two-dimensional difference gel electrophoresis; APE1, apurinic/apyrimidinic endonuclease 1; LC-MS/MS, liquid chromatography–tandem mass spectrometry; MALDI-TOF-MS, matrix-assisted laser desorption/ionization time-of-flight mass spectrometry; MS, mass spectrometry; NIHL, noise-induced hearing loss; SELDI-TOF, surface-enhanced laser desorption ionization; SNPs, single nucleotide polymorphisms; TCE, trichloroethylene; TDI, toluene di-isocyanate.

studies, only one focused on the (downstream) oil and gas industry with a study on asphalt workers exposed to bitumen (Rihs et al., 2011). In this research, the influence of polymorphisms in genes coding on urinary markers was evaluated, showing no significant effects on 1-hydroxpyrene for the studied SNP.

Epigenomics technologies were used to study brick makers exposed to PAHs (N = 39) and benzene-exposed workers engaged in printing, shoe making, or painting (N = 76) (Alegría-Torres et al., 2013; Zheng et al., 2017). With a cross-sectional study design, a pilot study in brick makers was conducted using DNA methylation analysis and identified epigenetic markers of PAHs exposure (IL-12 and P53 DNA methylation) (Alegría-Torres et al., 2013). For the other population indications for CpG-related DNA methylation (ERCC3 promoter region) involved in epigenetic modifications were observed, induced by benzene exposure and related to hematotoxicity (Zheng et al., 2017).

Four studies used transcriptomics technology and were part of a larger study (Vermeulen et al., 2005; Lan et al., 2009) which focused on workers in shoe factories exposed to benzene (McHale et al., 2009, 2011; Thomas et al., 2013, 2014). A method was developed and tested for this population, using two microarray platforms which makes it possible to identify more robust biomarkers than by using a single-platform array (McHale et al., 2009). Furthermore, a different method on RNA-sequencing technology was tested and used in a pilot study (Thomas et al., 2013). Subsequently, both methods were applied in a larger study (N = 125 and 83, respectively) and focused on relatively low levels of benzene exposure (McHale et al., 2011; Thomas et al., 2014).

The studies using proteomics technologies focused on workers exposed to benzene (Vermeulen et al., 2005; Zhang et al., 2018; Li et al., 2019), PAHs (Pacheco et al., 2013; Alhamdow et al., 2019), mercury (Motts et al., 2014), and metal fumes/$PM_{2.5}$ (Chuang et al., 2015). Using agnostic approaches by screening broad protein expression, two potential biomarkers of early effects (expression of PF4 and CTAP-III proteins) were identified using surface-enhanced laser desorption ionization (SELDI)-TOF MS (Vermeulen et al., 2005), while two other studies identified in total ten proteins in a population with chronic benzene poisoning, using 2D-DIGE and MALDI-TOF-MS (Zhang et al., 2018; Li et al., 2019). The other four studies on proteomics used mass spectrometry for a similar purpose (identifying new biomarkers of exposure and/or early effect and understanding pathways of disease).

Three studies used metabolomics technologies for workers exposed to metal fumes, trichloroethylene (TCE) and benzene, respectively (Wei et al., 2013; Walker et al., 2016; Sun et al., 2018). The study on metal fumes identified a dose-depending decreased amount of unsaturated fatty acids in a welder's population, which can be used as a potential biomarker (Wei et al., 2013). For Chinese workers exposed to benzene with a low number of white blood cells, it was found that the fatty acid oxidation was involved in hematotoxicity (Sun et al., 2018). Lastly, a systemic metabolic response was observed associated with exposure to TCE (Walker et al., 2016).

Discussion

In summary, 72 articles were included in this scoping review on technologies relevant for exposome research. Some of these focused primarily on the oil and gas industry, but the majority were focused on other industrial sectors because of the lack of sufficient papers in the oil and gas industry. Exposures are not ignored in the oil and gas sector but more traditional methods are used driven by regulatory requirements. Since these methods are single chemical focused and data is often time integrated, results are of limited value for exposome research. Interestingly, the oil and gas industry is used to applying the more invasive approaches (e.g. biomarkers for known carcinogens both for regulatory monitoring and for research) while it is theoretically easier to encourage the use of other noninvasive techniques. With new technologies evolving, it is expected that in the (near) future more relevant data for exposome research will be collected using a combination of both targeted and untargeted technologies to study more agnostically the external and internal exposome. Below we discuss per technology the identified key challenges and next steps (using additional literature beyond what was included in the scoping review) for a successful application in the oil and gas industry.

Personal sensors

From the peer-reviewed literature identified in this scoping review, we identified no reported applications of personal sensors in the oil and gas industry. We did identify papers on the use of personal sensors in pilot studies for other workers exposed to chemicals like PM, VOCs, formaldehyde, hydrocarbons and acids, and non-chemical stressors like heat and noise. In addition, the use of technologies for capturing real-time location of workers in several industries have been described. The benefits of personal sensors over more traditional methods are clear as they could provide more high resolution data, potentially in (near) real-time at often lower costs and are often easy of use

(Goede et al., 2020). However, the main challenges for a successful large-scale application in the oil and gas industry are related to the robustness of the sensors, the measurement repeatability and the sensitivity and specificity of the sensor at low concentrations for regulatory purposes (Duarte et al., 2014; Castell et al., 2017). In addition, ATEX certification (intended for use in potentially explosive environments) is a key requirement in the oil and gas industry, and it is essential that this is taken into account prior to application. Together with the aforementioned limitations of current sensors, technologies capable of measuring multiple (chemical) exposures (possibly in combination with nonchemical stressors), more in line with the exposome concept, are still limited and need priority from sensor developers, preferably integrating solutions in work clothes and helmets (Jovanov et al., 2011; Pronk et al., 2020).

External exposure modeling

Similarly for the personal sensors, the use of new types of external exposure models based on high resolution data is limited with only one application identified in the oil and gas industry (Sarigiannis et al., 2009). Currently, only more traditional exposure models like ECETOC TRA and ART are largely used in the oil and gas industry for regulatory (REACH) purposes (Hesse et al., 2018). Several peer-reviewed articles in other occupational sectors have described data-driven models capable of including both temporal and spatial resolution for PM, noise, and benzene. More data are needed, preferably in real-time to fully benefit from the potential of these new models for exposome research in the often highly dynamic environments characteristic of the oil and gas industry. As technology continues to evolve the application of sensors in workplace is likely to rise and data from these sensors can provide new possibilities for (new types of) exposure modeling like personal sensor networks (over currently used static networks) for detection and early warning systems. For exposures associated with more acute health effects and with personal sensors not available, other mathematic techniques like computational fluid dynamic (CFD) models could be applied to predict personal exposures starting to model at the source (e.g. leakage of a chemical) (Dong et al., 2017).

PBK modeling

PBK models, being the crucial link between external and internal exposure assessment, are applied in the regulatory context in the oil and gas industry from a single chemical perspective (often benzene), mainly for extrapolation of kinetics between species, exposure routes and exposure scenarios (U.S. EPA., 2006). In this scoping review, we identified several peer-reviewed articles describing applications in, or applicable to oil and gas industry workers, using often more complex PBK models for additional purposes including to conduct aggregated exposure assessment (for multiple routes of exposure) and the characterization of physiological and pharmacokinetic variability and uncertainty in e.g. predicting internal BLVs (Tan et al., 2018). In the near future, PBK models are expected to be used more regularly in combination with biomonitoring data in the 'exposure reconstruction' concept to estimate historical external personal exposures (Brown et al., 2015), which is currently ongoing in e.g. the European Human Biomonitoring Initiative (HBM4EU project). In general, the most important challenge for PBK technology is to develop reliable models for chemicals which are classified as data-poor with no or limited data on chemical specific tissue/plasma concentrations.

Biomonitoring and biomarkers

Biomonitoring is regularly applied in the oil and gas industry (even before 2005), with research mainly focusing on exposure to benzene and other VOCs with markers of exposure, effect and susceptibility to verify compliance with a BLV. However, to study working-lifelong effects of exposures, longitudinal studies are needed in the oil and gas industry to study trends over time. With omics technologies identifying more new biomarkers in the (near) future, the storage of biological material in biobanks is recommended for petrochemical workers to be able to conduct future retrospective analyses (Bocato et al., 2019). In addition, with more markers of early disease development coming from omics research, more effective prevention will become possible by applying these biomarkers.

Omics and bioinformatics

Omics technologies have been applied in workers exposed in particular in relation to benzene exposure in several industries including the oil and gas industry, with most of the identified studies on genotyping and proteomics, followed by changes in transcriptomics, epigenomics, and metabolomics. In addition, from other non-petrochemical studies, the successful application of omics to understand biological responses and susceptibilities to noise and other chemical such as PAHs and metal fumes became evident. Despite the use of omics technologies in research, standardized and validated

omics technologies are largely missing (Sauer et al., 2017), which is important in relation to ultimate regulatory application (e.g. compliance with an OEL). Furthermore, for the ultimate meaningful application of omics into the occupational setting, novel bioinformatics and chemical analytical approaches are needed to (i) help identify differentially expressed biomolecules in a consistent manner, and (ii) aid in the further identification of these using reference protein/chemical databases or advanced analytical chemistry. Last, by studying multiple endpoints and using a hypothesis-free (agnostic) study design, the interpretation of the study results requires new statistical approaches for the interpretation of the high-dimensional data from high-throughput omics techniques, as false-positive results are more likely to occur (Vlaanderen et al., 2010).

Conclusions

The occupational exposome concept offers some great promise for the oil and gas industry to more effectively reduce staff turnover by protecting workers from work-related diseases. The scoping review revealed that currently only PBK models and biomonitoring are (regularly) used for research and practical purposes in the oil and gas industry focused predominantly on workers exposed to benzene. The use of sensors, new types of exposure models, and omics/bioinformatics in this setting are in their infancy but are crucial for a successful application of the exposome concept, as it provides exposure and effect data at much higher resolution. The current challenges identified, include the technological readiness of applications which can be applied at the workplace (personal sensors, omics data analyses), the availability of data (sensor data, time integrated external exposure data, kinetics data), standardized and validated methods (personal sensors, external exposure models, PBK models, omics), and new study designs for longitudinal (working-lifelong) studies. More applied research is needed to overcome these challenges, also considering more practical barriers like ethics and costs, with industry and researchers from different domains working together, and exposome lessons learned from petrochemical scenarios, can be applied to new energy sources, including the finding of the emerging risks.

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Data Availability

There are no new data associated with this article.

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