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PERSPECTIVES

Advances and perspectives in environmental health research in China

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HIGHLIGHTS

- Environmental health research has surged in China over the past decade
- The scope extends beyond health effects of classic pollutants to include those of emerging pollutants and climate change
- Future research priorities and opportunities are proposed

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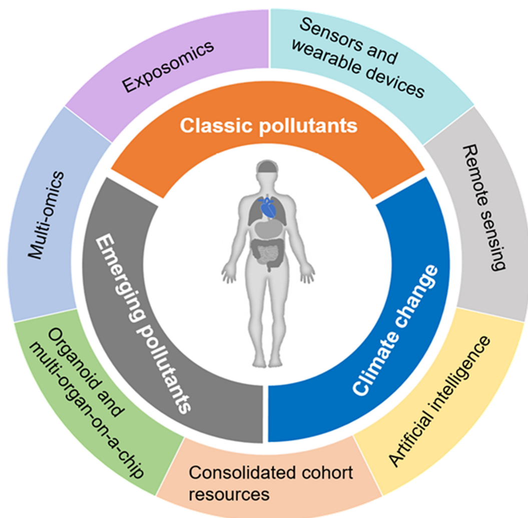

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Special issue—Towards a pollution-free planet

A B S T R A C T

Environmental health research aims to identify environmental conditions suitable for the healthy living and reproduction of human beings. Through the interdisciplinary research bridging environmental sciences and health/medical sciences, the impacts of physical, chemical, and biological environmental factors on human health are investigated. This includes identifying environmental factors detrimental to human health, evaluating human exposure characteristics to environmental factors, clarifying causal relationships between environmental exposure and health effects, analyzing the underlying biochemical mechanisms, linking environmental factors to the onset and progression of diseases, establishing exposure-response relationships, and determining effect thresholds. Ultimately, the results of environmental health research can serve as a scientific basis for formulating environmental management strategies and guiding prevention and intervention measures at both the public and individual levels. This paper summarizes the recent advances and future perspectives of environmental health research in China, as reported by a group of Chinese scientists who recently attended a workshop in Hainan, China. While it is not intended to provide a comprehensive review of this expansive field, it offers a glimpse into the significant progress made in understanding the health impacts of environmental factors over the past decade. Looking ahead, it is imperative not only to sustain efforts in studying the health effects of traditional environmental pollution, but also to prioritize research on the health impacts of emerging pollutants and climate change.

1 Key research areas of environmental health

The landscape of environmental health research continuously evolves in response to emerging environmental challenges. Pollution is the most recognized environmental issue confronting human society and its health effect has thus been central of environmental health research (Fig. 1). The related research can be broadly categorized based on the pollutants under investigation: (1) those already subject to regulation and (2) those not regulated yet but of emerging concern. In addition to pollution, climate change has emerged as another pressing environmental issue. Its impact on human health has gained increasing attention over the past decade (Fig. 1). This section provides a brief overview of these three key areas of research.

1.1 Classic pollutants and human health

Environmental pollution includes pollution of air, water, and soil among others. Over the past decade, frequent occurrence of air pollution represented by "haze" in developing countries such as China and India, has propelled extensive efforts on studying the health effects of air pollution, particularly focusing on the health risks associated with particulate matters (PM). The depth and breadth of research have been continuously expanded through the fusion of environmental science, public health, geographic information, and other disciplines. Regarding exposure characterization, not only has personal exposure assessment been accomplished for small-scale research, e.g., panel and interventional studies, but also the regional exposure assessment of air pollution has been achieved through combining satellite remote sensing, ground observation networks, and atmospheric transport models for large-scale studies. In terms of study population, research has expanded to populations with different susceptibilities, such as ordinary adults, pregnant women, infants and children, the elderly, and people with various unhealthy conditions. In terms of health effects, the focus has expanded beyond the respiratory system to encompass the cardiovascular system, immune system, nervous system, reproductive development, and other aspects. The underlying biological mechanisms have been investigated with the aid of advanced technologies such as multi-omics, high-resolution mass spectrometry, organoids, and artificial intelligence. The resultant refined assessments of the multidimensional health effects of air pollution on diverse regions and vulnerable populations provided the World Health Organization (WHO) with more comprehensive and systematic scientific evidence for revising the Global Air Quality Guidelines (AQGs) (WHO, 2021).

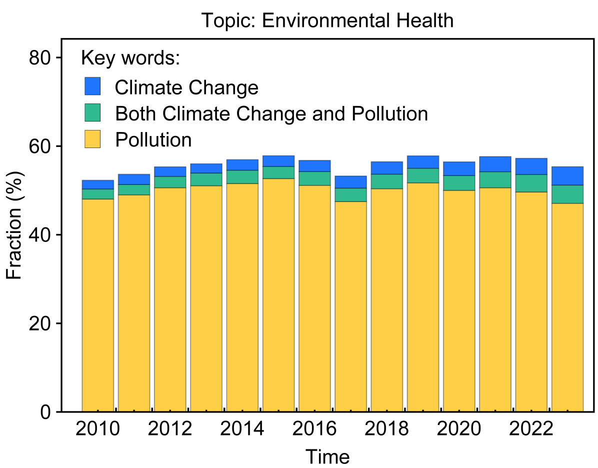

Fig. 1 Proportion of publications within the topic of "environmental health" that feature "climate change" and "pollution" as keywords from 2010 to 2023. Data are obtained from the Web of Science Core Collection database.

1.2 Emerging pollutants and human health

Emerging pollutants, also called new pollutants, encompass not only newly discovered contaminants resulting from the development of new products, but also previously existing pollutants not regulated yet. With the increasing production and widespread utilization of unregulated synthetic chemicals, these substances may come into direct contact with the human body, and may also accumulate within it through the bioaccumulation and biomagnification processes within the food web. This poses significant risks to both human and ecosystem health, potentially impeding the sustainable development of human society. Due to the wide variety, complex chemical behavior, and diverse mechanisms of toxicity of emerging pollutants, they present significant challenges in terms of screening, evaluating, and controlling. Over the past decade, key research endeavors concerning emerging pollutants include, but are not limited to: (1) the development of screening methodologies, including both the "bottom-up" approach (i.e., quantitative structure-activity relationship prediction and mass-spectrometric non-targeted screening) and the "top-down" approach (i.e., effect-directed analysis), to identify emerging pollutants with significant hazards, high exposure concentrations, and potential health and ecological risks; and (2) the assessment of health effects of emerging pollutants such as plasticizers, flame retardants, per- and polyfluoroalkyl substances (PFAS), including whole life cycle health impacts, disease risks, endocrine disruption effects, neurotoxicity, immunotoxicity, carcinogenicity, and reproductive developmental toxicity.

1.3 Climate Change and Human Health

Climate change is one of the greatest global health challenges facing humanity in the 21st century. Climate change can affect population health through a series of complex pathways and processes, including but not limited to global warming, more frequent extreme weather events (such as heatwaves, hurricanes, floods, and droughts), spread of pathogens, air pollution from dust storms and wildfires, water distribution and supply, and agriculture and food security. Recognizing the urgent need to address the nexus of health and climate change, the Lancet established a commission on health and climate change. In 2015, it published a seminal report titled "Health and Climate Change: Policy Responses to Protect Public Health" and launched the "Lancet Countdown 2030: Tracking Progress on Health and Climate Change" project, aiming at monitoring global responses to climate change and safeguarding human health. At the 28th Conference of the Parties to the United Nations Framework Convention on Climate Change (COP28) in 2023, health was included in the official agenda for the first time. The host country and the WHO jointly issued the "Declaration on Climate and Health," which "places health at the core of climate action and accelerates the development of climate-resilient, sustainable and equitable health systems." The declaration has been signed by more than 130 countries including China and the United States. Key research topics related to climate change and human health over the past decade include: (1) health issues resulting from the complex interplay of climate change factors and their spatial-temporal distribution in vulnerable regions; (2) the health impacts and underlying mechanisms of climate change trends, climate variability, and the spatial distribution of extreme climate events; (3) methodologies for a comprehensive assessment of health risks associated with climate change; (4) health co-benefits derived from climate change mitigation.

2 Research progress in China in the field of environmental health

With rapid social and economic development in China, environmental pollution issues have become increasingly prominent. In particular, the frequent occurrence of "haze" presents a significant public health challenge for local governments. In 2016, the "Healthy China 2030" blueprint emphasized the inclusion of protecting the ecological environment and public health as a fundamental strategy for national development. Consequently, the National Natural Science Foundation of China, Ministry of Science and Technology, National Health Commission, Ministry of Ecology and Environment, and local governments have allocated substantial funds and resources to support environmental health research. This investment has led to a surge in research activities in this field in China. As shown in Fig. 2, the number of publications on environmental health contributed by Chinese authors has surged from ~2000 in 2010 to ~20000 post-2020 within the Web of Science Core Collection, and the global share has tripled. Simultaneously, there has been a notable improvement in the research quality, characterized by enhanced population representation, increased accuracy of exposure assessment, and deeper understanding in underlying mechanisms. This section is not intended to provide a comprehensive review of the expansive field of environmental research, but it offers a glimpse into the significant progress made in China over the past decade.

2.1 Health effects of classic pollutants

With sustained funding support from Chinese government, Chinese scholars have made outstanding contributions in the research field of health risks of environmental pollution, and even occupied a leading

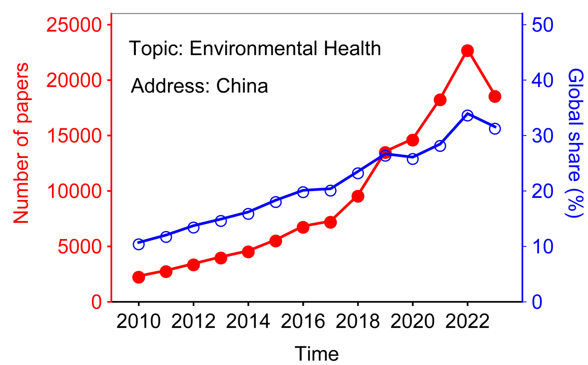

Fig. 2 Number of publications within the topic of "environmental health" contributed by Chinese authors from 2010 to 2023. Data are obtained from the Web of Science Core Collection database using the following sets of keywords: topic: environmental health; address: China.

position in certain fields such as the health impact of classic air pollutants. Based on systematic cohort and panel studies, the effects of air pollution were quantified on various health outcomes. For example, Haidong Kan from Fudan University led a team of scholars over the globe to update the concentration-response curves of ambient PM and daily mortality based on monitoring data from 652 cities worldwide (Liu et al., 2019), providing important supporting data for the revision of WHO air quality guidelines. The team led by Tong Zhu from Peking University found through a study of 697,148 single-birth newborns in 54 low- and middle-income countries that exposure to ozone (O_3) during pregnancy may have a significant impact on birthweight, and the burden of O_3-related birthweight reduction is particularly severe in South Asia, the Middle East, and North Africa (Tong et al., 2023). Through environmental intervention studies, Jicheng Gong from Peking University discovered new mechanisms by which atmospheric pollutants damage cardiopulmonary health, verifying the causal link between air pollution and cardiopulmonary health effects (Sinharay and Gong et al., 2018; Hu et al., 2020). Based on the national population-based birth defects surveillance system, Fangchao Liu from Chinese Academy of Medical Sciences and Hanmin Liu from Sichuan University found that high maternal $PM_{2.5}$ exposure, especially during the preconception period, increases the risk of congenital heart defects in offspring (Yuan et al., 2023). As for the health risk of indoor air pollution, the team led by Tangchun Wu from Huazhong University of Science and Technology conducted a cohort study of more than 270000 rural residents for up to 10 years, revealing that indoor air pollution caused by household solid fuel cooking and heating is an important cause of premature death among residents (Yu et al., 2018). Their results also suggest that switching to clean energy is the key to reducing resident deaths and effective ventilation can also be beneficial.

Although PM has traditionally been studied and regulated based on mass concentration, increasing evidence suggests that chemical composition might play a key role in determining its health impact. For example, research from Mei Zheng's group at Peking University revealed that the mass concentration of $PM_{2.5}$ emitted from residential coal burning was not always positively correlated with the amount of reactive oxygen species generated by $PM_{2.5}$ (Luan et al., 2022). In ambient $PM_{2.5}$ samples from a coal-burning area, the Nan Sang team at Shanxi University identified several chemicals (e.g., tributyl phosphate, 2-bromotetradecane, and methyl decanoate) interacting with transcription factors and thereby activating epithelial-mesenchymal transition pathway and promoting lung tumor metastasis (Ji et al., 2024). In addition, studies from multiple groups have highlighted black carbon as an important hazardous component of $PM_{2.5}$ (Dong et al., 2024).

2.2 Health effects of emerging pollutants

Initially, research on emerging pollutants mainly focused on the presence and distribution of emerging contaminants in the environment. In the last decade, researchers, including those in Europe, USA, and China, have begun to investigate the health effects of emerging contaminants. Various research teams in China have made significant advancements in identifying emerging pollutants. Targeted, suspect, and non-targeted approaches have been developed to identify emerging pollutants based on high-resolution mass spectrometry and applied to complex environmental media such as the atmosphere, indoor dust/air, soil, natural water, and sediments, leading to the discovery of a variety of new, toxic environmental pollutants with novel structures (e.g., Jiang et al., 2021; Meng et al., 2020; Qiu et al., 2021; Ye et al., 2021). New insights have also been gained concerning the distribution and transport of emerging pollutants across various environmental media, as well as their implication for human exposure (e.g., Li et al., 2020; Li et al., 2023a). In addition, the Jingwen Chen team at the Dalian University of Technology has constructed a series of environmental computational toxicology models for predicting environmental persistence, bioaccumulability, and toxicity of chemicals, as well as for integrative screening of hazardous chemicals (e.g., Wang et al., 2023; Liu et al., 2023a).

Substantial progress has also been made in assessing the risks of emerging pollutants to human health. For example, the team led by Shunqing Xu at Huazhong University of Science and Technology has conducted systematic studies of endocrine-disrupting chemicals (EDCs) exposure during pregnancy and long-term health hazards based on both birth cohort and animal studies, and found that prenatal exposure to EDCs (e.g., bisphenol A (BPA)) impaired fetal development and increased the risk of metabolic diseases in adulthood (Hu et al. 2019; Wei et al. 2011). The European Union's EFSA has repeatedly adopted their findings to support the health risk assessment of BPA. Many research groups contributed to understanding the health impacts of PFASs and organophosphorus flame retardants (e.g., Wang et al., 2022; Zhou et al., 2023; Ji et al., 2024). In particular, the team of Jiayin Dai at Shanghai Jiao Tong University has focused on the identification, exposure, toxicology, and health effects of PFAS (e.g., Pan et al., 2019), including some unique alternatives in China such as F-53B (Shi et al., 2018). The team of Guanghui Dong at Sun Yat-sen University also made a significant contribution to assessments of the health risks associated with PFAS (Dong et al., 2009; Zahm et al., 2024). Their research findings have been adopted by European and American regulatory agencies for establishing related standards.

2.3 Health effects of climate change

In terms of climate change, much of the current research centers on evaluating the impacts of climate change through the lenses of air pollution and ambient temperature. Epidemiological studies have indicated that both extreme high and low temperatures elevate the risk of population mortality. The 2023 China report of the Lancet Countdown on health and climate change showed that heatwave-related mortality was estimated to reach a record high of about 50900 deaths in 2022 (Zhang et al., 2023). Over the last five years (2018−2022), the average annual mortality was 169% higher than the historical reference point, highlighting the urgent health risks posed by extreme heat under a changing climate. Moreover, based on birth registry data from Guangzhou, China, the study from the group of Cunrui Huang now at Tsinghua University indicates that exposure to heatwaves during the final gestational week can trigger preterm birth, independent of $PM_{2.5}$ exposure (Wang et al., 2020). Furthermore, they have quantified the burden of heatwave-related preterm births and associated human capital losses in China (Zhang et al., 2022). In a panel study, Tong Zhu's group at Peking University reported the susceptibility of hypertensive individuals to acute increases in blood pressure in response to the reduction of environmental temperature at the personal level (Xu et al., 2024).

Efforts are now expanding to encompass other facets of climate change. For example, Tiantian Li's team from the Chinese Center for Disease Control and Prevention analyzed data from 153 counties across China and revealed that exposure to tropical cyclones increased the risk of both accidental and non-accidental mortality (Liu et al., 2023b). Wei Ma and Qi Zhao from Shandong University and coauthors revealed that climate change induced hydrometeorological conditions can affect the growth environment and virus activity of insect vectors, indirectly increasing the transmission risk of dengue, hand foot and mouth disease, and mumps (Li et al., 2023b). Furthermore, John S. Ji from Tsinghua University led a coalition of Chinese scientists advocating for climate change adaptation initiatives in China with a focus on safeguarding public health (Ji et al., 2023).

3 Perspectives of environmental health research in China

Revealing the health risks posed by environmental factors is a crucial step toward establishing an environmental governance system focused on safeguarding public health, ultimately contributing to the realization of a "Healthy China" guided by the principle of "prevention first." Thus, environmental health will continue to be a key national research priority in China. This section outlines potential research priorities in environmental research, highlights the technological and methodological advances potentially important for future progress (Fig. 3), and emphasizes the need of transforming scientific findings into policies and practices. For tackling complex emerging environmental health challenges, collaboration among Chinese researchers is vital, but international cooperation is equally essential.

3.1 Research gaps and priorities

Classic pollutants: Research on the health effects of environmental pollution in China has primarily focused on the impacts of ambient $PM_{2.5}$. At present, the health effect mechanisms of $PM_{2.5}$ on the cardiopulmonary systems are relatively clear, with causal relationships established, and $PM_{2.5}$ is also recognized internationally as a carcinogen. However, for other ambient air pollutants such as ozone, there are still many unknowns regarding their impact on human cardiovascular and respiratory health, and causal relationships are not yet clear. In terms of PM, further investigation is also warranted regarding health implications of its major chemical constituents and smaller size fraction, such as ultrafine particles ($PM_{0.1}$). Moreover, there is pressing need to broaden our focus from ambient air pollution to encompass other crucial yet less explored domains. These include pollution in indoor environments, such as residences, schools, and office buildings, where individuals spend 80%−90% of their time. Additionally, pollution in urban transportation systems, such as subways, warrants attention due to the high density of population present. In light that individuals are commonly exposed to a mixture of pollutants in real-world settings, future research should also broaden its scope from examining single-pollutant

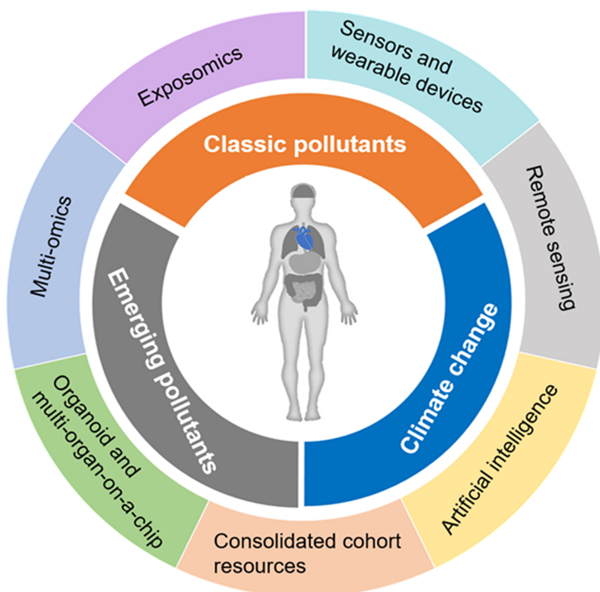

Fig. 3 Illustration depicting key areas of environmental research as well as technological and methodological advances potentially important for future progress.

exposure to encompassing the complex interplay of compound exposure. Furthermore, it is also necessary to assess the health benefits derived from government policies in environmental pollution prevention and control. Such evaluation can incentivize continued governmental investment in research concerning the health risks of environmental pollution.

Emerging pollutants: Despite significant advancements made by Chinese scholars in the field of emerging pollutants, current research has only addressed a small fraction of the chemicals introduced into the market annually. Faced with a multitude of chemicals characterized by sheer volume, diverse categories, and varying physicochemical properties, the primary challenge lies in identifying high-risk substances from complex environmental matrices based on their exposure characteristics and toxicological and health effects, while operating under constraints of time and resources. It is imperative to integrate available screening approaches and establish consensus on screening criteria. It is recommended to prioritize screening in indoor environments, where synthetic chemicals are extensively used and where human exposure mainly occurs. Furthermore, it is valuable to build a national-level environmental specimen bank which can offer standardized longitudinal data, baseline information, traceable detection capabilities, and exposure assessment tools. In terms of population study of the health effects of emerging pollutants, vulnerable populations such as pregnant women and infants should be prioritized. Alongside screening efforts, it is also important to design and use green alternative chemicals for achieving social, economic, and environmental sustainability.

Climate change: Climate change and health research has progressed from historical impact assessment to predicting future risks, and from merely quantifying the health impact of climate change to also assessing the health responses to climate change. These findings feed back into the policy-making process. Future efforts should focus on enhancing vulnerability assessment of the health effects of climate change, analyzing spatial-temporal difference, researching the impact mechanism of climate change on health, predicting future health effects of climate change and regional differentiation patterns, and assessing the effectiveness of response measures to mitigate the health effects of climate change. When assessing the health risks associated with climate change, future focus should expand to mental and psychological health, nutritional health, allergic diseases, and infectious diseases. At the same time, attention should be placed on the synergistic effects of compound exposure within the climate change framework, such as multiple extreme weather events occurring simultaneously or in quick succession, as well as joint exposure to meteorological factors and air pollution. Future efforts should also emphasize enhancing surveillance, forecasting, and early warning mechanisms for health impacts linked to localized climate shifts across diverse time frames. Additionally, establishing comprehensive public health management principles, methodologies, and adaptive strategies is essential for effectively mitigating the health hazards induced by climate change.

3.2 Advanced technologies and methodologies

Precise assessment of personal exposure and exposure-response relationships with multidimensional health, disease, and molecular phenotypes: Humans are exposed to a multitude of pollutants from various sources, but the traditional pollution exposure assessments often rely on measurements in certain environmental media where data are more convenient to obtain. This approach, while useful, may not capture the true exposures individuals experience. The rapid development of exposomics, wearable devices, remote sensing, and geographic information systems have the potential to enable more precise assessment of short-term and long-term personal exposure across different environmental settings. Meanwhile, the development of multi-omics technology facilitates the comprehensive characterization of biological responses to environmental exposures across molecular, cellular, tissue, and organization levels. For future population studies, it is recommended to conduct precise environmental exposure assessment on individual levels, to evaluate multidimensional phenotypic outcomes such as genes, biomarkers, target organs, senses, and disease/health, and to employ new statistical methods.

Multi-organ-on-a-chip and effect-oriented technology for identifying environmental pollutants, exploring mechanisms of toxicity, and screening intervention schemes: Traditional screening methods for environmental toxicants, which rely on *in vitro* experiments and animal models, are costly and time-consuming. These methods often lag behind the pace of research and development of new chemicals, thus failing to adequately address the need of pollutant control. Moreover, there is significant uncertainty when extrapolating results to the population level. Therefore, there is an urgent need to develop new technologies capable of simulating true human exposure, enabling rapid and cost-effective identification of toxins. The rapidly evolving technologies of organoid and organ-on-a-chip offer promising solutions. These technologies allow for the culture of cells from different organs and tissues on a chip, creating biologically relevant systems that closely mimic the human body. This provides new avenues for identifying environmental toxicants, conducting risk assessments, exploring toxicological mechanisms, and developing prevention and intervention strategies.

Integrating the cohort resources and data to develop a sharing mechanism and management system:

Cohorts serve as a critical foundation for environmental health research. Despite the establishment of numerous cohorts by researchers throughout China, their full potential remains largely untapped due to limited sharing capability. Additionally, many cohorts face challenges in sustainability once initial projects conclude, as continuous financial support is often lacking. To address these issues, it is recommended to integrate cohort information at the national level, establish a sharing mechanism and management system, and prioritize representative population cohorts for long-term stable financial support. The consolidation of cohort resources from various regions facilitates evaluation of robustness of the association between environmental exposure and specific health outcomes, as well as cross-regional comparisons of exposure-response relationships.

Machine learning and artificial intelligence (AI) approaches for predicting chemical risks, designing green alternatives, and analyzing big epidemiological data: With a vast number of chemicals on the market, only a small subset has experimental data on their environmental persistence, bioaccumulation, and toxicity, posing a significant challenge for comprehensive risk assessment. Rapid developments in deep learning techniques make it possible to develop models for high-throughput screening by leveraging a curated list of hazardous chemicals. Moreover, integrating techniques such as generative AI algorithms into environmental computational toxicology models facilitate the design of molecular structures for green alternatives and strategic planning of retrosynthetic pathways that conform to the principles of green chemistry. Additionally, AI holds the potential to revolutionize environmental epidemiology, particularly in light of the growing size and complexity of data sets in this field.

3.3 From science to policy

Furthermore, efforts should prioritize leveraging scientific findings in environmental health to inform and guide the development and implementation of policies for environmental protection and public health. Environmental health research provides evidence-based insights into the impacts of environmental factors on health, highlighting the need for formulating policies that mitigate these risks. It helps policymakers understand the direct correlation between environmental quality and public health outcomes, guiding the prioritization of interventions that can reduce disease burden and lead to significant health benefits. Additionally, environmental health research identifies specific pollutants and practices that pose health risks, enabling targeted regulatory actions. It also supports the design of comprehensive, integrated policies that address the complex interplay between air pollution, climate change, and health.

Based on reviewing a large number of scientific publications, WHO released its Global Air Quality Guidelines (AQGs) in 2005, and an updated version in 2021. In 2012, for the first time, China added $PM_{2.5}$ to its updated National Ambient Air Quality Standards (NAAQSs), based on the interim target 1 of AQGs for $PM_{2.5}$. In 2013, China launched the National Action Plan on Air Pollution Prevention and Control, resulting in a notable reduction of air pollution levels approaching NAAQSs over the following decade, thereby yielding substantial health benefits. Looking into the future, enhanced collaboration between scientists, policymakers, and the public is crucial for transforming research findings into effective policies and practices that protect the environment and public health, ensuring sustainable development and promoting a healthier future for all.

4 Conclusions

In China, significant strides have been made in environmental health research over the past decade. These findings have been instrumental in guiding actions led by government authorities at all levels to combat air, water, and soil pollution. Looking ahead, addressing the health effects of classic pollutants, emerging pollutants, and climate change will remain central to the field of environmental health. Anticipated advancements are expected to arise from the continued utilization of advanced technologies and methodologies.

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