Perspective

Progress on Wastewater-based Epidemiology in China: Implementation Challenges and Opportunities in Public Health

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Wastewater-based epidemiology has emerged as a transformative surveillance tool for estimating substance consumption and monitoring disease prevalence, particularly during the COVID-19 pandemic. It enables the population-level monitoring of illicit drug use, pathogen prevalence, and environmental pollutant exposure. In this perspective, we summarize the key challenges specific to the Chinese context: (1) Sampling inconsistencies, necessitating standardized 24-hour composite protocols with high-frequency autosamplers (≤ 15 min/event) to improve the representativeness of samples; (2) Biomarker validation, requiring rigorous assessment of excretion profiles and in-sewer stability; (3) Analytical method disparities, demanding inter-laboratory proficiency testing and the development of automated pretreatment instruments; (4) Catchment population dynamics, reducing estimation uncertainties through mobile phone data, flow-based models, or hydrochemical parameters; and (5) Ethical and data management concerns, including privacy risks for small communities, mitigated through data de-identification and tiered reporting platforms. To address these challenges, we propose an integrated framework that features adaptive sampling networks, multi-scale wastewater sample banks, biomarker databases with multidimensional metadata, and intelligent data dashboards. In summary, wastewater-based epidemiology offers unparalleled scalability for equitable health surveillance and can improve the health of the entire population by providing timely and objective information to guide the development of targeted policies.

Introduction

Public health authorities worldwide have adopted wastewater-based epidemiology (WBE) to monitor population health, particularly since the onset of the coronavirus disease 2019 (COVID-19) pandemic. WBE is a powerful surveillance tool for monitoring substance use and facilitating early warning of pathogen transmission and prevalence[1]. In China, WBE has been routinely used by anti-drug authorities to monitor the consumption of illicit drugs and by the Center for Disease Control and Prevention (CDC) to evaluate the prevalence of pathogens in the population[2,3]. In the annual report of the Drug Control Bureau of the Ministry of Public Security, WBE results are important for reflecting geotemporal consumption patterns and the effects of intervention campaigns. The tool could serve as part of the nationwide comprehensive public health strategy—Healthy China 2030. Our literature search revealed that over 300 WBE studies in China have been published since 2013[4]. However, although this rapid research increase has expanded opportunities for public health surveillance, challenges in maximizing the benefits of WBE remain. The objectives of this review were to i) summarize recent

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advancements in the WBE methodology in China and its applications for public health benefits; and ii) identify challenges of using WBE in China and propose potential solutions to enhance its utility in shaping comprehensive public health policies.

Integrated Sampling Framework for Large-Scale Studies

China currently has several large-scale WBE programs, including one involving more than 500 wastewater treatment plants nationwide [5]. The accuracy and representativeness of WBE data depend on consistent and high-quality sampling protocols. The implementation of 24-hour composite sampling using autosamplers at an appropriate sampling frequency (≤ 15 min/sampling event) and low-temperature storage is recommended. However, owing to the difficulty in deploying autosamplers in remote regions, passive samplers may serve as an alternative for both remote rural areas and community-level monitoring[6]. The performance of passive samplers can be affected by multiple factors, such as flow conditions, temperature, and suspended solids, resulting in lower sensitivity and potentially reduced representativeness compared with those of autosamplers. These limitations should be carefully considered, particularly when comparing data obtained from different sampling approaches. To address biomarker-specific excretion variations, establishing a WBE knowledge repository alongside adaptive tiered sampling network guidelines will be essential. Additionally, the systematic planning and development of multi-scale wastewater sample banks are required to advance research and enable retrospective tracing (Figure 1).

Identification and Suitability Evaluation of New Biomarkers

Despite the potential usefulness of clinical biomarkers in WBE, their excretion patterns, detectability in wastewater, and stability must be assessed. Recent WBE studies in China have demonstrated a strong analytical capacity to extend the number of target analytes beyond pharmaceuticals[7], pollutants[8], and viral RNAs[9]. Reports have documented the use of WBE biomarkers in China to evaluate chemicals such as ketamine[10], dextrorphan[11], 1,3-diphenylguanidine[12], and drugs for hypertension, diabetes, and gout[13], as well as pathogens such as the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Omicron variant[14], respiratory syncytial virus[15], and *Bordetella pertussis*[16]. Our evaluation encompassed several aspects, including the detection capability, urinary excretion ratios of chemical parent compounds to their metabolites, fecal shedding rates and pathogen loads, in-sewer

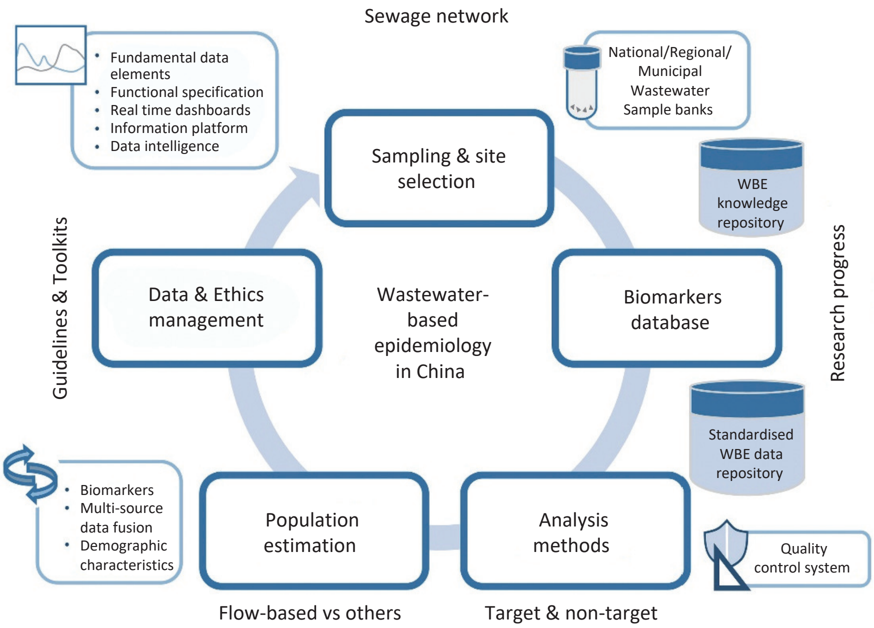

Figure 1. Framework for advancing wastewater-based epidemiology implementation in China. This framework underscores the potential of the tool for the large-scale monitoring of public health in China, aligning with national health strategies such as Healthy China 2030.

and in-sample stability, and quantitative associations with other indicators. However, we lack a detailed investigation of the excretion or shedding profiles of a broader panel of biomarkers, especially in the Chinese population. The current excretion factors used are mostly derived from pharmacokinetic studies with a limited number of participants, and existing evidence proves that such excretion factors can have considerable errors when applied to WBE[17]. The stability of biomarkers is another crucial parameter, not only for their selection but also for accounting for their loss during in-sewer transport. We previously incorporated in-sewer biomarker degradation (e.g., ethyl sulfate) and excretion profiles into the correction factor to improve the estimation accuracy[18]. In the future, WBE data can be used to systematically evaluate a broader range of biomarkers to derive appropriate correction factors for those that are important[19]. Therefore, a comprehensive biomarker database with multidimensional metadata linkages should be developed to support further exploration and implementation.

Target and non-Target Analysis Methods

Given that analytical methods form a fundamental pillar of WBE research, their quality assurance must be maintained through regular proficiency testing. Standardized detection methodologies and certified reference materials are crucial for ensuring analytical comparability and supporting validation frameworks across multiple laboratories. An annual inter-laboratory test of analytical methods is recommended to ensure data quality. Although technical standards for wastewater SARS-CoV-2 enrichment and nucleic acid detection (WS/T 799-2022)[20] and high-throughput variant analysis (T/SZAS 92-2024)[21] have been released in China, broader standardization efforts should be promoted. Moreover, fully automated pretreatment equipment, on-site sensors, and other online monitoring instruments should be developed to accelerate the collection of analytical results and reduce time and monetary costs. Efforts have been made to develop sensors for illicit drugs[22]; however, their adaptability and sensitivity require further improvement to meet regular monitoring requirements. In national narcotic laboratories, on-line solid-phase extraction (SPE) is being used in addition to traditional benchtop SPE methods for the routine analysis of illicit drugs. Conversely, non-targeted detection methods have significant potential to expedite data mining in wastewater, particularly in metagenomics and metaviromics to identify unknown pathogens[23], or to screen for new psychoactive substances that emerge in the illicit drug market[24].

Population Estimation for WBE Purpose

Real-time *de facto* population estimation is a significant challenge, with large uncertainties associated with migration and commuters[25]. Most WBE studies in China rely on data provided by wastewater treatment plants. Authors of some early studies proposed the use of hydrochemical parameters (e.g., ammonium nitrogen) or population biomarkers to reduce estimation errors[26]. Mobile data have also been used for dynamic population estimations in other countries[27]. Although these data can capture daily variations, they raise cost and privacy concerns. Alternatively, flow-based estimates could be a simpler solution for catchments without industrial discharges, although caution should be taken owing to seasonal variations in per capita water use and potential sewage overflow. Concurrently, conducting demographic investigations within catchments would strengthen population-WBE data linkages.

The Need for Data Management and Ethics Considerations

Over the past decade, studies on various biomarkers across multiple catchments have yielded valuable insights into nationwide public health trends. The integration of these datasets into a unified platform would improve these insights. Different stakeholders have emphasized standardizing full-process protocols and building collaborative networks to ensure the long-term consistency and utility of data[28]. National academic conferences such as the China Conference on Environment and Health and the National Conference on Environmental Chemistry have increasingly organized dedicated sessions on WBE to facilitate knowledge exchange and strengthen national research capacity. The development of intelligent data analysis toolkits and dashboards will enhance the efficiency and responsiveness of WBE. The National Wastewater Drug Monitoring Report, an example of a WBE data platform in China, is released to the public without disclosing specific site-level information. A similar platform for pathogen surveillance was established internally by the CDC.

Ethical challenges should be considered in WBE. For example, identifying illicit drug use among lowcount populations via the analysis of small catchments can run the risks of discrimination and stigma. WBE studies must de-identify sensitive information and ensure the privacy of target populations. To date, Chinese WBE studies have focused on populations of at least a few thousand people, avoiding individual identification. In the future, balancing public health and law enforcement benefits with ethical challenges will be required.

Despite the abovementioned challenges, WBE in China presents a great opportunity for extensive public health surveillance on a scale unmatched by other methods. WBE can promote health equity by expanding public health surveillance to rural areas and vulnerable populations. Moreover, the understanding of international stakeholders can be enhanced through international and inter-institutional collaborations, such as with the European Union Drugs Agency and the Global Consortium for Wastewater and Environmental Surveillance for Public Health.

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Competing Interests The authors declare that they have no competing interests.

Ethics Not applicable

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