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### Waves of pharmaceutical waste

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The viral waves observed during the coronavirus disease 2019 pandemic (COVID-19) are suggesting a new global phenomenon by which a global change, e.g., a viral wave, is inducing a wave of waste, that is a sudden rise of waste and associated pollution due to sharp and time-limited changes of human behavior. The originality of this phenomenon is that the crisis—here the pandemic -is fast and global, com-pared to previous crises which were slower, more restricted, and local, and that the crisis is limited in time, like a wave. This wave-of-waste phenomenon fits well with the entrance into the Anthropocene, theorized by Nobel Prize winner Paul Crutzen, where humans now influence the planet glob-ally. Here we argue why such waves-of-waste are likely to occur more frequently in the next global crises, on the basis of the sudden rises of pharmaceutical waste observed during the pandemic.

The World Health Organization declared COVID-19 as a global pandemic on March 11, 2020 (WHO 2020). Now more than two years into the pandemic, there have been more than 500 million confirmed cases, including over six million deaths around the globe, making it the largest public health crisis in the past one hundred years (WHO 2022a). With the recent emergence and spread of new variants, global weekly new infections surged to new records at the beginning of

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2022 (Wang and Han 2022; WHO 2022a, 2022b). The pandemic has strongly affected almost all countries, thus inducing an unprecedented sharp rise of waste production.

#### **Booming pharmaceuticals**

Therapeutic agents, most notably synthetic pharmaceuticals, play a pivotal role in managing the global public health crisis. Since the onset of the pandemic, sales of prescription and over-the-counter drugs surged in Europe, Brazil and North America (Smith and Elsayed 2020). The strong demand for pharmaceutical products persisted in regions experiencing re-emergent outbreaks with large numbers of new infections. For example, in India, pharmaceutical sales were boosted through the second quarter of 2021 as the second wave of COVID-19 swept across the world's secondmost populous country, resulting in year-on-year growth of 134% in anti-infectives (Leo 2021). In the United States (US), sales of pharmaceutical drugs also reported strong growth throughout 2020, with the largest increases in antivirals, of 78.3%, hormones, of 16.7%, and diabetes, of 11.5%, compared with the previous year (Tichy et al. 2021). Pharmaceuticals used for treating mental disorders also experienced high demand. In December 2020, about 42% of 3,904 adults surveyed by the US Census Bureau reported depression or anxiety (Abbott 2021), and 34.0-71.5% of healthcare workers in China reported mental disorders related to COVID-19 (Moses 2020).

#### A forecasted major impact on the environment

Concerns have been raised on the increasing discharge of sanitary waste containing antiviral drugs and metabolites, which are often inadequately treated at municipal wastewater treatment plants and pose threats to the receiving environments (Gwenzi et al. 2022; Kumar et al. 2020; Kuroda et al. 2021). Meanwhile, huge quantities of pharmaceuticals dispensed to or purchased by the general public are left unused or expired throughout the COVID-19 pandemic. This is creating an unintended, yet massive legacy of bioactive substances that are ending in the environment (Fig. 1). These drugs include expired, unused, e.g., from recovered or deceased owners, and excess pharmaceuticals caused by over-prescription, patient incompliance, panic buying, and stockpiling, i.e., hoarding. Without proper management and regulatory oversight, these unwanted pharmaceuticals may induce an ecological disaster given their high quantities and



Fig. 1 Pandemic-induced drug pollution, an ecological disaster at an unprecedented scale. As the world enters the third year of the coronavirus disease 2019 (COVID-19) pandemic, high quantities of pharmaceuticals dispensed to or purchased by the public are left unused or expired in households, creating an invisible, toxic environmental legacy that requires urgent regulatory oversight. Without proper collection and safe disposal, unwanted pharmaceutical products accumulating in households are often disposed of in the trash or flushed in the toilet by owners. Trashed pharmaceuticals mostly ends up in municipal solid waste landfills, where these bioactive compounds can induce drug resistance in microorganisms and, through landfill leachate, emissions and leakage, pollute the surrounding soil and groundwater environments. Pharmaceuticals are only partial degraded in municipal wastewater treatment plants, where hydrophobic pharmaceutical compounds and degradation products would accumulate in the sludge, while more soluble, less hydrophobic products are discharged into the receiving surface water. Some pharmaceuticals have high persistence to environmental and drinking water treatment processes and can enter the municipal water supply.

toxicities to aquatic and terrestrial biota. While contamination of water, soils and sediments by traces of drugs has already been observed a long time ago, the global magnitude of the pandemic is very likely to induce an unprecedented, huge wave of drug waste in the natural environment.

#### Two-thirds of prescribed drugs are unused

In an awakening paper, Daughton and Ternes described pharmaceuticals as *agents of subtle change* (Daughton and Ternes 1999). Since then, numerous studies have reported their adverse effects and risks on environmental and public health. Pharmaceuticals constitute a notorious class of anthropogenic waste, often with high toxicities and persistence in the environment if disposed of inappropriately (Caban and Stepnowski 2021; Han 2022; Monisha 2022; Morin-Crini et al. 2022; Zare et al. 2022). At parts per trillion levels, those bioactive substances elicit undesired responses in aquatic or terrestrial biota, bioaccumulate and pose direct risks to humans through food and drinking water (Miège et al. 2009; Nakada et al. 2006; Velpandian et al. 2018; Wee et al. 2020). Unwanted household pharmaceuticals, in particular, pose longstanding challenges to environmental regulators due to their low collection rates and often improper disposal by owners (Law et al. 2015; Manocha 2020).

A survey of the US households revealed that about twothirds of prescription drugs remain unused after being dispensed to patients (Law et al. 2015). As a result of not knowing how to properly dispose of unwanted drugs, 29% of Americans would place their unused or expired medications in the trash, and 26% would flush them down the drain (Stericycle 2020). Surveys in developing countries painted an even bleaker picture. For instance, a survey in India showed that 73% of the 956 survey respondents threw their unused or expired medicines in the trash, 20% flushed them down the drain, and only 6% returned their unused medicines to local pharmacies (Manocha Manocha). Similar findings were reported in China where both awareness and collection programs are lacking for managing unwanted pharmaceuticals in households (Zhang and Chen 2022).

#### **Drug resistance**

A significant portion of pharmaceuticals thrown into household trash ends up in municipal solid waste landfills. A recent report by the US Environmental Protection Agency stated that more than 50% of municipal solid waste were landfilled across the country (EPA 2021a). Under the selected pressure exerted by pharmaceuticals, landfills provide favorable environments for the growth of antimicrobial resistance in microbes, which can transmit their drug-resistant genes to other pathogens that may eventually reach the outer environments through leachate and bioaerosols (Anand et al. 2021).

Leakage or inappropriate management of landfill leachate is known to cause pollution in adjacent groundwater (US GAO 2019; Yu et al. 2020). Indeed, active pharmaceutical ingredients were detected at elevated or alarming levels in groundwater near municipal landfill sites (Velpandian et al. 2018). On the other hand, pharmaceuticals flushed into sewers often show persistence during biological treatment processes at municipal wastewater treatment plants, where removal rates vary widely for different pharmaceutical compounds (Kuroda et al. 2021; Miège et al. 2009; Nakada et al. 2006). For example, removal rates for COVID-19 drugs ranged only from less than 6% to 47-92% for antivirals and antibiotics approved for treating COVID-19 and bacterial co-infections (Kuroda et al. 2021). Meanwhile, much of the pharmaceutical compounds and their transformational products are accumulated in sewage sludges (Tarazona et al. 2021). These compounds can re-enter the environment via the application of biosolids on agricultural soils, a common practice in European Union member states and the Organisation for Economic Co-operation and Development countries (ECHA 2019; OECD 2021). Such a tremendous wave of pharmaceutical compounds and their degradation products would aggravate the already pressing issue of drug resistance facing the scientific community and environmental regulators (Maxmen 2017; Nguyen et al. 2022; Popova et al. 2021).

#### Cancellation of the drug take-back day

Regulatory bodies have taken actions to mitigate the inappropriate disposal of unwanted pharmaceuticals in households. These actions have achieved varying degrees of success in the past. Nonetheless, under the impact of the current pandemic, actions have either been hindered or come to a stall (DEA 2020). Furthermore, these actions have been implemented only in countries and regions with stringent environmental regulations. Prior to the COVID-19 pandemic, Sweden was the sole member state in the European Union requiring legally that all unused drugs must be returned to local pharmacies (Meddisposal 2021; SMPA 2019). In most countries, however, there is no such mandate in place, and participation in these programs requires voluntary efforts by the general public (DHTGA 2019; EPA 2021b). Lockdowns, reduced trips and the perceived risk of COVID-19 transmission in public settings could all hinder the willingness and actions of the public to return their unwanted pharmaceuticals to collection points, a similar behavior observed for other waste recycling programs (UMICH 2020; Zand and Heir 2021).

The National Prescription Drug Take Back Day, the largest collection event for expired and unwanted prescription drugs in the United States that is normally held twice a year, was canceled on April 25, 2020, due to the ongoing pandemic (DEA 2020). While the event was resumed in October 2020 and 2021, the number of collection sites available was among the lowest on record, and the total weight of drugs collected in the most recent event, of 372 tons, was the lowest since April 2016 (DEA 2022).

# Trillion dollars spent globally on pharmaceuticals

Recent discussions have focused on the mounting waste of single-use plastics, e.g., face masks, discarded into the environment during COVID-19 (Brock 2020). By contrast, a less visible and more acutely toxic environmental legacy is the enormous amounts of excess and unwanted pharmaceuticals that are left with owners in common households. The US House Committee reported that prescription drug spending exceeded 500 billion USD a year and was growing three times faster than inflation rates even prior to the COVID-19 pandemic (Kovner 2020). Around the globe, an estimated total of 1,270 billion USD were spent on pharmaceuticals in the year of 2020 (Mikulic 2021). With active community transmission and strict infection prevention and control measures in place (Wang et al. 2020, 2021), it will not be surprising to find that the old 'throw-in-the-trash' and 'flushing-down-the-drain' methods regained favor in common households in the current pandemic.

We call for regulators to promote the awareness of the public to keep or dispose of their unwanted pharmaceuticals in a safe manner and, resource permitting, reinstate or initiate drug take-back programs in communities, e.g., at grocery stores and pharmacies. As an emergency response, pharmaceutical manufacturers or public health authorities can provide households with paid mail-back envelopes to collect non-liquid pharmaceutical products for centralized treatment, e.g., incineration with medical waste. Meanwhile, we urge individuals not to throw their expired or unwanted pharmaceuticals into the household trash or flush them in the toilet, and when it is necessary to do so, do these in a safer manner by following the instructions to reduce their harm and impact on the environment (FDA 2018, 2020). Overall, future global crises such as pandemics are likely to induce waves of unwanted chemicals in the environment. There is therefore an urgency to design a society with zero waste or 100% recycled waste, to stop contamination of nature and, indirectly, humans.

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#### Declarations

Conflict of interest The authors declare no conflict of interest in this work.

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