First, do no harm: time for a systems approach to address the one is the one is the the one is the one is the the one is the one one is the one is the one is the one one is the one one on problem of health-care-derived pharmaceutical pollution



Chemical pollution is considered one of the nine planetary boundaries, and increasing evidence suggests that we are already operating outside of this, risking irreversible environmental change.¹ Pharmaceutical chemicals are vital components of modern health care, but their contamination of global waterways is threatening environmental and human health, contributing to biodiversity loss, driving antimicrobial resistance, and jeopardising progress towards the sustainable development goals.^{2,3} With the global pharmaceutical market now worth more than US\$1.25 trillion4 and continuing to grow as populations age and suffer from more chronic, non-communicable diseases,⁵ there is an urgent need to integrate pharmaceutical pollution into sustainable health-care strategies, alongside efforts to reduce carbon and plastic waste.

The long-term detrimental impacts of some pharmaceuticals in the environment have been known for decades, and it is now widely recognised that ambitious legislative and non-legislative measures are required to address this issue.³ Progress to date has been restricted largely because of a focus on improving human health and financial outcomes, and the complexity of global pharmaceutical value chains.³ High-income countries (HICs) are the major consumers of pharmaceuticals,³ and face a substantial challenge in mitigating rising local pollution levels emanating from patient excreta and inappropriate disposal,³ while simultaneously taking responsibility for the considerable manufacturing pollution externalities created through globalising their supply chains. Here, we present a UK case study that illustrates the scale of the problem and demonstrates the need for a cohesive, cross-sectoral systems approach.

The UK is a HIC with a large pharmaceutical industry (£36.7 billion turnover in 2019),⁶ a well recognised healthcare pharmaceutical market (the UK National Health Service [NHS]), and a diverse water industry comprising both private and public operators working on regional and national scales. Efforts to reduce pharmaceutical pollution derived from UK health care face numerous significant challenges: first, NHS pharmaceutical supply chains are complex and traverse institutional, sectoral, and national

boundaries, so defining the environmental impacts of manufacture and supply, and assigning accountability for them, is difficult and disjointed;³ second, pharmaceutical usage is extensive and rising, with pharmaceuticals being the second biggest cost of the NHS (£16.8 billion annually);7 third, UK regulations do not allow recycling of pharmaceuticals,⁴ with a substantial proportion of unused and expired drugs inappropriately disposed of into land or water waste;⁴ fourth, removal of pharmaceuticals from UK wastewater treatment plants is incomplete and highly variable,³ with treated effluent water and waste (sludge) containing pharmaceutical residues of concern often directly released to the environment; fifth, untreated waste containing health-care pharmaceuticals regularly enters the UK environment directly, through off-grid, septic-tank systems and combined sewer overflows; sixth, environmental levels of most pharmaceuticals are not regularly monitored, and of the 1912 pharmaceuticals registered in UK health care,5 only eight are regularly monitored in UK waters (EU watch list 2022/1307); and finally, few pharmaceuticals used in UK health care have comprehensive data on environmental impacts, with only 11% having any substantive ecotoxicology data in the public domain.5

Systems thinking is increasingly used to interpret and manage complex issues. We charted the flow of pharmaceutical stock used in UK health care, and the most important factors influencing this flow (figure). Our systems map illustrates the inherent interconnectivity between the health, pharmaceutical, and environmental sectors, and outlines pathways for the integration of policies and frameworks between these. For example, the recent Organisation for Economic Co-operation and Development report on the Management of Pharmaceutical Household Waste⁸ could be integrated into health-care system strategies, including NHS net-zero and over-prescribing policies.7 Our map also identifies opportunities to improve cross-sectoral interconnectivity, for example it highlights the scarcity of feedback from the environmental sector into points controlling the flow of pharmaceutical stock through the system (licencing, reimbursement, procurement, and prescription), and the complete absence of feedback

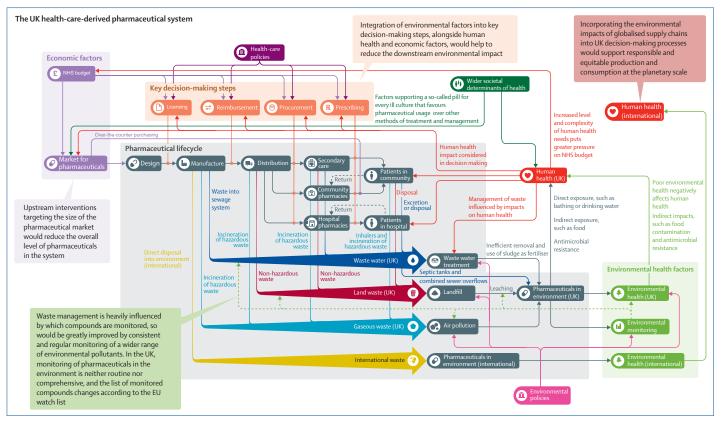


Figure: The UK pharmaceutical system derived from health care

The system map follows the flow of pharmaceuticals (the stock) through their life cycle, from design (left) to environmental contamination (bottom right). Aqueous and solid waste is produced at several stages of the life cycle, both within the UK and internationally. Permitted disposal of aqueous waste is via waste-water treatment plants and disposal of solid waste is by incineration, which produces gaseous breakdown products (also pollutants, such as CO₂, CO, and NOX). Asthma inhalers and other drugs, such as anaesthetic gases, also produce gaseous waste. Human health, economic, policy, and other social factors have influence across the system. Environmental factors have no direct influence throughout the life cycle other than through their impact on human health. The green lines from the environmental monitoring box are dashed to indicate that monitoring of pharmaceuticals in the environment is neither comprehensive nor routine.

relating to international manufacturing pollution. This demonstrates the need for expansion of environmentally responsible initiatives to cover global supply chains, for example in ecopharmacovigilance schemes developed by UK pharmaceutical companies, and in NHS procurement policies.

See Online for appendix

For more on the **One Health** Breakthrough Partnership see https://ohbp.org/ An abundance of potential interventions already exist across the UK health-care-derived pharmaceutical pollution system (appendix). Many of these interventions are aimed at reducing the rate or impact of pharmaceuticals flowing into the environment, for example through greener pharmaceutical design, improved disposal or increased removal from wastewater. From a broader systems perspective, the most effective way to reduce pharmaceutical outflow is likely to be through reducing inflow—ie, by addressing the upstream market forces driving unnecessary pharmaceutical usage. This strategy echoes calls from wider sustainable health-care strategies for greater prioritisation and investment into preventative health care and non-pharmaceutical treatment options. However, like many of the interventions identified (appendix), this is not straightforward, demonstrating the need to consider competing social, health, economic, and environmental factors when designing system-wide intervention strategies. As such, adoption of a systems approach will require dedicated cross-sectoral platforms, with resources and funding to engage and support the major stakeholder groups in jointly discussing, researching, prioritising, and adopting system-wide approaches. The One Health Breakthrough Partnership in Scotland is a successful model of such a multiagency systems approach.

With pharmaceutical production predominantly (and increasingly) based in low-income and middleincome countries (LMICs),³ these populations face the greatest burden of manufacturing pollution despite an estimated 2 billion people still no having access to essential medicines and sanitation.⁹ There is also a long tradition of sending unused medical products near their expiry date to LMICs, potentially leaving them with large stocks of out-of-date medicines without safe disposal options.¹⁰ Thus, HICs have an urgent responsibility to identify and implement strategies to mitigate their global pollution footprint. Initiatives such as the PREMIER project are supporting this, by addressing the scarcity and access to data on the environmental impacts of pharmaceutical pollution,³ to inform decision making.

Mitigating global pharmaceutical pollution derived from health care is essential for achieving sustainable health-care systems, and for helping to restore humanity back within the safe operating space of the chemical pollution planetary boundary.¹ Future efforts must also be integrated with broader sustainable development issues, such as those targeting equitable access to health-care pharmaceuticals and veterinary pharmaceutical usage. These issues are inextricably linked to pharmaceutical pollution derived from health care and pose key barriers to a sustainable global pharmaceutical future.

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For more on the **PREMIER project** see https://imi-premier. eu/mission-vision/