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Supplementary appendix

This appendix formed part of the original submission. We post it as supplied by the authors.

Supplement to: Thornber K, Adshead F, Balayannis A, et al. First, do no harm: time for a systems approach to address the problem of health-care-derived pharmaceutical pollution. *Lancet Planet Health* 2022; **6:** e935–37.

Annex 1: Potential intervention points across the system. Based on the UK healthcare-derived pharmaceutical system presented in Figure 1, we compiled a list of potential interventions to reduce the environmental impacts of healthcare-derived pharmaceutical pollution across the system. An initial list of suggestions was identified from numerous reviews and reports on the subject (see reference list at the end); this was adapted for a UK context and extended through discussions amongst our group at two half-day online workshops. It must be noted that these are not recommendations; some have considerable resource implications and feasibility constraints that must be explored in more detail through further cross-sectoral discussions before recommendations can be developed. Acronyms used: ERA (Environmental Risk Assessment), API (Active Pharmaceutical Ingredient), REACH (Registration, Evaluation, Authorisation and restriction of CHemicals), HTA (Health Technology Assessment), WWTP (Waste Water Treatment Plant), AMR (AntiMicrobial Resistance), CSO (Combined Sewer Overflow), LMIC (Low- and Middle-Income Country).

MARKET FOR PHARMACEUTICALS

Sustainability aim	**1. Reduce consumer need for pharmaceuticals (improve disease prevention)**
Suggested interventions	• Increase spending on public health and preventative healthcare, encouraging greater investment earlier in disease pathways • Greater prioritisation of a (proactive) value- and health promotion-based healthcare service, rather than the current (reactive) commodity- and treatment-focus. • Reduce time constraints on primary care consultations and make better use of wider primary health care teams, to allow time for shared decision making on evidence based, non-pharmaceutical interventions (see reference Department of Health & Social Care, 2021 for definition of this)
Sustainability aim	**2. Reduce consumer demand for pharmaceuticals**
Suggested interventions	• Raise awareness and understanding of pharmaceutical fate and impacts, across all stakeholders, including the public • Restrict advertising of pharmaceuticals • Develop clear guidance for eco-labelling • Incorporation of environmental impacts and responsible disposal into healthcare training

DESIGN

Sustainability aim	**Design (or re-design) of pharmaceuticals that are less harmful or persistent in the environment**
Suggested interventions	• Agree on criteria to define "green" pharmaceuticals • Increase weight of ERA in licensing decisions and ensure they are enforced • Develop better models for predicting environmental impact across species, including general toxicity and antimicrobial resistance minimal inhibitory concentrations • Promote sharing of data on environmental impacts of pharmaceuticals, e.g. through a central, international database of

	ERA and environmental monitoring data with access rights and independent oversight, to minimise duplication of testing and improve consistency • Provide more incentives for pharma companies to focus on greener design • Develop new business models that reward (profit) based on results and clinical outcomes to break the link with price per pill and promote innovation in better longer-term healthcare • Develop/use better targeted delivery systems in the patient • Develop internationally acceptable environmental standards for drug production to encourage greener design • Develop drug classification scheme based on environmental criteria, to inform procurers and incentivise greener drug development

MANUFACTURE

Sustainability aim	**Reduce pollution from pharmaceutical manufacture**
Suggested interventions	• Expand regulatory framework for good manufacturing practice to include mandatory disclosure of environmental criteria (e.g. effluent discharge levels across supply chain), to increase transparency and make origin of APIs and other ingredients easier to trace • Improve understanding of pharmaceutical fate, toxicity, ecological risk; develop a priority list for the APIs that pose greatest risk, to expedite action • Impose appropriate regulatory limits (specific to each compound) for effluent discharge • Identify water bodies/environments of highest concern, and incorporate these risks into ERA/licensing processes • Include APIs in UK REACH and Industrial Emissions Directive regulatory criteria • Ensure prescription-only and post-approval monitoring for drugs with high environmental risk • Improve transparency and sharing of information across the supply chain for more accurate demand forecasting • Develop clear guidance for eco-labelling • Use of green engineering to recover APIs from unused medicines and recycle • Make it compulsory for pharmaceutical companies to publicly disclose supply chain information

LICENSING

Sustainability aim	**1. Include environmental risk assessment data in the licencing decision-making process, to restrict or ensure risk intervention and mitigation strategies are in place for pharmaceuticals with high environmental risk**
Suggested interventions	• Establish central, international database of ERA and environmental monitoring data with access rights to minimise duplication of testing and improve consistency, with independent oversight

	• Revisit pharmaceuticals authorised before ERAs became mandatory (01/12/2006) and do retrospective assessments; develop a priority list for the APIs that pose greatest risk, to expedite action • Improve transparency of licencing decision-making process • Ensure post-marketing environmental impacts are monitored and reported (i.e. through including environmental impacts in pharmacovigilance systems) • Replace current product-based environmental assessment systems with a substance-based review system, to reduce admin, increase transparency and reduce animal testing • Review and update ERAs when new environmental risk data becomes available • Use ERA outcomes to drive more data collection where necessary
Sustainability aim	**2. Increase the robustness and transparency, and minimise duplication of environmental risk assessments**
Suggested interventions	• Establish central, international database of ERA and environmental monitoring data with access rights to minimise duplication of testing and improve consistency, with independent oversight

REIMBURSEMENT/HEALTH TECHNOLOGY ASSESSMENT

Sustainability aim	**Include environmental risks in HTA economic evaluation**
Suggested interventions	• Public/policy maker acceptance of environmental protection as equal/high priority • Change HTA policy to incorporate environmental risk criteria in decisions on reimbursement. This will require: i) development of methods guidance for integrating environmental risk in reimbursement decisions, including methods for determining health and cost impacts of environmental risk, and methods for comparing health technologies with different environmental impact; and ii) calculate costs of environmental impacts on society for incorporation in cost-benefit analyses • Provide HTA panels with access to a central database of pharmaceuticals to allow easy comparison of environmental criteria, and decision-making support tools • Include environmental experts on HTA panels

PROCUREMENT

Sustainability aim	**Include environmental risks in NHS procurement policies/decision-making framework**
Suggested interventions	• Provide procurers with access to a central database of pharmaceuticals to allow easy comparison of environmental criteria across the pharmaceutical life cycle, alongside validated and agreed decision-support tools. For example, building upon the www.fass.se database that exists for Swedish healthcare • Develop healthcare provider frameworks to ensure procurers can identify companies who engage in environmental protection and improvement, in line with NHS Procurement Policy Note 06/20 (see reference list)

	• Public/policy maker acceptance of environmental protection as equal/high priority • Quantify economic and human health impacts of integrating environmental impacts into decision-making

PRESCRIBING

Sustainability aim	**1. Include environmental risks in NHS prescribing policies, to prescribe environmentally-friendly alternatives where possible**
Suggested interventions	• Provide prescribers with access to database of pharmaceuticals, to allow easy comparison of environmental criteria, alongside validated and agreed decision-support tools • Public/policy maker acceptance of environmental protection as equal/high priority • Quantify economic and human health impacts of integrating environmental impacts into decision-making
Sustainability aim	**2. Minimise risk of pharmaceutical wastage**
Suggested interventions	• Optimise patient treatment • Provide access to stock availability to encourage the usage of medicines in stock and avoid wastage • Explore alternative pharmaceutical supply approaches, e.g. sale or return

DISTRIBUTION

Sustainability aim	**Reduce level of waste from expired medication**
Suggested interventions	• Restrict storage time of medication through effective inventory policies and use of advanced logistical systems to optimise stocking • Review stipulated product shelf-lives to maximise them by better aligning with product stability wherever possible • Improve the definition/understanding of expiry dates, through education of prescriber, distributor, consumer risk (i.e. both human health and litigation risks) • Develop system to encourage and support movement of stock that is close to expiry between pharmacies

DISPENSING

Sustainability aim	**1. Reduce level of waste from unused medication**
Suggested interventions	• Explore sustainability costs/benefits of smaller packaging sizes (which may dispense only what patients need, but may have greater manufacturing carbon/energy/plastic costs) • Recycling of unused medication • More frequent evaluation of repeat prescriptions • Limiting prescription durations to discourage overprescribing • Synchronisation of repeat medication, such that new prescriptions are in sync with the supply date of existing prescriptions
Sustainability aim	**2. Reduce level of waste from expired medication**

Suggested interventions	• Restrict storage time of medication through greater uptake of effective inventory policies and use of advanced logistical systems to optimise stock management (e.g. to automatically dispense medication close to expiry date) • Encourage cooperation and exchange between pharmacies • Procurement of smaller sized packaging or products with longer expiry dates • Review stipulated product shelf-lives to maximise by better aligning with product stability wherever possible Timing the preparation of compounded medication to simultaneously process patients that receive the same medication, to reduce wastage, or sharing vials across pharmacies/clinics • In care homes, bulk prescribing medication for occasional use (for multiple residents), rather than individual packaging (this is already happening in many care homes) • Consistent use of patient's own medication during hospitalisation • Minimise patient stockpiling/over-ordering of prescriptions (e.g. due to fear over loss of drug through non-use) • Incorporation of environmental impacts and responsible disposal into all healthcare training

CONCORDANCE/USE

Sustainability aim	**Optimise patient adherence to prescriptions to minimise need for subsequent treatments**
Suggested interventions	• Consider sustainability cost/benefits of alternative delivery methods, e.g. deliver medication to patient's home could reduce bulk storage through inconvenience of regular pharmacy trips but may increase carbon footprint. • More shared decision-making between prescribers and patients (e.g. through longer GP consultations or engagement of patients with clinical pharmacists) to encourage adherence and timely cessation • Explore alternative therapies for "treatment-resistant" patients, or isolated/vulnerable people at raised risk of experiencing problems in medicine taking • Conduct audits of monitored dosage systems • Toolkits to support optimal use of medicines (e.g. as developed for Asthma; see www.greenerpractice.co.uk)

DISPOSAL

Sustainability aim	**Reduce inappropriate pharmaceutical disposal**
Suggested interventions	• Public (including healthcare practitioner) education and awareness campaigns on responsible disposal • Make it compulsory to feature disposal information for patients on outer drug packaging and in pharmacies • More active pharmaceutical collection schemes for unused drugs, with dedicated resources and implementation guidelines to support this (e.g. Extended producer responsibility schemes)

	• Bespoke disposal schemes for pharmaceuticals with high environmental risk (e.g. as initiated for inhalers and anaesthetic gases). • Research/innovation into capture and reuse of released drugs (e.g. as proposed for anaesthetic gas waste, see www.sagetechmedical.com) • Policies that allocate more responsibility for waste to manufacturers, for example UK policy makers could require a maximum percentage of waste from manufacturers (e.g. Extended producer responsibility legislation), to encourage more producer responsibility for waste • Change of regulations to allow use of unused drugs where medicines are considered viable, e.g. using packaging sensors to monitor heat exposure • Maximise shelf-life to better align with product stability

WASTE TREATMENT

Sustainability aim	**1. Reduce pharmaceuticals in wastewater entering the environment directly**
Suggested interventions	• Incorporate environmental impacts from global manufacturing wastewater into healthcare sustainability strategies • Improve pharmaceutical manufacturing regulatory and management structures relating to supply chains based LMICs with little or no wastewater treatment infrastructure • Create strong economic and political drivers to address pollution from across the whole pharmaceutical life cycle • Improve the management of CSOs • Reduce pharmaceutical contamination of sludge before application to farmland
Sustainability aim	**2. Reduce pharmaceuticals entering the environment from WWTPs**
Suggested interventions	• Upgrade traditional WWTPs to increase removal of pharmaceuticals • Reduce risk of land contamination through use of sludge containing pharmaceutical residues • Develop guidance on household disposal of pharmaceuticals, especially for those off mains WWTPs (i.e. septic tanks)
Sustainability aim	**3. Reduce point-source healthcare pharmaceutical pollution**
Suggested interventions	• Incorporation of environmental impacts and responsible disposal into healthcare training • Develop guidance for healthcare institutions to reduce the discharges of pharmaceutical residues into municipal wastewater • Promote separate collection of urine of patients administered with persistent (e.g. x-ray or MRI contrast agents) and ecotoxic medicines (e.g. cytostatic drugs) • Regulate the management of human waste beyond cytostatic and cytotoxic substances (the only pharmaceuticals explicitly classified as hazardous waste under the Water Framework Directive) • Dedicated WWTPs for hospitals or care settings, where a significant risk to the wider water cycle and environment has been identified • Adequate regulation of pharmaceutical incineration plants

PHARMACEUTICALS IN ENVIRONMENT

Sustainability aim	**Reduce impact of pharmaceuticals on individuals and ecosystems**
Suggested interventions	• Uptake of new/better monitoring and modelling methods, and incidence reporting • Streamline/simplify regulatory system for chemical/pharmaceutical to improve transparency • Improve co-ordination across institutions/sectors to share data and reduce knowledge gaps • Develop standards for data collection, quality, analysis, storage, prioritisation and reporting • Work directly with water industry to develop pharmaceutically-intelligent drinking and waste water safety plans, monitoring and incidence reporting • Make pharmaceutical companies contribute to financing post-registration monitoring and water treatment costs, in line with the "polluter pays" principle • Improve understanding of pharmaceutical fate, toxicity, human health risks, ecological risks, including mixtures, and our ability to trace pharmaceuticals from source to sink

CROSS-CUTTING/SYSTEMS

Sustainability aim	**Integration of environmental impact across the healthcare system**
Suggested interventions	• Prioritisation of sustainability across the pharmaceutical life cycle on the agenda of policy-makers • Develop evaluation criteria for the health, economic and environmental impacts of interventions • Collect better data on current levels of pharmaceutical usage and wastage across the system, in order to accurately measure impact of interventions and overall trends • Better methods to measure the human health, economic and social impacts of *pharmaceutical pollution* • Better methods to measure the human health, economic, social and environmental impacts of *health prevention strategies* • Measure and quantify the risks across the system, in order to prioritise intervention areas

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