Sustainable medicines use in clinical practice - a clinical pharmacological view on eco-pharmaco-stewardship

Adeyeye, Elizabeth; New, Benjamin Jaa Ming; Chen, Fangyue; Kulkarni, Spoorthy; Fisk, Marie; Coleman, Jamie J.

Published in:
British Journal of Clinical Pharmacology

DOI:
10.1111/bcp.15140

Publication date:
2022

Document Version
Peer reviewed version

Adeyeye Elizabeth (Orcid ID: 0000-0003-3245-4739)

New Benjamin JaaMing (Orcid ID: 0000-0002-1692-8204)

TITLE PAGE

Sustainable medicines use in clinical practice - a clinical pharmacological view on eco-pharmaco-stewardship

Elizabeth Adeyeye[1], Benjamin JaaMing New[2], Fangyue Chen[3], Spoorthy Kulkarni[4,5], Marie Fisk[4,5], Jamie J Coleman[6,7]

[1] Department of Clinical Pharmacology, Cardiovascular Medicine, Barts Health NHS Trust, London, UK
[2] Ninewells Hospital & Medical School, NHS Tayside, Dundee, DD1 9SY, UK
[3] University College Hospital, 235 Euston Road, London, NW1 2BU, UK
[4] Experimental Medicine and Immunotherapeutics (EMIT), Department of Medicine, University of Cambridge, Trinity Lane, Cambridge
[5] Cambridge University Hospitals NHS Foundation Trust, Addenbrooke's Hospital, Cambridge, UK
[6]Institute of Clinical Sciences, College of Medical and Dental Sciences, University of Birmingham, Birmingham B15 2SP, UK
[7]University Hospitals Birmingham NHS Foundation Trust, Edgbaston, Birmingham, B15 2TT, UK

Elizabeth Adeyeye MB ChB, MRCP(UK)
Specialty Registrar in Clinical Pharmacology and Therapeutics, and General Internal Medicine, Barts Health NHS Trust
ORCID ID: 0000-0003-3245-4739

Benjamin JaaMing New MRCP(UK)
Specialty Registrar in Clinical Pharmacology and Therapeutics, and General Internal Medicine, NHS Tayside
ORCID ID: 0000-0002-1692-8204

Fangyue Chen MA, MB BChir
Critical Care, University College London Hospitals NHS Foundation Trust
ORCID ID: 0000-0002-5440-3206

Spoorthy Kulkarni MBBS, MD (General Medicine), MRCP(UK)
Specialty Registrar in Clinical Pharmacology and Therapeutics,
Cambridge University Hospitals NHS Foundation Trust, University of Cambridge
ORCID ID: 0000-0003-0598-9834

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/bcp.15140

Marie Fisk MRCP(UK), PhD
Specialty Registrar in Clinical Pharmacology and Therapeutics,
Cambridge University Hospitals NHS Foundation Trust and Clinical Lecturer, University of Cambridge
ORCID ID: 0000-0002-1292-7642

Jamie J Coleman MD, MA, MRCP(UK)
Honorary Professor of Clinical Pharmacology and Medical Education, University of Birmingham and Consultant Physician, University Hospitals Birmingham NHS Foundation Trust
ORCID ID: 0000-0002-7512-5153

Corresponding Author: Elizabeth Adeyeye,' Department of Clinical Pharmacology, Cardiovascular Medicine, Barts Health NHS Trust, London, UK
Tel: +44 (0)7947 144 355 Email: Elizabeth.adeyeye@nhs.net

Running title: Sustainable medicines use in clinical practice - a clinical pharmacological view on eco-pharmaco-stewardship

Word count: 4449 + 0 figure(s) + 0 table(s)

Keywords: Adherence, prescribing, drug utilisation, public health

Abstract
Climate change continues to pose a dangerous threat to human health. However, not only is health impacted by this crisis, healthcare itself adds to the problem, through significant contributions to greenhouse gas emissions. In the UK, the National Health Service (NHS) is responsible for an estimated 4% of the overall national carbon footprint. Medicines account for a quarter of this and whilst they are vital for health now, through sustainable use they can also positively influence the environmental health of the future. In this review, we explore how clinical pharmacologists and other health care professionals can practice sustainable medicines use or eco-pharmaco-stewardship. We will discuss current and near future environmental practices within the NHS, which we suspect will resonate with other health systems. We will suggest approaches for championing eco-pharmaco-stewardship in drug manufacturing, clinical practices and patient use, to achieve a more a sustainable healthcare system.

Introduction

The climate change emergency is one of the most momentous challenges we face in the twenty-first century.1 Countries around the world have joined forces to limit further global warming and reduce the risk of subsequent environmental catastrophes. The Paris Agreement, a legally binding treaty committing countries to meet the long-term goal of keeping the increase in global average temperature to well below 2°C compared to pre-industrial levels, came into force in 2016. This has been adopted by 190 countries to date.2

Society, organisations, and individuals all have a part to play in tackling the drivers of climate change, and the healthcare sector is no exception. In a 2017 paper on environmental sustainability, the World Health Organisation (WHO) advocated for health systems to 'improve, maintain or restore health, while minimizing negative impacts on the environment and leveraging opportunities to restore and improve the environment to the benefit of the health and well-being of current and future generations'.3 In the United Kingdom, the National Health Service (NHS) has set out a clear aim to reduce carbon emissions to net zero in its Greener NHS campaign.4

Within a health system such as the NHS, challenges to create a more sustainable organisation may appear to compete with increasing demands in care and economic factors. However, it is well recognised that providing sustainable healthcare is essential not only to protect the environment but to prevent the inevitable health hazards of climate change, which is a potential meta-problem and threat multiplier to human health.5,6

The health sector contributes to carbon emissions in several ways, including direct emissions from health facilities and indirectly in the supply chain, for example whilst transporting goods. Medicines account for an estimated 25% of the overall emissions within the NHS, and although there is a significant focus on specific groups such as anaesthetic gases and inhaler devices, there are many other enabling actions that can be taken to reduce this impact.4 We use the term 'eco-pharmaco-stewardship' to focus on sustainable medicines use and believe that all healthcare professionals have the potential to impact climate change in their practice.7 In this commentary, we examine how the clinical pharmacology community can play a role within the NHS to positively drive changes for medicines sustainability, from everyday practices in wards and GP surgeries, through to impacts on policy at regional and national levels. We will discuss what has been done in the UK to address this to date and share ideas about how we can work together towards a more sustainable NHS.

Outline

Eco-pharmaco-stewardship is relatively young and there is a lack of robust evidence on this topic, however we will build on this knowledge, along with personal experience and clinical pharmacological principles to structure this discussion. We will consider the topic from three distinct vantage points – drug manufacture (the pharmaceutical perspective); drug use at a population and hospital level (the physician and pharmacy perspective); and drug use at an individual level (the patient use perspective). Additionally, we will look at the specific cases of anaesthetic gases and respiratory inhalers as these account for a significant proportion of direct emissions at the point of use.3,8

The pharmaceutical perspective

The pharmaceutical industry exerts a huge impact on the environment, and this so called 'pharmaceutical pollution' is increasingly acknowledged as a global danger to the health of humans and our ecosystem.9 This damage comes in many forms, such as pharmaceutical products entering the environment into water supplies and significant contributions to greenhouse gas emissions, the latter being the focus of this commentary. We will discuss the current and future sustainable practices within the pharmaceutical industry most relevant for health care professionals working within the NHS.

Environmental accountability procedures already exist in the drug manufacturing process. For example, in Europe, companies are required to provide an environmental risk assessment (ERA) for newly licensed products.10 There are calls for extensions of the ERA beyond the initial marketing authorisation stage to span the product lifecycle for enhanced accountability. Other methods that could promote environmental responsibility include the development of universal greenhouse gas emissions metrics and disclosure of these metrics by pharmaceutical companies. This information can be used to 'eco-label' products, increasing the ease of making sustainable purchasing decisions.11

Enhancing the drug development process is a key step towards sustainability. Green chemistry techniques, such as designing reactions to run at room temperature and increased use of catalysts, are increasingly adopted to reduce chemical waste and emissions from the carbon resource intensive manufacturing process.12 Improvements in the stability of drugs can impact on sustainability also. For example, improving the temperature stability of pharmaceutical products can reduce energy consumption from storage and transport.13 In addition, optimising stability prolongs shelf life and reduces the risk of expiration before use. Drug dosing formulation could be optimised to avoid wastage. Where appropriate, producing multi-dose vials and increasing the range and availability of vial sizes and pre-filled syringes can reduce partial usages of 'drawn up' medications.14 This is particularly relevant in paediatric prescribing for which there are more body-weight dosage calculations and wider dosage ranges.

Pharmaceuticals are increasingly being combined with medical device delivery systems which improve accuracy of dosing, pharmacy efficiency time, patient convenience and usability, and require less packaging15. Examples of this include subcutaneous auto-injectors for insulin delivery or longer-term implantable devices. However, the increase in single use delivery systems causes some contention given the potential for considerable waste compared to reusable products. Innovative steps have been made to reduce the impact of these systems. For example, devices can be designed to keep contaminated parts separate and readily disposable, so that the remainder of the device can be used again, therefore maximising reusability.15,16 There is also increasing use of replacing standard materials in these devices with biocompatible and biodegradable materials.1516

Packaging and transportation are clear targets to reduce the environmental impact of medicines. The development of green packaging must be balanced with strict criteria regarding Good Manufacturing Practice (GMP), material traceability, product protection including sterility and waste disposal.17 Packaging must also be made with the patient in mind to maximise user adherence, which itself reduces pharmaceutical waste. Sustainable

packaging aims to be light and compact to improve efficiency in storage and transportation. It should be structurally sound to reduce the need for additional shipping materials like corrugated boxes. Also, if primary and secondary packaging steps are combined with drugs in a single process at one location, this maximises efficiency of the supply chain and further reduces waste from transportation.18

Packaging material optimization is crucial and there is growing interest in using novel biodegradable materials, recyclable plastics, and materials from renewable sources. Plastic waste is a significant ecological hazard and efforts have been made to reduce this burden. For example, there is increased utilisation of PET (Polyethylene terephthalate), the most recyclable plastic, which can be used for medication liquid bottles, caps, ampoules, and syringes. Blister packs are widely used in pharmaceutical packaging. They are traditionally made of composite materials, such cardboard with a plastic, making them difficult to recycle. However, some progress has been made to improve their sustainability. In 2019, the Wasdell group, a manufacturing and packing company based in Swindon, manufactured the world's first plastic blister pack that is biodegradable when exposed to water or landfill.19 The Australian-American packing giants Amcor this year announced trialling the world's first fully recyclable polyethylene-base thermoform blister pack.20

Optimised packaging also reduces direct environmental costs through transportation. Transportation is a particular area in which close collaboration and strategic planning between NHS organisations and suppliers could significantly improve efficiency and reduce waste. Changes can be made to streamline transportation processes, such as improving distribution load and restructuring routes.18 Additional reductions in carbon footprint can be made by utilising lower emission and electric vehicles.

The NHS cannot control emissions from the pharmaceutical industry directly, but it can use its considerable purchasing power to drive change. For example, by incorporating environmental requirements in procurement processes.3 Furthermore, by forming alliances with other health systems, purchasing power agreements can be made, creating an even more influential force to be reckoned with. Whilst the pharmaceutical industry is making progress to reduce its environmental impact, those working within health organisations can positively influence this progress through greater awareness, collaboration, and definitive action.

The physician and pharmacy perspective

Although occupying a relatively small carbon footprint in medicines emissions, both physicians and pharmacists hold unique positions in healthcare systems as 'gatekeepers' to the use of medicines and are therefore important in the process of eco-pharmaco-stewardship. Sustainable changes can be made in many parts of healthcare — in hospitals and the community with better prescribing, in regulatory meetings through carbon-conscious medicines optimisation decisions, and in lecture halls through educating the next generation of environmentally conscious health care professionals.

Careful prescribing and medication use can help reduce both carbon and financial costs within healthcare. In hospitals, this includes timely medication use before expiration dates, supported by efficient stock logistics; using patient's own drugs during their inpatient stay;

providing smaller supplies of new medications or 'starter packs' to mitigate wastage from poor tolerability; and regular medication reviews with appropriate deprescribing. Medication wastage can also be significantly reduced with practical measures such as vial-sharing in cytotoxics and the use of low dead volume syringes in vaccination.21 Vial-sharing is not always achievable in every drug class as it depends on the stability of the drug over time, and whether patients can get grouped together to administer this.

There are physicians and pharmacists involved in the procurement of medicines and optimisation of their use through local committees such as Medicines Advisory Groups and Drug and Therapeutic Committees in addition to the national procurement processes. While these meetings highlight the clinical efficacy, safety and cost-effectiveness of current and new drugs, the environmental costs are not routinely discussed. By incorporating sustainability assessments using the available environmental product information, greener medicines choices can be made, and we can start to develop 'carbon-friendly' formularies. A good example of a sustainability switch is seen with flupentixol. This is one of the most commonly administered long-acting antipsychotic injections and in the UK is often prescribed at higher doses and more frequently than studies suggest is beneficial.22 Evidence-based reductions of this not only reduces potential harm to patients from over exposure but could also cut down on emissions by 170,000 kg CO_2e and save an estimated £300,000 per year across England.22

Aside from improving current practices, the conversations around eco-pharmaco-stewardship should extend to the next generation of healthcare professionals. The GMC has stated that "newly qualified doctors must be able to apply the principles, methods and knowledge of population health and the improvement of health and sustainable healthcare to medical practice".23 Some medical schools have also started to incorporate planetary health and education for sustainable healthcare, in either a student-selected component or as part of the core curriculum.

There may be staff barriers to fully realise the potential of sustainable medicines use within the NHS such as diffusion of responsibility and not being able to see the environmental cost of their clinical practices.24 Clinical pharmacologist, along with others interested in medicine use, have the potential to overcome these barriers not only by ensuring environmentally friendly medicines optimization, but through education, engagement and empowerment of others to make the changes in practices today that lead to a greener, safer and more sustainable tomorrow.

Eco-pharmaco-stewardship case study 1 – Anaesthesia: gases and other practices
Anaesthetic gases, notably nitrous oxide and halogenated hydrocarbons, represent over 2% of the NHS's overall carbon footprint.4. Anaesthetists and critical care physicians are therefore in a position to make valuable contributions towards the practice of eco-pharmaco-stewardship.

Over half of anaesthetic gas carbon emissions are due to nitrous oxide (N_2O). It has a global warming potential (GWP_{100}) that is 298 times that of CO_2.25 In addition, nitrous oxide is now the dominant ozone-depleting substance emitted by human activity and has been recognised as one of the most of environmentally damaging gases in the atmosphere.25,26

Within the field of anaesthesia, nitrous oxide is a popular agent in obstetrics as an alternative to neuraxial analgesia. It also offers some benefit as a carrier gas for other volatile anaesthetic agents, such as decreasing the latter's effect on cardiac depression and reducing systemic vascular resistance.26 Outside of the operating theatre, nitrous oxide is used extensively for minor procedures amongst the paediatric population, in the emergency department for procedures such as fracture reduction.26 Despite being a highly versatile agent with a relatively efficacious and safe profile, its environmental impact must not be overlooked. Considerations must be made with regard to standardizing and limiting its usage, and opting for alternative agents where possible.

Of the halogenated hydrocarbon based gases, desflurane has the greatest environmental impact, with a GWP_{100}) 2,540 times that of CO_2.27 The greenhouse gas emissions of desflurane are around 2,600 times greater than propofol, a non-volatile anaesthetic agent.27To look at it another way, using desflurane with a modern anaesthetic machine for 1 hour produces the same CO_2 emissions as a 230-mile trip in a modern car.28

The choice of anaesthesia is influenced by patient, surgical and anaesthetic factors, as well as the individual preferences of the anaesthetist. Use of inhalational agents can be reduced by adopting alternative techniques, such as regional anaesthesia and Total Intra-Venous Anaesthesia (TIVA). When this is not possible, carbon footprint can be minimized by rationalizing the agent of choice and minimizing the quantity of agent by monitoring the depth of anaesthesia and flow rates. Inhalation anaesthesia offer advantages compared with TIVA, including the ease of use for paediatric patients, improved cerebral and cardiac protection, reduced postoperative pulmonary complications and decreased mortality following cardiac surgery. TIVA on the other hand has a favourable profile for post-operative recovery and is the preferred agent for cancer resection surgeries.29

Beyond anaesthetic gas use, there are other practices contributing to medicines wastes within the speciality. Anaesthetists and intensivists are frequently called to initiate emergency pharmacological treatments under time-limited conditions. Therefore, it is standard practice to prepare the main anaesthesia and emergency drugs in advance, to mitigate the risk of medication error under stressful situations and this leads to significant medication wastage. An estimated 20 – 50% of drugs drawn up are unused and discarded.30 A recent multicentre study in Italy of over 13,000 prepared drug syringes found a variation of drug wastage from 7.8% (urapidil) to 85.7% (epinephrine), with an average wastage rate of 38%.31 Potential strategies to reduce medication waste include the use of prefilled syringes, especially for high acuity, low-usage rate emergency drugs such as atropine and ephedrine. The use of prefilled syringes in pre-diluted forms with enhanced labelling can also help to reduce the risk of medication errors, as well as variations in drug concentrations.

In the UK, the Royal College of Anaesthetists, Association of Anaesthetists of Great Britain and Ireland and the College of Anaesthesiologists of Ireland joined forces in 2013 to establish a task group called the Environment and Sustainability Committee. They produced an environmental policy statement in July 2017 to identify and act on opportunities to improve the sustainability of the anaesthetic practice.32 Environmental impact modules have been incorporated into anaesthetic curricula. There have been a range of educational

events and updated clinical guidelines to encourage greener practices.33 Furthermore, to assist with real time decision making, an anaesthetic impact calculator mobile application has been created to help clinicians to calculate and compare the CO_2 emissions of inhaled anaesthetic agents.34

Eco-pharmaco-stewardship in anaesthetic practice is still in it's early stages and will take time for it to fully impact clinical practice; but with growing recognition of this problem comes increased opportunities for practical solutions, with the potential for huge environmental gains.

Eco-pharmaco-stewardship case study 2 – Metered-dose inhalers

Medications delivered via inhalers form the mainstay of the management of chronic respiratory conditions such as asthma and COPD. The use of pressurised metered-dose inhalers (MDIs) account for around 3% of the NHS's greenhouse gas emissions.4 Since their introduction in 1956, MDIs have become the leading inhaled therapy delivery modality.35 In 2019, an estimated 480 million MDIs were prescribed globally, which equates to 2,400 doses inhaled every second.35 Currently around two-thirds of inhalers prescribed are MDIs.35 Inhalers further impact the environment via their contribution to plastic waste.

The main source of their carbon footprint comes from the propellant used to deliver the medication to the airways rather than the medication itself. Previously, the propellant gases in MDIs were chlorofluorocarbons (CFCs) but due to their recognised contribution to ozone layer destruction, they were banned under the enforcement of the Montreal protocol in 1989.35 Hydrofluoroalkanes (HFAs), also referred to as hydrofluorocarbons (HFCs), have taken their place as the propellant gas of choice. Whilst HFAs do not contribute significantly to ozone damage, they are extremely powerful greenhouse gases. Of the 11,500 tonnes of HFA propellant produced worldwide per year, 92% is HFA-134a (norflurane) and the remainder is HFA-227ea (heptafluoropropane).36 They have high 100-year global warming potentials, up to 1,300 and 3,350 times that of CO_2, respectively.36

The challenge of lowering HFA MDI related emissions is underway, with cross cutting efforts from health organisations, environmental groups, pharmaceutical companies, regulatory authorities and governments working to reduce this impact by developing strategies from drug development to clinical usage.

Within MDI manufacture, emissions can be limited by decreasing the production of inhalers using the more damaging HFA-227ea propellant in favour of HFA-134a. There is growing interest in using alternative propellants with better emissions profiles, such as HFA-152a (1,1-difluoroethane). It is estimated that an MDI using HFA-152a as the propellant reduces carbon emissions by 90% compared with an equivalent HFA-134a MDI. 37 Major pharmaceutical companies such as GSK have made commitments to focus on production of alternative propellant free inhalers.38

Some of the most impactful changes occur at the healthcare provider-patient level. Strategies here can broadly be split into two groups: increased use of propellant free inhalers and optimising HFA MDI use to limit emissions. Clinical pharmacologists can work with other healthcare professionals championing these strategies.

Dry powder inhalers (DPIs) or soft-mist inhalers (SMIs) are inhaler devices that do not use propellants, therefore increased use of these types of inhalers can reduce overall HFA related emissions. It is advised that where clinically appropriate these inhalers should be used preferentially. DPIs have the advantage over MDIs in that their use does not require breath coordination.36 However, they are not suitable for children or patients who cannot generate sufficient inspiratory flow rates such as advanced airflow limitation in severe COPD.36

Healthcare providers can prescribe MDIs to minimise the quantity of propellant used. For example, for beclomethasone, prescribing 1 puff of a 200mcg MDI versus 2 puffs of a 100mcg MDI, halves the amount of propellant required for the same dose.36 Correct inhaler technique can help to improve therapeutic efficacy and reduce wasted doses. Furthermore, for demonstration of technique, propellant free placebo MDIs can be used.36 Ensuring patients have awareness of how many doses their inhalers contain can further reduce unused inhaler content.

Non-pharmacological management is also important. Respiratory conditions are exacerbated by smoking and air pollution and where possible this should be minimised. Improving respiratory reserve with increased physical activity and pulmonary rehabilitation can also assist with better disease control and potentially reduce inhaler use, particularly with reliever therapies.

The patient use perspective

Physicians, pharmacists, nurses, and allied health professionals have vital roles to play in working with patients to optimise the benefits of medicines and to promote sustainable medicines use. We have discussed the environmental impacts of pharmaceutical waste but there are also significant financial implications of this. Each year, around £300 million NHS prescribed medicines are wasted and at any given time, an estimated £90 million worth of medicines lie unused in patients' homes.39 In this section we will focus on medicines waste related to patient use and how we can support our patients to reduce the impact of this. The key areas we have identified to target this are adherence issues, reduction in issued prescriptions and medicinal product disposal.

Non-adherence to medications presents a major challenge both therapeutically and environmentally. An estimated 50-60% of patients are non-adherent to medicines they have been prescribed.40 According to the WHO, "increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatment."40

Healthcare professionals often encounter patients in whom medicines are not used as prescribed despite their efforts to come to shared decisions about appropriate therapy. The issues underlying this can be complicated and not always fully appreciated by the healthcare professional. Warning signs of medicines not used as prescribed may come in the form of fear of lifelong treatment, poor understanding of the condition, poor mental wellbeing, concerns about adverse effects and apparent lack of expected treatment effects.41

Identifying medicines not used as prescribed is an important step as it helps to initiate an honest discussion between the patient and healthcare professional. However, there is more

that we can do beyond traditional patient education. We can use tools that support patient's adherence to treatment. Health coaching through telephone-based support can provide regular contact with patients to help them build better medicine taking habits and improve self-monitoring. There is growing interest in advancements in technology that can enhance such information delivery as well as improve engagement of patients with their own health and with healthcare providers. This has become especially pertinent during the COVID-19 pandemic, where the way that we communicate with our patients has shifted and virtual communication formats have become increasingly important. Online initiatives such as Me & My Medicines42 are tools that can assist in the understanding of medicines for patients and aid in empowering patients to have open conversations about issues regarding compliance. Factors leading to unintentional adherence such as forgetfulness in either taking medications or regular collection of prescriptions can be targeted with medication-taking reminder applications and pharmacy-to-door medicines delivery services. For example, the NHS app has a prescription ordering service. However, as with all technological progress, we should be mindful that there is a potential for exclusion of patients who may not have the digital literacy to fully utilise this.

Reducing the number of prescriptions can help cut down on unused medicines, and a balance needs to be achieved between giving appropriate therapy without omitting potentially important medications. The recently published UK National Overprescribing Review advised that tackling this complex problem will require a system-wide approach that supports both health professionals and patients.43 It suggested that at least 10% primary care prescriptions items were unnecessarily issued. Strategies outlined to reduce prescriptions that are not needed focused on improving digital systems, interoperability, performing structured medication reviews, and promoting personalized care. Clinical pharmacologists who have expertise in evidence-based and stratified therapies can be of valuable here, through using population medicines optimisation approaches that aim to maximise therapeutic efficacy and minimise harm and waste.

Polypharmacy, though appropriate for many patients, can increase the risk of non-adherence, and inadvertently lead to requests for more medications than is needed and stockpiling. Medication reviews and the use of tools such as the STOPP/START criteria are increasingly employed to tackle inappropriate polypharmacy.44 However, for further change we need to empower our patients to take control of their medication supplies. This could perhaps start with open conversations about medication requirements and building relationships with their local pharmacies. Organisations such as Medicine Waste UK45 campaign to increase awareness on prevention of prescriptions, their tagline message being 'order only what you need'.

The number of unused medications that resides in patients' homes indicate that current methods of ensuring appropriate use are sub-optimal and additional measures are needed to influence and change behaviour amongst patients.45For patients who pay for their prescriptions, there is a disincentive to dispose of medicines not being taken as there may be a view that they will be required in the future. Better medicines ordering systems and general practice repeat prescribing processes may ensure that only what is actually required is ordered.

For disposal of pharmaceuticals including packaging, currently the main route is via the pharmacy with the onus on the patient to do this. Medicine Waste UK gives advice on how to safely dispose of medications. For medication packaging, Teracycle offer free recycling at drop off options in participating Superdrug stores across the UK.46 Further development of systems that collect and dispose of household pharmaceutical waste in the UK, including medicines and their packaging could represent an important measure to protect the environment, while also protecting human health from unintended exposure and inappropriate use. Such collection schemes for unused medicines are available and indeed compulsory by law in many other developed countries.47

Conclusion

Time is short for making the substantial changes in carbon emissions reduction worldwide to achieve the ambitious goals set out over the next few years and decades. Every sector must make decisions and create actions to improve sustainability and within the health sector clinical pharmacologists, working with other specialties and disciplines especially clinical pharmacists, can make innovative choices and plans to support climate change ventures. We have set out some the principles of eco-pharmaco-stewardship from a variety of perspectives which focus on areas such as optimising prescribing, substituting high carbon products for low-carbon alternatives, and improvements in production and waste processes. If these principles are considered and actioned widely across the health service, then we too can play a part in reducing the global crisis we face through climate change and improve the health of the world and the population for future generations.6

Acknowledgments

We are grateful to Mr Graham Prestwich, Public and Patient engagement lead for the Yorkshire and Humber Academic Health Science Network, for useful comments on the draft of this article.

Contributors

All authors have contributed to the drafting of the manuscript. EA, JJC and MF revised the manuscript critically. All authors approved the manuscript prior to submission.

Competing interests

The authors have no conflicts of interest to declare.

References

1. United Nations. The climate crisis - a race we can win. Published online 2019:2. Accessed September 10, 2021. https://www.un.org/sites/un2.un.org/files/un75_climate_crisis.pdf. WB
2. United Nations. The Paris Agreement. Accessed September 10, 2021. https://www.un.org/en/climatechange/paris-agreement
3. World Health Organization Regional Office for Europe. Environmentally sustainable health systems: a strategic document. Published online 2017. Accessed September 4, 2021. https://www.euro.who.int/en/health-topics/Health-systems/public-health-

services/publications/2017/environmentally-sustainable-health-systems-a-strategic-document-2017

4. NHS England and NHS Improvement. Delivering a “Net Zero” National Health Service. Accessed September 8, 2021. https://www.england.nhs.uk/greenernhs/wp-content/uploads/sites/51/2020/10/delivering-a-net-zero-national-health-service.pdf

5. Salas RN. The Climate Crisis and Clinical Practice. *https://doi.org/101056/NEJMp2000331*. 2020;382(7):589-591. doi:10.1056/NEJMP2000331

6. Atwoli L, Baqui AH, Benfield T, et al. Call for emergency action to limit global temperature increases, restore biodiversity, and protect health. *BMJ*. 2021;374:n1734. doi:10.1136/BMJ.N1734

7. Eco-pharmco-stewardship (EPS). A holistic environmental risk management program. Accessed September 4, 2021. https://www.efpia.eu/media/25628/eps-a-holistic-environmental-risk-management-program.pdf

8. Fisk M, Zecharia A, Payne R, et al. Sustainable medicines development and use: Our collective responsibility for action to mitigate the natural world crisis. *British Journal of Clinical Pharmacology*. Published online September 6, 2021:bcp.15067. doi:10.1111/BCP.15067

9. Milanesi M, Runfola A, Guercini S. Pharmaceutical industry riding the wave of sustainability: Review and opportunities for future research. *Journal of Cleaner Production*. 2020;261:121204. doi:10.1016/J.JCLEPRO.2020.121204

10. European Medicines Agency. Guideline on the environmental risk assessment of medicinal products for human use. Published online 2018. Accessed September 8, 2021. www.ema.europa.eu/contact

11. Salas RN, Maibach E, Pencheon D, Watts N, Frumkin H. A pathway to net zero emissions for healthcare. *BMJ*. 2020;371:m3785. doi:10.1136/BMJ.M3785

12. Tucker JL, Faul MM. Industrial research: Drug companies must adopt green chemistry. *Nature 2016 534:7605*. 2016;534(7605):27-29. doi:10.1038/534027a

13. Envirotainer. 5 key steps to find the best pharma cold chain solution to reduce carbon emissions. Accessed September 6, 2021. https://www.envirotainer.com/resources/industry-insights/2019/5-key-steps-reduce-carbon-emissions/

14. Hatswell AJ, Porter JK. Reducing Drug Wastage in Pharmaceuticals Dosed by Weight or Body Surface Areas by Optimising Vial Sizes. *Applied health economics and health policy*. 2019;17(3):391-397. doi:10.1007/S40258-018-0444-0

15. Patel M, Sheridan E. Sustainability in drug delivery: A green future without compromising safety and efficacy. Chemistry Today. Published 2017. Accessed September 10, 2021. https://www.paconsulting.com/newsroom/expert-

opinion/chemistry-today-sustainability-in-drug-delivery-a-green-future-without-compromising-safety-and-efficacy-7-april-2021/

16. I'ons G. From Design to Disposal: Achieving Sustainability in Medical Devices. ONdrugDelivery. Published 2020. Accessed September 6, 2021. https://ondrugdelivery.com/from-design-to-disposal-achieving-sustainability-in-medical-devices/

17. World Health Organization. Guidelines on packaging for pharmaceutical products. Accessed September 6, 2021. https://www.who.int/medicines/areas/quality_safety/quality_assurance/GuidelinesPackagingPharmaceuticalProductsTRS902Annex9.pdf

18. Lithgow T. Six steps to pharmaceutical packaging sustainability. Healthcare Packaging. Published 2009. Accessed September 5, 2021. https://www.healthcarepackaging.com/machinery-materials/adherence-delivery/news/13281351/six-steps-to-pharmaceutical-packaging-sustainability

19. World's first biodegradable blister packs for pills & food supplements developed in Swindon. Business & Innovation Magazine. Published 2019. Accessed September 5, 2021. https://www.businessinnovationmag.co.uk/worlds-first-biodegradable-blister-packs-for-pills-food-supplements-developed-in-swindon/

20. Amcor: Recyclable Blister Packaging From: Amcor | Healthcare Packaging. Healthcare Packaging. Published 2021. Accessed September 5, 2021. https://www.healthcarepackaging.com/machinery-materials/package-design/product/21403890/amcor-amcor-recyclable-blister-packaging

21. Smith RS. A 2-year retrospective review of vial sharing options for the compounding of cytotoxics. *European Journal of Hospital Pharmacy*. 2015;22(3):161-164. doi:10.1136/EJHPHARM-2014-000547

22. Maughan DL, Lillywhite R, Cooke M. Cost and carbon burden of long-acting injections: a sustainable evaluation. *BJPsych Bulletin*. 2016;40(3):132-136. doi:10.1192/PB.BP.114.049080

23. General Medical Council. Outcomes for graduates. 2020. Accessed September 11, 2021. https://www.gmc-uk.org/education/standards-guidance-and-curricula/standards-and-outcomes/outcomes-for-graduates/outcomes-for-graduates

24. Naylor C, Appleby J. Sustainable health and social care Connecting environmental and financial performance. *The King's Fund*. Published online 2012. Accessed September 4, 2021. https://www.kingsfund.org.uk/sites/default/files/field/field_publication_file/sustainable-health-social-care-appleby-naylor-mar2012.pdf

25. Muret J, Fernandes TD, Gerlach H, et al. Environmental impacts of nitrous oxide: no laughing matter! Comment on Br J Anaesth 2019; 122: 587–604. *British Journal of Anaesthesia*. 2019;123(4):e481-e482. doi:10.1016/J.BJA.2019.06.013

26. Lew V, McKay E, Maze M. Past, present, and future of nitrous oxide. *British Medical Bulletin*. 2018;125(1):103-119. doi:10.1093/BMB/LDX050

27. McGain F, Muret J, Lawson C, Sherman JD. Environmental sustainability in anaesthesia and critical care. *BJA: British Journal of Anaesthesia*. 2020;125(5):680. doi:10.1016/J.BJA.2020.06.055

28. Gordon D. Sustainability in the Operating Room: Reducing Our Impact on the Planet. *Anesthesiology Clinics*. 2020;38(3):679-692. doi:10.1016/J.ANCLIN.2020.06.006

29. Lim A, Braat S, Hiller J, Riedel B. Inhalational versus Propofol-Based Total Intravenous Anaesthesia: Practice Patterns and Perspectives among Australasian Anaesthetists: *https://doi.org/101177/0310057X1804600509*. 2018;46(5):480-487. doi:10.1177/0310057X1804600509

30. Rinehardt. EK, Sivarajan. M. Costs and wastes in anesthesia care. *Current opinion in anaesthesiology*. 2012;25(2):221-225. doi:10.1097/ACO.0B013E32834F00EC

31. Barbariol F, Deana C, Lucchese F, et al. Evaluation of Drug Wastage in the Operating Rooms and Intensive Care Units of a Regional Health Service. *Anesthesia and analgesia*. 2021;132(5):1450-1456. doi:10.1213/ANE.0000000000005457

32. Environment and sustainability committee. Joint Environmental Policy Statement (July 2017). Published 2017. Accessed September 4, 2021. https://anaesthetists.org/Portals/0/PDFs/Environment/Joint%20Environmental%20Policy%20Statement%20-%20FINAL.pdf?ver=2019-05-12-081735-747

33. The Royal College of Anaesthetists. Sustainability Strategy 2019–2022. Accessed September 4, 2021. https://www.rcoa.ac.uk/about-college/strategy-vision/environment-sustainability/sustainability-strategy-2019-2022

34. The Royal College of Anaesthetists. The Anaesthetic Impact Calculator. Accessed September 4, 2021. https://rcoa.ac.uk/about-college/strategy-vision/environment-sustainability/anaesthetic-impact-calculator

35. Pritchard JN. The Climate is Changing for Metered-Dose Inhalers and Action is Needed. *Drug Design, Development and Therapy*. 2020;14:3043. doi:10.2147/DDDT.S262141

36. Wilkinson AJK, Anderson G. Sustainability in Inhaled Drug Delivery. *Pharmaceutical Medicine 2020 34:3*. 2020;34(3):191-199. doi:10.1007/S40290-020-00339-8

37. Jeswani HK, Azapagic A. Life cycle environmental impacts of inhalers. *Journal of Cleaner Production*. 2019;237. doi:10.1016/j.jclepro.2019.117733

38. GSK Public policy positions A publication of GSK Communications and Government Affairs 1 Respiratory Products and Global Warming. Accessed October 30, 2021. https://ec.europa.eu/clima/policies/ozone_en

39. Pharmaceutical Waste Disposal | Direct365. Accessed September 4, 2021. https://www.direct365.co.uk/waste/clinical-and-healthcare-waste/pharmaceutical-waste?utm_source=Bing&utm_medium=cpc&utm_term=pharmaceutical%20waste&utm_campaign=CWC-Clinical-Waste&infinity=ict2~net~gaw~ar~~kw~pharmaceutical%20waste~mt~p~cmp~CWC%20-%20Clinical%20Waste&msclkid=b66947b7e0b11009122e268496fc4769&utm_content=CWC%20Broad%20-%20Pharmaceutical%20Waste

40. Sabaté E, World Health Organization. Adherence to long-term therapies: evidence for action. Published online 2003. Accessed September 4, 2021. https://www.who.int/chp/knowledge/publications/adherence_full_report.pdf?ua=1

41. Mackenzie IS, MacDonald TM. Identifying poor adherence to antihypertensive medications in patients with resistant hypertension. *British Journal of Clinical Pharmacology*. 2019;85(1):5-7. doi:10.1111/BCP.13806

42. Me & My Medicines, Medicines Communication Charter, It's OK to Ask – Home. Accessed September 4, 2021. https://meandmymedicines.org.uk/

43. of Health D, Care S. Good for you, good for us, good for everybody: a plan to reduce overprescribing to make patient care better and safer, support the NHS, and reduce carbon emissions. Published online 2021.

44. National Institute for Health and Care Excellence. Medicines optimisation: the safe and effective use of medicines to enable the best possible outcomes NICE guideline. Published online 2015. Accessed September 8, 2021. www.nice.org.uk/guidance/ng5

45. Medicine Waste UK. http://www.medicinewaste.com/. Accessed September 4, 2021. http://www.medicinewaste.com/didyouknow

46. TerraCycle UK. The Medicine Packet Recycling Programme | TerraCycle® UK · TerraCycle. https://www.terracycle.com/en-GB/brigades/medicine-packet-uk. Accessed September 4, 2021. https://www.terracycle.com/en-GB/brigades/medicine-packet-uk

47. Pharma Environment – Safer medicine for a safer world. Accessed September 7, 2021. https://pharmaenvironment.org/#home