Inhalers and the environment: Pollution, plastics and policy

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ABSTRACT

The effects of the climate crisis have been well established with the first global efforts to address the issue made over 30 years ago. The global healthcare sector is a large contributor to the total greenhouse gas (GHG) emissions, with the recent focus on the respiratory care sector. However, recent directives to address these emissions include 'blanket unconsented switching' of stable respiratory patients from pressurized metered dose inhalers (pMDIs) to dry powder inhalers (DPIs), which has the potential to cause a multitude of serious consequences for the patient. This article reviews the broad consequences and provides recommendations to encourage an environmentally friendly patient-centered approach without causing harm to the patient.

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INTRODUCTION

The planet's climate crisis is unequivocally an emergency with the effect of human consumption and distribution of resources well documented to present the scale of the crisis and the consequences that impact the well-being of the global population and environment. The World Health Organization (WHO) has projected that by 2030, at least 300000 deaths per year will occur due to climate change. which would heavily impact countries with weak healthservices infrastructure¹. The wealthiest 10% of nations have contributed 52% of the cumulative CO₂ emissions over the last 25 years². Globally, the healthcare sector has a carbon footprint equivalent to 4.4% of net global emissions, equivalent to 2 gigatons of CO23, and the top healthcare emitters are high-income countries (HICs) such as the United States, China and the European Union, which account for over half of the total footprint³. In contrast, lowand middle-income countries (LMICs) share the greatest burden of climate change and climate-sensitive health risks⁴. The climate crisis is therefore a healthcare crisis in which appropriate measures must be introduced to de-carbonize the individual sectors worldwide.

Increasingly, the global warming contributions by the respiratory healthcare sector are being debated; specifically, the use of hydrofluorocarbons (HFCs) as propellants in pressurized-metered dose inhalers (pMDIs). These propellants account for <0.1% of the total global greenhouse gas (GHG) emissions and it is estimated that 0.052% of GHG emissions in Greece are due to pMDIs^{5,6}. Although the contribution appears minuscule, there are calls, particularly amongst policymakers and governments, to reduce the carbon footprint of pMDIs, which could reform the respiratory treatment guidelines in action. However, often, the environmental impact of pMDIs is discussed in the context of preventer inhalers rather than relievers, thus omitting the significant contribution of short-acting b-agonists (SABAs) to global warming. Whilst it seems that a combination of long-acting b-agonists (LABA) and inhaled corticosteroids (ICS) dominate the global respiratory market, SABAs alone contribute to half of the market share based on the number of doses prescribed⁷. This is also coupled with the findings from the CARBON program that show that SABA use is common in Europe and Canada, with significant SABA GHG emissions⁸. When compared to total inhaler emissions, Greece contributes 62% of SABA GHG emissions, followed by the UK (68%) and Romania (80%)8. Therefore, it is not unreasonable to conclude that a large part of pMDI emissions are due to reliever use.

However, the international response to these findings has been scrutinized by the respiratory field. In particular, the UK Government's Environmental Audit Committee (EAC) has introduced a controversial directive targeting respiratory treatments to reduce the global warming potential (GWP) impact, with an emphasis to switch patients from pMDIs to dry powder inhalers (DPIs)⁵. The UK National Healthcare System (NHS) has since established a longterm plan for England to include this target and will aim to reduce prescribing of pMDIs by 50% by 2030⁹. Alarmingly, prescribers are also being incentivized to 'blanket switch' stable patients, often without their consent in order to meet these targets. Indeed, patients are being admitted to the hospital with acute respiratory attacks as a consequence of

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blanket unconsented switching.

However, these directives provide little consideration regarding the patient's needs and the potential negative healthcare outcomes. The consequences to patient health must be evaluated and included by policymakers to ensure appropriate reform is undertaken. By following uncritiqued guidelines, there is now a risk to the access to personalized medicine which should otherwise be non-negotiable with patient outcomes as the priority. With increasing pressure, healthcare professionals (HCPs) are thus expected to balance the risk of negative patient outcomes with the benefit of saving the planet¹⁰. An unguided and uncritical approach to initiatives such as these can pose a greater risk of harm not only to the patient but also to the planet. Therefore, a call for greater collaboration across sectors is urgently required to align our environmental goals with greater consideration of patient outcomes.

DEVELOPMENTS

The impact of fluorinated gases on the environment The contribution of fluorinated gases (F-gases) to the global warming crisis has called for attention to the issue. Before the 1987 Montreal Protocol, chlorofluorocarbons (CFCs) were primarily used as refrigerants and propellants; however, their GWP is considerably higher than that of hydrofluorocarbons (HFCs)^{11,12}. The legislation allowed for the successful phasing out of CFCs both due to their contribution to stratospheric ozone depletion and their contribution to the greenhouse effect¹³. Medical devices such as pMDIs were exempt to allow for the identification of suitable alternative propellants (i.e. HFCs) that did not cause stratospheric ozone damage.

The search for an alternative propellant and healthcare strategy

However, the extension of the Kigali Amendment recognizes the environmental impact of HFCs and has enforced their gradual phasing out^{12,14}. Medical aerosols are yet protected, wherein essential use is encouraged if a suitable alternative is lacking. This coincides with the development of lower GWP propellants [HFC-152a and HFO-1234ze(E)] that are scheduled to be on the market by 2025 that could reduce emissions by up to 92%¹⁵. The development of these low-GWP propellants is encouraging and sustains the need to allow for the innovation of alternative propellants and devices, rather than restricting HCP and patient access to their preferred inhaler device.

Affordability of alternative propellants must also be considered as seen in the transition from CFCs in which the manufacture of CFC pMDIs became more expensive than HFC pMDIs⁷. The same trend may be seen with the new low-GWP propellants and, thus, could influence the timing that pMDIs with lower GWP gases enter the market. In particular, HFO-1234ze(E) seems to be comparable to the commonly used HFC-134a of which approximately 30% of the \$0.80 cost to manufacture a pMDI is due to this propellant¹⁶. Therefore, an

environmentally friendly and economically feasible propellant is desired. However, widespread implementation of these new propellants will, of course, take time.

Environmental breakdown of the healthcare system

The European Union's healthcare footprint contributes to 4.7% of the national footprint emissions, compared to the United States which is almost double (7.6%)³. Greece falls below the EU average and contributes to 3.7% of the healthcare footprint, whilst countries such as the UK (5.4%) and Germany (5.2%) exceed the EU and global average^{3,17}. Greece's healthcare sector has also experienced a decline in GHG emissions between 2007–2016¹⁸, however, this may be due to public healthcare cuts that occurred during this time. Nevertheless, the national figures provide the incentive for all regions to de-carbonize their healthcare sector with netzero pledges in action to reach the Paris Agreement target by 2050.

Some countries have pledged to reach net-zero targets ahead of the Paris Agreement, such as by the NHS in England which was the first healthcare system to announce its target of 2040¹⁷. However, it is important to recognize all areas that contribute to GHG emissions within the healthcare sector. For example, 3.5% of all road travel within England is associated with the NHS, with 5% of NHS emissions due to patient travel¹⁷. In comparison, HFCs in pMDIs account for 3% of the NHS total emissions⁵. Whilst it is positive that these figures provide areas for change, the potential consequences must be acknowledged with the ambition to achieve netzero amongst all nations. In the context of respiratory health, unintended negative consequences could indeed be observed by initiating widespread switching of pMDIs under the guise of saving the environment¹⁹.

Unintended consequences of inhaler switching

Future directives and guidelines must consider the environmental impact of respiratory treatments, but this should not be at the expense of the patient or the healthcare system. However, unconsented inhaler switching from pMDIs to DPIs has the potential to have many consequences (Table 1).

Clinical consequences

Unconsented switching to DPIs can have a damaging effect on the HCP-patient relationship, which could taint patient perceptions of the healthcare system and the resultant inhaler treatment²⁰. Whilst it is notable that patients and HCPs should indeed partake in reducing their carbon footprint, this must be carefully administered in the healthcare setting in which both parties are involved in the decision-making process. It must also be stressed that patients should not be made to feel as though the onus is theirs, which may encourage the feeling of self-blame and reduce patient confidence.

A great concern is also warranted particularly if switching

Clinical	Environmental	Economic
Loss of patient trust and confidence of the healthcare system	Little consideration of inhaler recycling and waste issues	Prescription costs will increase which add burden to the healthcare systems
Loss of personalization of inhaled treatment, including patient preference and acceptability	DPI waste contributes to marine eutrophication and human toxicity	Potential escalation of treatment and hospitalization will increase healthcare costs
Not all inhalers are clinically suitable for every patient	Does not address the environmental impact of low-GWP propellants in pMDIs	May directly affect patient costs and affordability of care
Increased risk of hospitalization and in- person visits	Indirect increase of transport emissions to clinics/hospitals due to poor clinical outcomes	

Table 1. The unintended consequences of unconsented inhaler switching from pMDIs to DPIs

pMDI: pressurized metered dose inhaler. DPI: dry powder inhaler. GWP: global warming potential.

SABA pMDIs to their DPI equivalent⁷. This would also be impractical, especially due to the challenges of DPIs in which particular patient groups such as children, the elderly and those with active exacerbations struggle to provide the necessary inspiratory effort to achieve the flow rate to disperse the medication^{21,22}. Therefore, the access to the pool of inhalers should not be reduced for those patients that require them and where an alternative does not exist. Removing pMDIs from patient care would be detrimental and thus limit the tailoring of treatment.

Patients that have been switched without their knowledge also carry the risk of being uninformed of the inhaler technique necessary. With reports stating that over a third of patients are already unsure of how to use their inhaler²³, the potential for critical errors is large and can increase the risk of hospitalization, emergency care visits and thus poor patient outcomes²⁴. Therefore, this may also contribute to the indirect economic consequences on the healthcare system^{10,25}.

Economic and environmental consequences

The direct consequence of switching SABA pMDIs to DPIs is significant in terms of the financial burden. Across the top 15 markets, the prescription costs are predicted to increase when switching to SABA DPIs by 290% for the UK, 304% for Spain and 277% for Italy, as examples⁷. The environmental effect of DPIs should also be considered, even though they do not contain F-gases, they can have a greater impact on marine and human toxicity¹⁵. However, when evaluating the best-case scenario for switching inhalers, the global reduction in emissions is most profound when maintenance and reliever pMDIs transition to the use of low GWP propellant (HFA-152a)²⁶.

Therefore, greater acknowledgement for low GWP pMDIs and alternative inhalers is needed to ensure patient access to appropriate treatment, in conjunction with optimizing existing inhaled therapy, which includes treating the whole airway tree²⁷.

A patient-centered approach to inhaler therapy

In order to implement successful patient-centered therapy, a whole-system approach is necessary to ensure the precision of care and to balance the environmental factors. By evaluating patient outcomes and environmental issues at each level of intervention, HCPs can ensure that the most appropriate medication and device are prescribed. By optimizing diagnosis, there is great potential to address the issue of healthcare waste and reduce the rate of hospital admissions due to sub-optimal management. Earlier and accurate diagnoses are necessary, alongside appropriate prescribing that can be assisted by adhering to local guidelines instead of single-disease guidelines that can exacerbate the issue of polypharmacy²⁸.

Substantial reduction in the healthcare system's expenditure and carbon footprint can be made by addressing the issue of medical waste. Medicine wastage within primary care is estimated to cost the Netherlands €100 million per annum²⁹ compared to the UK's £300 million per annum, of which 40–50% could be made avoidable^{30,31}. In conjunction, approximately £100 million of medicine waste is hoarded by patients³⁰ – why is this so? This could be explained by examining prescribing practices which have resulted in a 46.8% increase in the number of items dispensed from 2006 to 2016³². The rise in polypharmacy could also be attributed to this increase which can in turn increase the risk of hospitalization by 300% when prescribed more than 10 medicines³³. To put this into context, hospital admissions for lung disease have increased at three times the rate of general admissions over the past 7 years³⁴. This could be due to an ageing population; however, this highlights issues within the system that must be addressed to increase patient outcomes and reduce the impact on the carbon footprint. A responsible approach must be implemented to optimize prescribing and identify areas where de-prescribing may be deemed necessary.

Identifying SABA overuse and initiating the correct treatment regime

Firstly, the correct treatment must be initiated and at the most optimal dose. Compared to its other European counterparts, the UK has the greatest per capita use of SABA and controller inhalers, with 61% of prescriptions of pMDIs being for SABAs^{8,35}. Overuse of SABAs (more than three prescriptions a year) is a sign of uncontrolled asthma and an indicator of sub-optimal medicine management. Reports have shown that many patients are overprescribed to a SABA but underuse their inhaled corticosteroids (ICS)^{36,37}. This is supported by data that show that the majority of SABA prescriptions were given to patients that overuse, with a range of 69% (Italy and Sweden) to 85% (UK) in Europe⁸. Therefore, initiating a preventer inhaler that the patient can and will use regularly, could decrease the global warming impact as the patient is controlled by using the lowest effective dose and less propellant²⁵.

The Assess, Choose and Train (ACT) algorithm incorporates both patient and environmental factors to facilitate the informed-decision making process with the active involvement of the patient³⁸. The ACT focuses on the patient's ability to operate an inhaler, which is crucial in determining inhaler use²¹. This can ensure that the most appropriate inhaled therapy is chosen and assisted with frequent reviews, which can potentially result in a decrease in inhaler waste due to improper prescribing. Such guidelines thus strengthen the need to ensure access to different inhalers, rather than excluding the use of pMDIs based on questionable rationale which will hinder personalized treatment.

There is, however, sparse guidance regarding inhaler switching in terms of patient training. NICE has released a patient aid that compares the environmental impact of inhalers to increase patient awareness and potentially encourage patients to switch. However, it would not be sensible to initiate a switch unless the patient has had an assessment and patients that are currently stable with their prescribed inhaler should not be blindly switched over.

Optimizing management of medicines

Crucially, the management of medicines relies on effective communication between the patient and the HCPs. Systems to improve management are required to allow for greater patient support. Identifying non-adherence provides the basis for optimizing patient care, especially for patients with long-term conditions in which non-adherence is estimated between 30–50%³⁹. Efforts should be made at the initiation of their prescribed inhaled treatment, which could be pivotal in terms of their treatment journey. Inhaler technique must be addressed, which can improve adherence and thus reduce the need to escalate treatment and reduce potential hoarding or waste. This would thus reduce overprescribing and overordering by the patient which affirms a more responsible approach to medication management. It should also be considered that adherence can change with time and, consequently, should be assessed at every consultation to ensure optimal outcomes⁴⁰.

Prescribing practices must also be reviewed to ensure that patients with one or more inhaled devices are maintained with similar devices, where possible. Greater outcomes are associated with the familiarity of the device and similarity of the inspiratory manoeuvre⁴¹; thus, great care should also be taken when prescribing generic or innovator devices. Where applicable, prescriptions should specify the innovator device, which could otherwise result in the patient receiving a variety of generic devices.

Inappropriate prescribing must also be highlighted at the earliest stage of intervention and should encourage greater integration of the care system. Bronchodilators are prescribed for restrictive lung diseases that may be unnecessary for some patients and also have an unnecessary impact on the environment. For example, obesity can impact lung function and cause restrictive breathlessness⁴²; however, with lifestyle changes, this could be reversed and the use of SABA pMDIs is usually unnecessary.

Preventative measures and non-pharmacological treatment must also be considered to ensure optimal management of respiratory conditions, for example, vaccination, smoking cessation and earlier implementation of pulmonary rehabilitation. Therefore, it is paramount to ensure that regular audits and reviews are utilized within the system, which can lessen the environmental impact.

Engaging the patient

A patient-centered approach to inhaler therapy will most importantly require the involvement of the patient. The greatest variable is the patient, who will ultimately decide whether their treatment is acceptable for their needs. Patient-reported outcomes (PROs) are becoming increasingly utilized to address inhaler acceptability, including assessing the sustainability of the inhaler. Inhaler preference studies have shown that although patients acknowledge the environmental impact of their inhaler, their preference is more heavily influenced by whether the inhaler is easy to use and able to manage their condition⁴³. Inhaler misuse can affect these perceptions, which can decrease the stability of their condition due to decreased drug delivery to the lungs. In fact, studies have reported that 70% of patients could not use their pMDI correctly, which led to greater instability⁴⁴. Poor inhaler technique, poor adherence and poor patient perception can therefore directly worsen patient outcomes⁴⁵. There are also substantial cost implications attributed to poor inhalation technique, particularly the improper use of DPIs, that can have a high economic burden⁴⁶. A focus on patient education is thus desperately needed to optimize patient treatment and to assess whether this is the most appropriate inhaler before potentially escalating treatment. Empowering the patient and increasing their understanding of their condition will allow for better self-management. Patient

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attitudes and perceptions can thus change. For example, patients that are over-reliant on their SABA, based on perceived immediate action, can be supported to encourage the correct use of their treatment. By engaging the patient, HCPs can seek to reduce their overuse, which can increase asthma control and decrease the risk of exacerbations⁴⁷.

The resultant effect of a system-wide review can, therefore, lead to a decrease in wasted treatment and cost, a decrease in patient travel and a decrease in hospital admissions. These are a few examples in which healthcare systems can target their carbon footprint to overall decrease their environmental impact whilst maintaining optimal patient care (Table 2).

Inhaler policy and recycling

The societal approach to recycling has seen a shift in behavior in the last 10–20 years⁴⁸. In 2015, a mandatory single-use plastic bag fee was introduced in England that has had a positive impact; not only in reducing plastic waste but also by increasing wider awareness of waste disposal⁴⁸. In turn, a 'policy spillover' effect has been witnessed to encourage the appropriate disposal of other plastics. A recent example is the EU Directive of Single-Use Plastics which took effect in 2021 that implements the EU's plastics strategy⁴⁹. However, there seems to be a great disparity in attitudes and knowledge concerning medication waste^{50,51}. Concerningly, it has been reported that up to 80% of patients are unaware of how to dispose of their medicines appropriately, due to a lack of communication with their healthcare provider^{50,51}. This provides an opportunity for HCPs to educate the community, which can influence patient over-ordering of medicines and increase

the patient's understanding of their condition and the environmental issues. However, this also highlights the issue of the lack of a nationwide medication recycling approach.

In the UK, approximately 73 million inhalers are prescribed every year⁵² of which 63% are disposed of in domestic waste with almost half their propellant left inside, much of which will remain in landfills⁵³. The NHS also estimates that only 0.5% of pMDIs are recycled⁵. Unfortunately, this figure is also coupled with a statement from NHS England that they will not implement a national recycling scheme for inhalers at this time⁵⁴. However, it is imperative that we should evaluate the disposal lifecycle of these drug delivery systems to improve safe disposal avenues for patients. Indeed, incineration of inhalers and medical waste can also be an effective method to prevent landfill disposal. This is a viable option for pMDIs and components that cannot be recycled and will ensure that residual propellant is captured and thermally degraded resulting in lower GWP substances emitted into the atmosphere⁵⁵. However, the environmental savings are still lower than that of recycling inhalers as a whole⁵⁵, which also has the added benefit of recycling and re-using residual propellant and thus extending their use. Therefore, a widespread recycling scheme must be established with advocacy from the healthcare and pharmaceutical sector.

Individual pharmaceutical schemes have resulted in success such as the GSK Complete the Cycle program that had cut CO₂ emissions equivalent to approximately 8600 cars as the first inhaler recycling and recovery scheme⁵⁶. However, the GSK scheme was unable to reach the necessary scale intended as an independent service with a total of 2 million

Initiating appropriate therapy	Optimizing medicines management	Engaging the patient
Initiate the most appropriate therapy with the patient involved in the decision- making process	Identify sources of non-adherence and continue to review regularly	Ensure the patient is informed and involved in decisions regarding their treatment
Consider the environmental impact of treatment if the patient is stable and able to use the given inhaler	Ensure patient inhaler technique is optimized and address any sources of error	Consider patient preferences and acceptability of inhaled devices
Ensure the patient is controlled with a suitable maintenance inhaler	Ensure patients are prescribed similar devices where required and ensure patients are prescribed the same brand of inhaler to ensure continuity of care	Educate patients of their inhaled therapy to better understand their condition
Identify SABA over-use and over- prescribing by the use of regular medication reviews	Identify inappropriate prescribing and assess the associated clinical outcomes	Encourage patients to better self-manage their condition where appropriate
	Ensure preventative and non- pharmacological measures are initiated where appropriate	

Table 2. Areas within healthcare systems that can implement a patient-centered approach to improveenvironmental and clinical outcomes

SABA: short-acting β-agonists.

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inhalers recycled or recovered through the scheme⁵⁶. Other schemes, such as the Chiesi Take AIR pilot, aim to recycle inhaler plastics and canisters, recover and re-use propellants and convert energy from non-recyclable components through incineration⁵⁷. Although these schemes are promising, many are still in their infancy and are not available across the nation, whilst some may also only be applicable to inhalers from the manufacturer. It would be impractical to require a patient with multiple inhalers from different manufacturers to recycle according to the associated scheme; therefore, an industry-wide led approach will be necessary. With the ambition of the UK government to ensure that at least 50% of pMDIs are recycled⁵, a safe disposal and recycling scheme must be a priority. Additionally, from 2020, the European Commission adopted the new Circular Economy Action Plan which follows the model to design waste out of systems by re-using, repairing and recycling existing materials for as long as possible⁵⁸. A circular healthcare economy could offer an alternative and sustainable approach to medical waste and, thus, promote greener manufacturing⁵⁹, which is required to meet net-zero targets.

Engaging the patient in this discussion will also benefit their understanding of their inhalers. HCPs and recycling awareness campaigns can influence patients by encouraging them to use all their doses, to better manage their symptom control and ensure adequate inhaler technique. By encouraging inhaler recycling, an extra point of contact in the patient pathway is added which allows for the opportunity to discourage wasted doses and educate the patient. However, the responsibility should be shared at each level of contact and, therefore, a more integrated approach can result in less waste and greater patient understanding.

CONCLUSION

The responsibility of the climate crisis should not fall on the patient alone and they should not be stigmatized for their preferred care⁶⁰. The pharmaceutical industry, the healthcare system and the government must instead share this responsibility and acknowledge their unique positions to advocate for appropriate reform and encourage greater collaboration. This is crucial to allow for a multidisciplinary approach with the patient at the forefront of the discussion rather than compromising patient care based on environmental grounds solely.

A whole-system review should thus be the focus of reform to enhance collaboration across the board. Unsuccessful strategies now could indeed cause more harm to the patient and contribute to the greater waste of resources. Therefore, a critique of such proposals is warranted and exemplifies the need to encourage dialogue between these parties. Most importantly, the optimization of patient-centered care must retain precision and personalization. By doing so, the environmental impact of the prescribed inhaled treatment can be considered without harming the patient.

CONFLICTS OF INTEREST

The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none was reported.

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