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How do patients determine when their inhaler is empty? Insights from an analysis of returned inhalers and a patient survey

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ABSTRACT

Background Inhalers are widely used for the management of asthma and chronic obstructive pulmonary disease. However, there is little knowledge about the extent to which an inhaler is used and when it is disposed of, despite the implications for an individual's health (when used beyond the recommended number of doses (overused)), and medicine wastage, healthcare costs and the environment (when discarded with remaining doses (underused)). To explore inhaler use, we assessed the number of doses remaining in pressurised metered-dose inhalers (pMDIs) returned via a Chiesi Inhaler Recycling scheme.

Methods pMDIs were dismantled, and components recycled where possible. Each canister was weighed and the mass of the formulation remaining was calculated. pMDIs were categorised based on number of doses remaining (underused, used, empty (indicating correct use) and overused) and by dose counter presence/absence. A separate online survey was used to obtain patient feedback on inhaler use and disposal behaviours.

Results Overall, 2614 pMDIs were analysed (55.9% maintenance, 44.1% reliever inhalers); 1015 (38.8%) had an integrated dose counter. The proportion of pMDIs returned empty was greater for inhalers with dose counters than for those without (51.3% vs 25.1%; p<0.0001); the proportion of pMDIs returned underused was lower for inhalers with dose counters than for those without (5.2% vs 33.2%; p<0.0001). The proportion of pMDIs returned overused was substantial and similar for devices with and without dose counters (34.0% vs 23.2%; p>0.01). Most respondents (55.2%) using devices without a dose counter reported that they were not confident in identifying when their inhaler was empty. Furthermore, many respondents (20.6%) who used inhalers with a dose counter reported continued use beyond 'zero'.

Conclusions Our study suggests that many inhalers are returned underused or overused, with inadequate knowledge among patients about the number of therapeutic doses remaining in the device and appropriate inhaler disposal. These have concerning implications for patient health and the environment and highlight a need for high-quality education for patients and healthcare professionals.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Using pressurised metered-dose inhalers (pMDIs) beyond the labelled number of actuations may cause ineffective dosing of medication, leading to poor clinical outcomes; whereas disposing of pMDIs with doses remaining has implications in terms of medicine wastage, healthcare costs and the environment.

WHAT THIS STUDY ADDS

⇒ Our data show that many inhalers were returned underused or overused, with concerning implications for patient health and the environment; and that patients have poor knowledge in terms of recognising how many doses remained in pMDIs.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ There is a need for high-quality education materials to improve how efficiently patients use their inhalers and track the number of doses remaining, to help minimise the risks of patients overusing their inhalers and to reduce the environmental impact of underused inhalers.

INTRODUCTION

Inhalers play a central role in the management of respiratory conditions such as asthma and chronic obstructive pulmonary disease (COPD).[1–4] Pressurised metered-dose inhalers (pMDIs) and dry-powder inhalers (DPIs) are among the most commonly used devices worldwide.[1 5 6] A range of factors including patient preferences, physical ability, age, comorbidities, inspiratory rate and inhaler technique can affect how well an inhaler device suits a patient.[1 7–9]

Every multidose reservoir inhaler contains a labelled number of unit doses; however, to ensure reliable performance throughout its use, manufacturers include an 'overfill' of medication, such that each device contains a surplus above the stated number of doses.[10–12]

Some inhalers contain a dose counter or indicator that the patient can use to determine when the prescribed number of doses has been reached (declared 'zero' dose, considered as nominal 'empty'). If a dose counter is not present, the patient needs to remember their usage to determine when the prescribed number of doses has been reached.[12 13] Previous studies have reported that some patients struggle to identify when their inhaler is considered empty, particularly when a dose counter is not available.[12–16]

Correct inhaler use allows patients to manage their condition effectively.[9] While correct device use is critical for optimal disease management,[9 17 18] it is also important to consider the potential health concerns caused by continuing to use inhalers beyond their prescribed number of doses.[12 13] Although manufacturer overfill in pMDIs may result in the delivery of some residual medication in these circumstances, delivery becomes progressively less reliable with continued use. This phenomenon is referred to as 'tail-off', which begins to affect dose reproducibility as an inhaler runs out of formulation (ie, the drug that is either dissolved or suspended in a liquid propellant). Tail-off occurs only after the labelled number of doses have been delivered from the pMDI and may pose significant safety concerns for patients.[12 19] The amount of medication per unit dose that remains once the declared zero dose has been reached may be inaccurate or therapeutically insufficient, which may increase the likelihood of disease complications and hospital admission.[12–14 16]

By contrast, disposing of inhalers that are not empty has environmental implications. pMDIs contain hydrofluorocarbon propellants, which belong to the broader group of fluorinated propellant gases and are potent greenhouse gases (GHGs).[20 21] Hydrofluorocarbons are responsible for approximately 2% of global GHG emissions, with the majority arising from the refrigeration and air conditioning industries, rather than from pharmaceutical products.[5 21–23] Improper disposal of pMDIs, such as discarding them in landfills, releases propellants into the atmosphere even after the declared zero dose has been reached owing to the presence of the overfill; this has an impact on global warming.[10 24 25] In addition, there is a societal burden in terms of medication waste and potential suboptimal disease management if pMDIs are disposed of before the declared zero dose has been reached. Understanding the extent of premature pMDI disposal, and any underlying reasons for it, is therefore important for any initiatives that aim to implement correct inhaler use for effective respiratory disease management and to minimise the environmental impact of pMDIs.

In the UK, the environmental impact of pMDIs can be reduced by returning used and/or unwanted inhalers to pharmacies, where they are disposed of as clinical waste through incineration to reduce the impact of the leftover GHGs in accordance with the National Health Service (NHS) contractual framework.[26] However, qualitative data from patient surveys suggest that over 90% of patients dispose of their inhalers in household waste.[24 27] Recently, the Chiesi Take Action for Inhaler Recycling (AIR) scheme demonstrated the feasibility and effectiveness of a postal recycling scheme for patients to return inhalers.[28] As part of this scheme, canisters were crushed rather than incinerated and any remaining propellant was captured for recycling, which prevented an estimated 119.3 tonnes of carbon dioxide emissions from entering the atmosphere in a 12-month period.

Previous studies suggested that there is a lack of adequate understanding about the use of inhalers beyond the labelled number of doses (overuse) and associated implications on disease control and/or patient safety; or about discarding inhalers when not empty (underuse) and the impact on medicine wastage, healthcare-related costs and the environment.[12 13 16 28] This article provides insights into patient behaviour and environmental effects around inhaler use in the UK following a weighing study designed and implemented by Chiesi. This study aimed to estimate the number of medication doses remaining in returned pMDIs from the Take AIR scheme to understand how frequently inhalers are used beyond their specified number of doses or disposed of with doses remaining. To complement and aid the interpretation of the results from this study, a separate patient survey was also performed to obtain feedback about when and why patients dispose of their inhalers.

METHODS

Analysis of pMDIs returned for recycling

pMDIs returned through the Chiesi Take AIR scheme between 13 May 2022 and 15 July 2022 in the UK were included in the analysis. Full methodology and results from the initial Take AIR pilot study have been previously reported.[28] Briefly, Take AIR, a 12-month pilot postal recycling scheme across Leicester, Leicestershire and Rutland, was designed and funded by Chiesi and aimed to assess the feasibility of postal inhaler recycling as an alternative to the community pharmacy waste collection service. Royal Mail returned envelopes directly to the contracted waste management company, Grundon Waste Management Limited. At Grundon, the contents were sorted and separated into two waste streams: recyclable and non-recyclable. All pMDI canisters were separated from their actuators, and the brand, type of canister and expiry date were noted. Each canister was individually weighed with mass noted in grams and, once weighed, was disposed of through the Take AIR scheme.[28]

To calculate the mass of the formulation remaining in each canister, the mass of a completely empty/shell canister (ie, with no formulation or propellant remaining) was subtracted from that of each returned canister. The shell canister mass used in this calculation was determined by taking one of each device type (that was near-empty to minimise propellant wastage), cooling it to liquify the propellant, puncturing holes in

the canister and allowing the propellant to evaporate under a fume hood to ensure that it was completely empty. To categorise the extent of inhaler usage, it was also necessary to estimate the mass corresponding to declared zero. To this end, three of each type of product were purchased and the mean mass of the full canisters was calculated. The loss in mass from each actuation of the device ('shot weight') was estimated by measuring the loss in mass over a total of 20 actuations and calculating the mean. The declared zero mass of a canister was then calculated by taking the mass of a full canister and subtracting the shot weight multiplied by number of labelled doses.

All pMDIs were categorised based on the number of doses remaining: underused (defined as having a remaining formulation mass with >50% labelled doses remaining); used (defined as having a remaining formulation mass ranging from >10% to ≤50% of the declared zero dose); empty (defined as having a remaining formulation mass within 10% of the declared zero dose) and overused (defined as having a remaining formulation mass >10% below zero). Cut-off points were chosen to allow for a sufficient number of remaining doses to cater for minor inaccuracies in the weighing and estimating of the 'empty' mass point. Inhalers were analysed by pMDI type, including reliever devices, and further stratified by short-acting beta-agonists (SABAs), long-acting beta-agonists (LABAs), short-acting muscarinic antagonists (SAMAs) and maintenance devices, which were stratified by inhaled corticosteroid (ICS) strength. pMDIs were also categorised by the presence of dose counter. These analyses were intended to evaluate if the use of different types of reliever or maintenance inhalers may reflect variable recycling behaviours.

Statistical analysesf

Data were entered in Microsoft Excel and summarised by pMDI type and presence of dose counter. Data were tested using the two-sample Z-test for proportions. For all statistical tests, a p<0.01 was considered significant.

Inhaler usage survey

Chiesi developed a separate qualitative online survey to collect data on inhaler usage and disposal. Patients with a respiratory condition who had been prescribed an inhaler, and/or their carers, were invited to complete the survey on Microsoft Forms via links on the Chiesi UK LinkedIn page, the Chiesi Facebook page or the Asthma + Lung UK Respiratory Voices Network. Patients and/or carers provided their anonymised opinions in a multiple-choice form and answered one open-ended question on inhaler use and disposal methods. The survey remained open from 7 February 2023 to 5 June 2023, and data were summarised and presented using descriptive statistics.

Patient and public involvement

The patient questionnaire was provided to Asthma + Lung UK for review to ensure the language was appropriate for patients. While patients and members of the public were otherwise not involved in the design, conduct, reporting or dissemination of our research, we are grateful to all patients and caregivers who returned devices as part of the Take AIR initiative and/or contributed to the online survey.

RESULTS

Analysis of pMDIs returned for recycling

In total, 2694 pMDIs were returned to Grundon Waste Management through the Take AIR scheme and were weighed to estimate the amount of product remaining between 13 May 2022 and 15 July 2022 (figure 1). Of these, 80 pMDIs were excluded from the analysis for multiple reasons, including damaged labels, missing data obtained from Grundon (product information, expiry date or mass) and erroneous data (defined as values outside of the range of the plot axes); data from 2614 pMDIs were used for subsequent assessments. The returned and analysed pMDIs included both maintenance inhalers (n=1462; 55.9%) and reliever inhalers (n=1152; 44.1%). Over half of the analysed pMDIs (n=1480; 56.6%) had no dose counter. In total, 1015 (38.8%) of the pMDIs returned had an integral dose counter, all of which were maintenance inhalers.

When we explored the distribution of doses remaining in all pMDI devices according to the presence or absence of a dose counter, the proportion of inhalers returned empty (defined as having a remaining formulation mass within 10% of the declared zero dose) was significantly higher for inhalers with dose counters than without (521/1015; 51.3% vs 372/1480; 25.1%; p<0.0001, figure 2a). The proportion of pMDIs returned underused (defined as having a remaining formulation mass with >50% doses remaining) was significantly lower for devices with than devices without dose counters (n=53; 5.2% vs n=492; 33.2%; p<0.0001). The proportion of overused pMDIs (those with a remaining formulation mass >10% below zero) was similar for devices with and without dose counters (n=345; 34.0% vs n=344; 23.2%; p>0.01). The other inhalers were returned used, with the remaining formulation mass ranging from >10% to ≤50% of the declared zero dose.

Looking at maintenance pMDIs only, the proportion of inhalers returned empty was significantly greater for devices with dose counters than those without (521/1015; 51.3% vs 45/328; 13.7%; p<0.0001, figure 2b). By contrast, the proportion of inhalers returned underused or overused was significantly smaller for those with dose counters than without (underused: n=53; 5.2% vs n=80; 24.4%; p<0.01, figure 2b; overused: n=345; 34.0% vs n=146; 44.5%; p<0.001). The other maintenance inhalers were returned used, with the remaining formulation mass ranging from >10% to ≤50% of the declared zero dose.

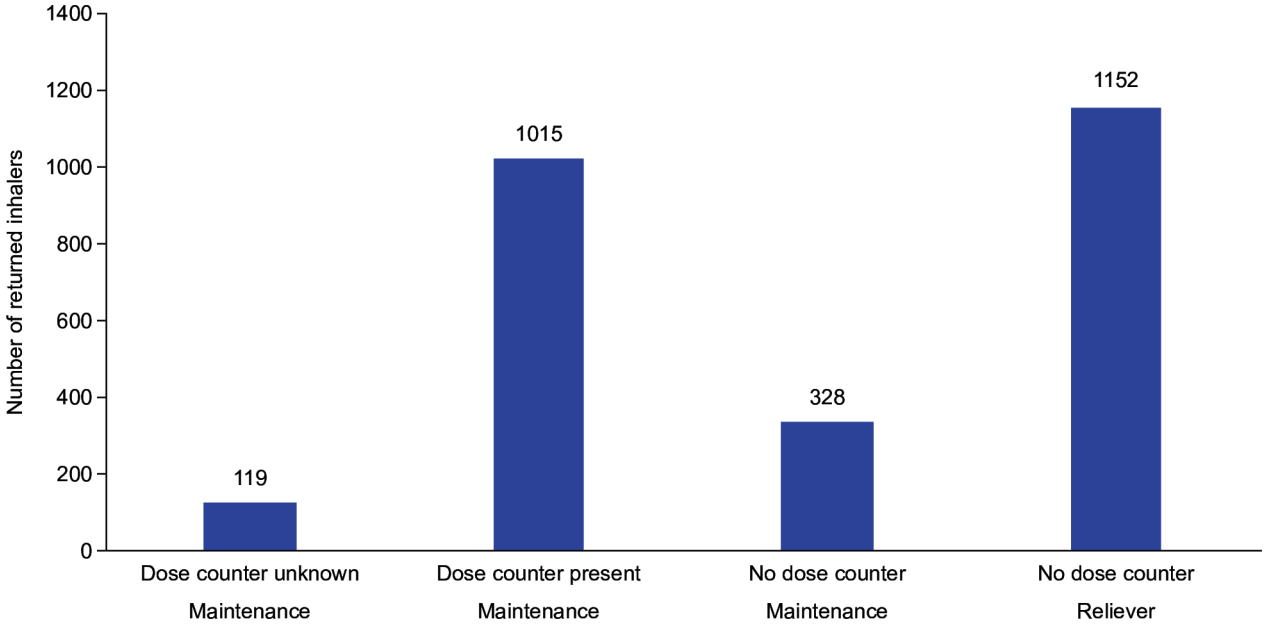


Figure 1 Summary characteristics of returned pMDIs included in weighing analysis. pMDI, pressurised metered-dose inhaler.

Most of the 1152 reliever pMDIs returned were SABA inhalers (n=1120; 97.2%), followed by LABA devices (n=26; 2.3%) and SAMA inhalers (n=6; 0.5%) (figure 3a). Reliever pMDIs were returned with a wide range of remaining doses: fewer than one-third (n=327; 28.4%) were returned empty, more than one-third of the pMDIs (n=412; 35.8%) were returned underused and 198 (17.2%) were returned overused. The remaining pMDIs were returned with residual doses between >10% and ≤50%.

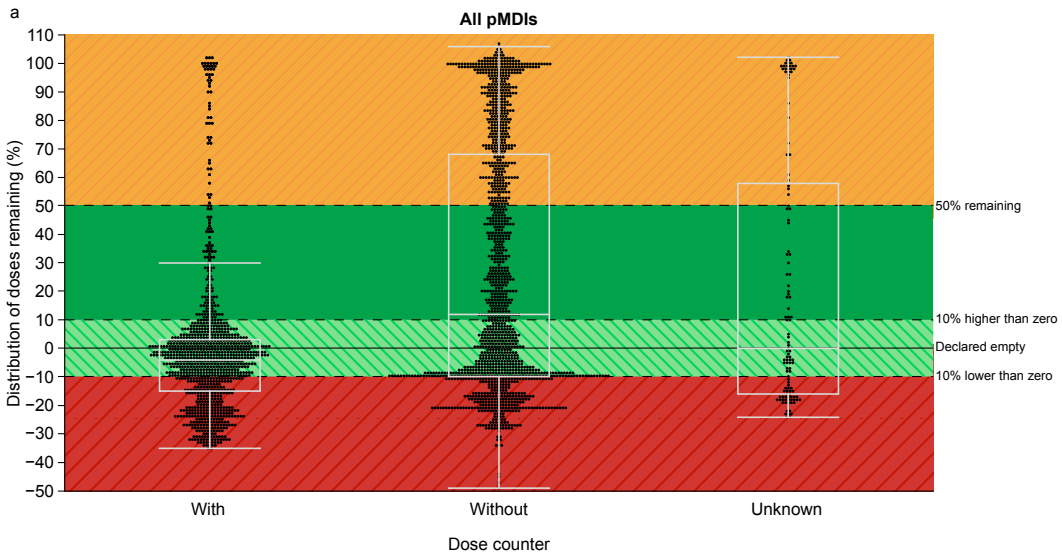
Returned maintenance pMDIs included inhalers with low-, medium- or high-dose ICS strength (figure 3b). Maintenance pMDIs had a wide range of doses remaining, with fewer than half (590/1462; 40.4%) returned empty. The proportion of maintenance devices returned overused was significantly higher than those returned underused (n=531; 36.3% vs n=166; 11.4%; p<0.0001). This contrasts with reliever inhalers, for which the opposite was true (198/1152; 17.2% vs 412/1152; 35.8%; p<0.0001). The proportion of inhalers returned underused was significantly lower for high-strength ICS inhalers compared with low-strength ICS inhalers (61/310 (19.7%) devices containing low-strength ICS had >50% doses remaining, compared with 96/708 (13.6%) devices containing medium-strength ICS, and 9/444 (2.0%) containing high-strength ICS; p<0.0001 for high-strength vs low-strength ICS).

Considering only those pMDIs without dose counters, significantly fewer maintenance pMDIs were returned empty than reliever pMDIs (45/328; 13.7% vs 327/1152; 28.4%; p<0.0001, figures 2b and 3a). The proportion of maintenance pMDIs without dose counters returned underused was significantly lower than that observed for reliever inhalers (n=80; 24.4% vs n=412; 35.8%; p<0.0001), whereas the proportion of maintenance pMDIs without dose counters returned overused was significantly higher than for reliever inhalers (n=146; 44.5% vs n=198; 17.2%; p<0.0001).

Patient-reported inhaler disposal and recycling behaviour

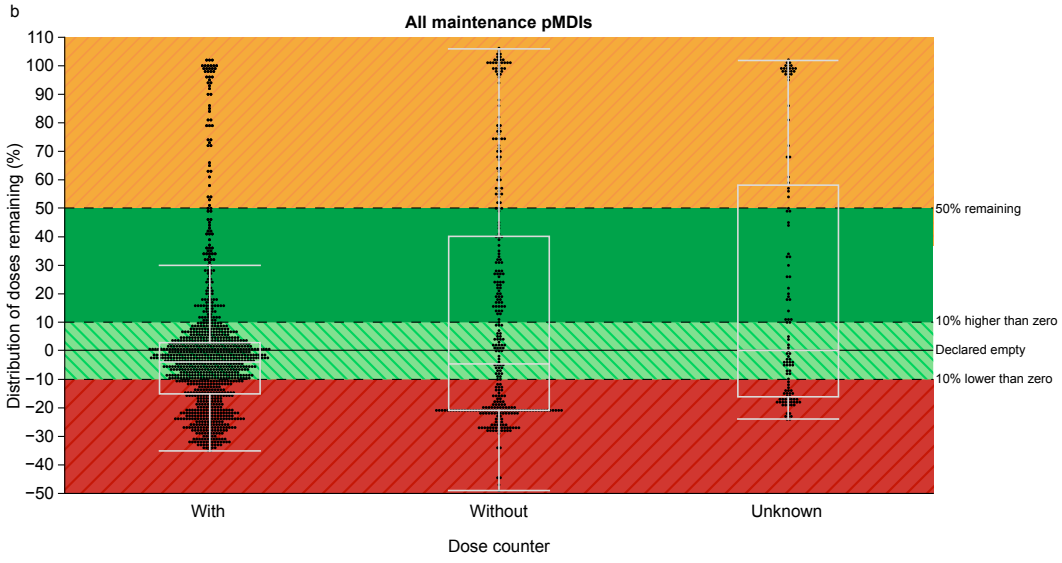
To complement and aid the interpretation of the results from the analysis of pMDIs returned for recycling, we conducted a survey to obtain feedback on when and why patients dispose of their inhalers. The online survey investigating the behaviour of the respondents around inhaler disposal collected 199 responses between 7 February 2023 and 7 June 2023. Almost half of the respondents (n=95; 47.7%) were prescribed only pMDIs; the remaining respondents were prescribed only DPIs (n=51; 25.6%), or a combination of pMDIs and DPIs (n=52; 26.1%). One patient did not know their inhaler type.

The most commonly reported method used by respondents to determine when their inhaler was empty (figure 4) was checking when the dose counter showed zero (74.9%). Other common indicators reported included when a dose of the medicine was no longer received (24.6%), when the pMDI felt empty on shaking (22.6%), and when the pMDI stopped 'puffing' (19.1%). Among 29 respondents using an inhaler without a dose counter, over half (n=16; 55.2%) did not know or were not sure about when their inhaler was empty. Most of the 199 respondents (n=170; 85.4%) reported that they were using at least one inhaler with a dose counter. Among these respondents, fewer than half (n=71; 41.8%) reported looking at the counter daily or every time they used their inhaler, and 15 (8.8%) only checked it when the inhaler felt empty (online supplemental figure 1a). Over three-quarters of the 170 respondents (n=131; 77.1%) reported starting a new inhaler as soon as their



Dose counter	With (n=1015)	Without (n=1480)	Unknown[a] (n=119)	Total of 'Without' and 'Unknown' (n=1599)
>50% doses remaining	53 (5.2%)	492 (33.2%)	33 (27.7%)	525 (32.8%)
>10% to ≤50% doses remaining	96 (9.5%)	272 (18.4%)	22 (18.5%)	294 (18.4%)
Within 10% of zero	521 (51.3%)	372 (25.1%)	24 (20.2%)	396 (24.8%)
>10% lower than zero	345 (34.0%)	344 (23.2%)	40 (33.6%)	384 (24.0%)

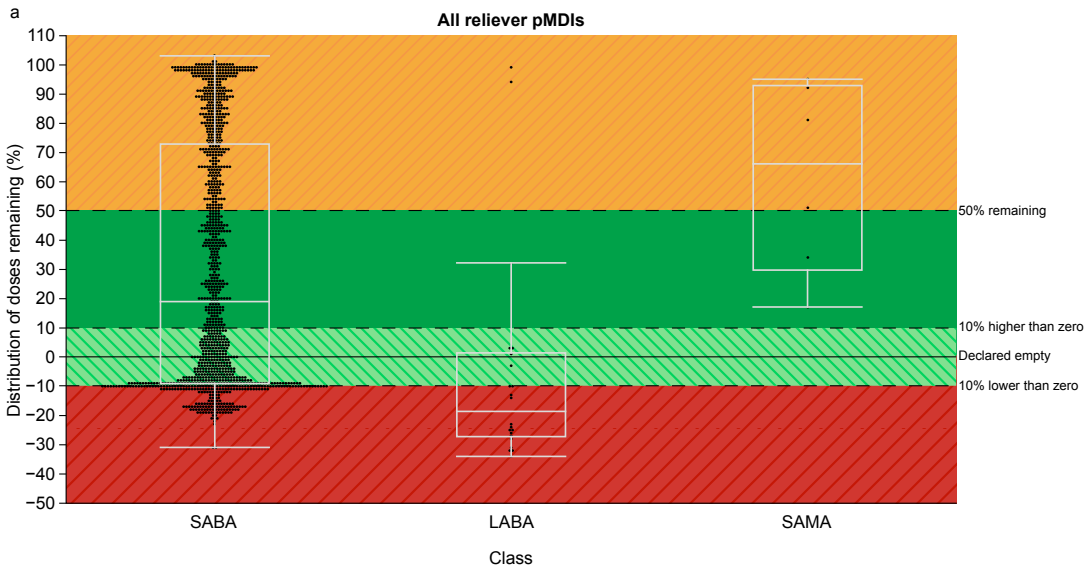
Key
Underused
Used
Empty
Overused



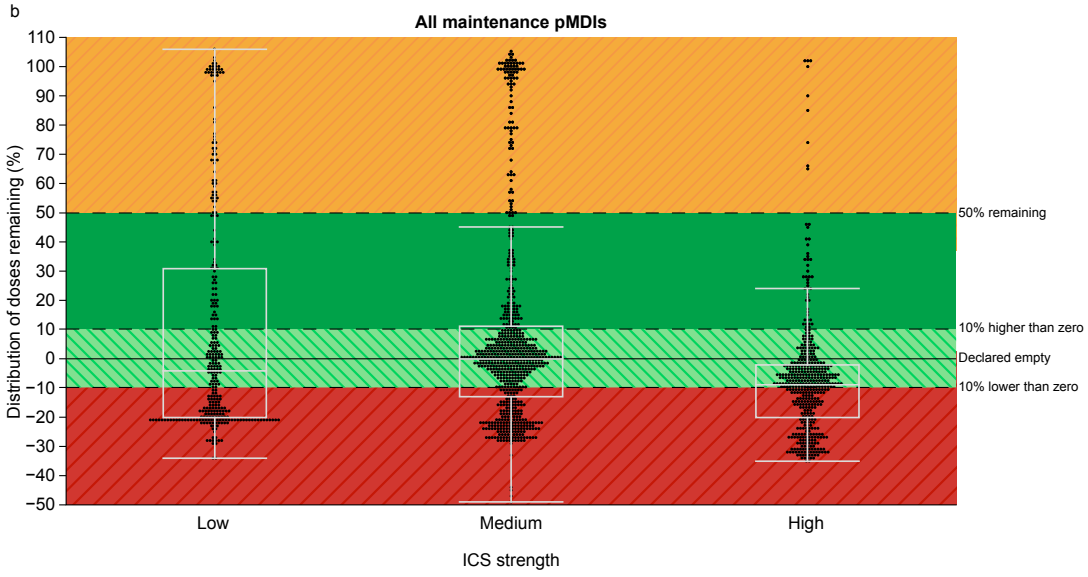
Dose counter	With (n=1015)	Without (n=328)	Unknown[a] (n=119)	Total of 'Without' and 'Unknown' (n=447)
>50% doses remaining	53 (5.2%)	80 (24.4%)	33 (27.7%)	113 (25.3%)
>10% to ≤50% doses remaining	96 (9.5%)	57 (17.4%)	22 (18.5%)	79 (17.7%)
Within 10% of zero	521 (51.3%)	45 (13.7%)	24 (20.2%)	69 (15.4%)
>10% lower than zero	345 (34.0%)	146 (44.5%)	40 (33.6%)	186 (41.6%)

Key
Underused
Used
Empty
Overused

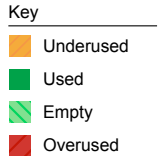
Figure 2 Distribution of doses remaining stratified by dose counter presence in (a) all pMDIs and (b) maintenance pMDIs only. [a]Inhalers which were subject to a change in the presence of dose counters over the study course were classified as 'unknown' because dose counter presence was not noted during data collection. The box and whisker plot shows data spread using a box for the middle 50% of data and lines (whiskers) extending to the minimum and maximum values. The box's ends mark the 25th and 75th percentiles, with the median inside. Points beyond the whiskers are considered outliers. pMDI, pressurised metered-dose inhaler.



Class	SABA (n=1120)	LABA (n=26)	SAMA (n=6)	Total (n=1152)
>50% doses remaining	406 (36.3%)	2 (7.7%)	4 (66.7%)	412 (35.8%)
>10% to ≤50% doses remaining	212 (18.9%)	1 (3.8%)	2 (33.3%)	215 (18.7%)
Within 10% of zero	323 (28.8%)	4 (15.4%)	0 (0%)	327 (28.4%)
>10% lower than zero	179 (16.0%)	19 (73.1%)	0 (0%)	198 (17.2%)



ICS strength	Low (n=310)	Medium (n=708)	High (n=444)	Total (n=1462)
>50% doses remaining	61 (19.7%)	96 (13.6%)	9 (2.0%)	166 (11.4%)
>10% to ≤50% doses remaining	46 (14.8%)	91 (12.9%)	38 (8.6%)	175 (12.0%)
Within 10% of zero	67 (21.6%)	322 (45.5%)	201 (45.3%)	590 (40.4%)
>10% lower than zero	136 (43.9%)	199 (28.1%)	196 (44.1%)	531 (36.3%)



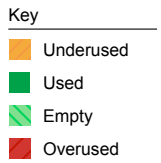


Figure 3 Distribution of doses remaining in (a) reliever pMDIs by type and (b) maintenance pMDIs by ICS strength. The box and whisker plot shows data spread using a box for the middle 50% of data and lines (whiskers) extending to the minimum and maximum values. The box's ends mark the 25th and 75th percentiles, with the median inside. Points beyond the whiskers are considered outliers. ICS, inhaled corticosteroid; LABA, long-acting beta-agonist; pMDI, pressurised metered-dose inhaler; SABA, short-acting beta-agonist; SAMA, short-acting muscarinic antagonist.

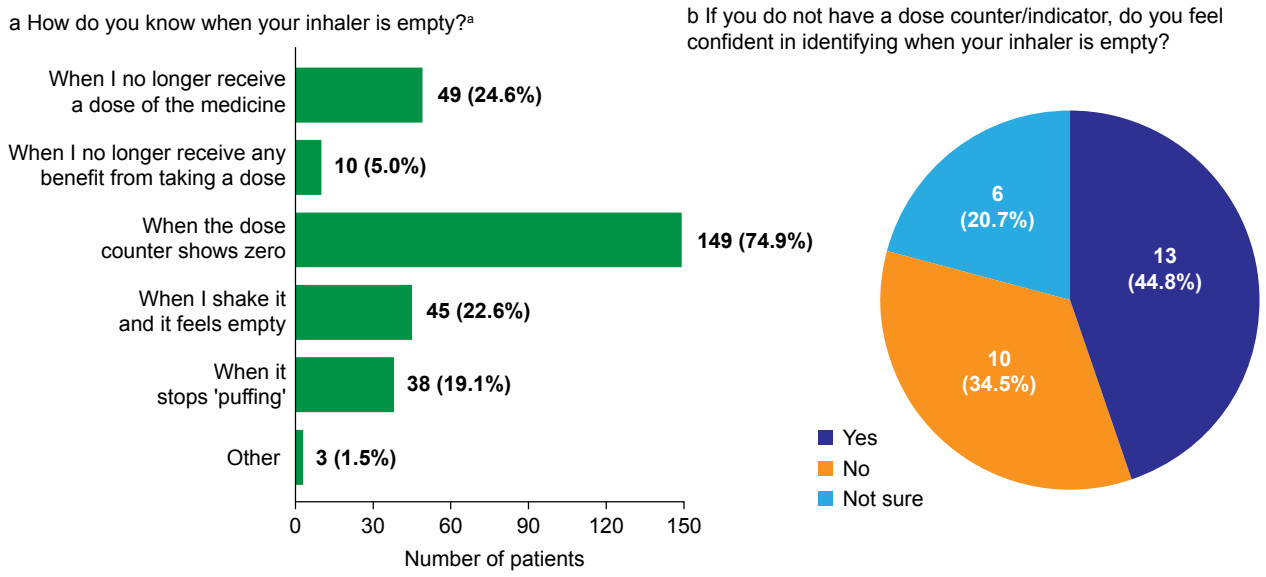


Figure 4 Respondent behaviour around determining when an inhaler is empty (a) and respondent confidence in identifying when an inhaler without a dose counter is empty (b), as reported in the online survey. Pie chart shows percentages of patients. [a]More than one response was permitted for this question.

dose counter indicated zero (online supplemental figure 1b); however, the remainder reported continuing to use it past zero or stopped using it despite not having a new inhaler. One-fifth of respondents (n=35; 20.6%) reported using the device beyond zero on the dose counter.

Among all 199 respondents (including those who were not using a device with a dose counter), the most commonly reported indicator that prompted disposal of an inhaler (figure 5a) was the dose counter showing zero (n=112; 56.3%). Other common indicators included no longer receiving a dose and/or benefit (n=84; 42.2%), the inhaler being out of date (n=37; 18.6%) and picking up a repeat prescription (n=35; 17.6%). Interestingly, over half of the respondents (n=105; 52.8%) disposed of their inhaler whether it was empty or not (figure 5b), and one-quarter (n=50; 25.1%) separated out the component

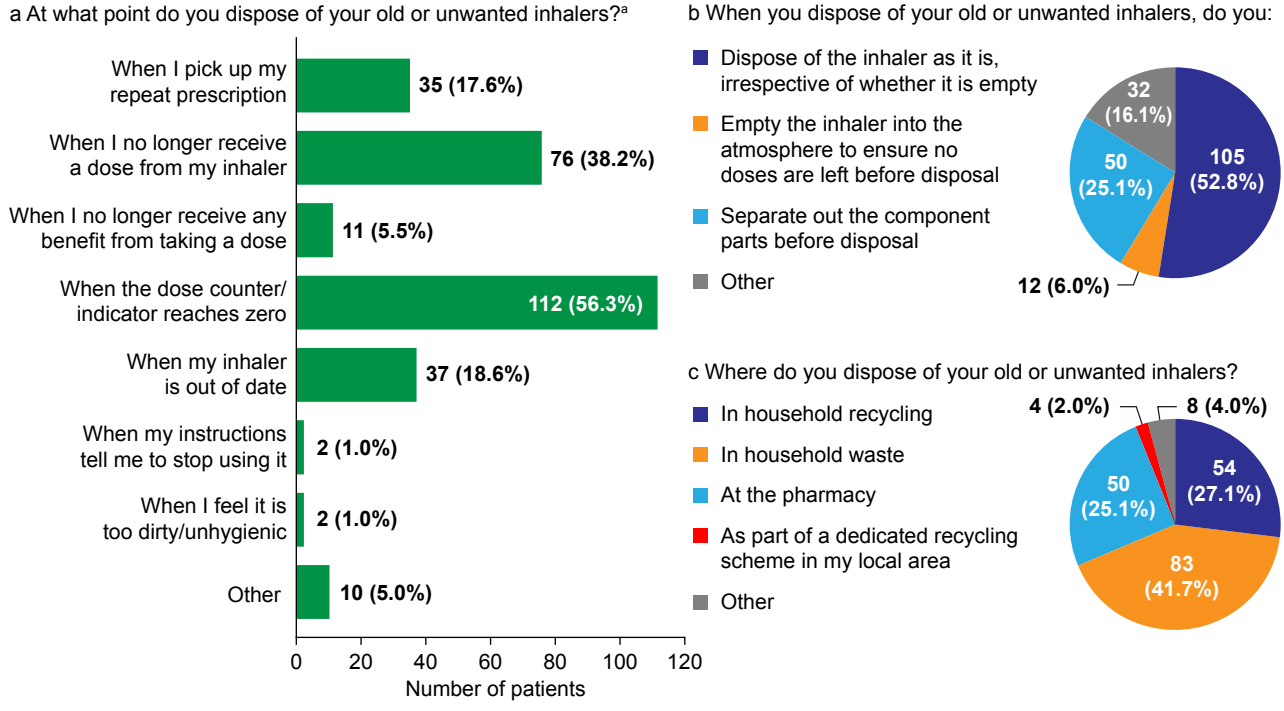


Figure 5 Respondent behaviour in determining when to dispose of old/unwanted inhalers (a) and respondent behaviour regarding disposal/recycling (b **and** c), as reported in the online survey. Pie chart shows percentages of patients. [a]More than one response was permitted for this question.

parts before disposal. Of the 168 survey participants with a SABA reliever inhaler, most (n=107; 63.7%) reported no difference regarding when they disposed of their device compared with their maintenance inhaler.

Almost half of the 199 respondents (n=83; 41.7%) reported disposing of their old and/or unwanted reliever and maintenance inhalers in general household waste, whereas 54 (27.1%) disposed of their inhalers in household recycling (figure 5c). Only one-quarter of those surveyed disposed of their inhalers at the pharmacy (n=50; 25.1%). When asked for any final thoughts relating to inhaler recycling, 70 respondents (35.2%) expressed a need for more information about recycling schemes, and 16 respondents proactively communicated that they had problems with the pharmacy accepting old inhalers.

DISCUSSION

Our findings highlight substantial variability in inhaler recycling behaviours among participants in the Take AIR recycling scheme. Ideally, all inhalers should be recycled or returned to a pharmacy for disposal, and it is preferable that this happens when the inhaler has been used up to the number of labelled doses. Inhalers recycled or discarded before this point will have unused medication doses, resulting in avoidable waste. Inhalers used beyond this point (overused) will have placed the patient at risk, as drug delivery falls significantly and somewhat unpredictably after complete utilisation.

In our study, pMDIs with an integrated dose counter were more likely to be sent for recycling within the optimal window (containing a formulation mass within 10% of the declared zero dose). Just over half of pMDIs with a dose counter were recycled at this point, while only one-quarter of pMDIs without a dose counter were recycled at this stage. This is consistent with previous studies,[13 14] demonstrating the importance of dose counters for patients to track the number of actuations, identify when the maximum labelled number of actuations has been reached and recognise when the inhaler should be replaced. Notably, the percentage of empty maintenance inhalers increased with ICS dose, potentially reflecting the increasing severity of the disease.

Disposing of an underused inhaler is particularly wasteful. We defined underused as inhalers that were recycled with more than 50% of doses remaining. Our analysis showed that just 5% of all pMDIs with a dose counter were returned underused compared with over one-third of devices without a dose counter. Integrated dose counters on pMDIs may, therefore, help to address the problems associated with inhaler underuse, such as medicine wastage, increased cost to the NHS and environmental damage, caused by patients disposing of inhalers with remaining medication and propellant.[28 29] Considering only those inhalers without dose counters, the proportion of returned underused maintenance inhalers was significantly lower than that of reliever inhalers, which is compatible with good patient adherence to the treatment regimen. Conversely, the higher proportion of underused reliever inhalers may reflect how these are used.[1 9 13 30] Prescribing of SABA inhalers is common in the UK and Europe[31]; as SABA reliever inhalers are typically used for symptom management,[32 33] patients are advised to use these devices intermittently, relying on the fast-acting relief to alleviate acute symptoms.[34] Patients may, therefore, not know how many SABA doses remain, and this is exacerbated by these devices typically lacking dose counters. The rapid relief of symptoms provided by reliever medications may be associated with over-reliance on them[35] and can in turn increase the risk of exacerbations and hospitalisation, particularly if their use contributes to reduced focus on achieving effective disease control with regular use of maintenance ICS medications.[36–38] A report published in February 2021 found that acute healthcare services in the UK were the largest contributor (from clinical activities) to NHS England's total GHG emissions.[39] Another study demonstrated that a history of severe or multiple COPD exacerbations can increase the carbon footprint of future healthcare resource utilisation and SABA prescribing by 50% for each year of follow-up.[40] Thus, addressing this over-reliance on SABA treatments and improving adherence to maintenance medication could help to improve patient outcomes and minimise the environmental burden.[41]

Patients may also be receiving unnecessary reliever devices in repeat prescriptions for their maintenance inhalers, regardless of how much of the reliever inhaler they may have used. Other potential factors for consideration are that patients may be prescribed multiple inhalers that they store at different locations, such as having one at home and another at work. They may be prescribed different devices for their maintenance and reliever inhalers, which creates further confusion about the number of doses remaining in an individual inhaler, especially for devices without dose counters.

It is concerning that a substantial proportion of pMDIs (for maintenance and reliever devices) were returned overused, with a remaining formulation mass amount >10% below zero. This pattern was observed regardless of the presence of a dose counter, although the greatest extent of overuse was among maintenance inhalers without a dose counter (44.5%). This shows that, while beneficial, the presence of dose counters does not guarantee that patients will recognise the remaining doses in a pMDI, underlining the importance of good patient and healthcare professional (HCP) training and ongoing education. Using an inhaler beyond its labelled number of doses could have serious implications for disease control and patient safety. The use of maintenance inhalers beyond the labelled number of doses may lead to poor disease control, with increased symptoms and increased risk of exacerbations, which is not ideal given that these are designed to keep the disease under long-term control and prevent symptoms from occurring.

In contrast, using reliever inhalers beyond the labelled number of doses can result in patients not receiving the immediate benefit required in critical situations, as these are intended for quick relief during acute asthma attacks. This potentially leads to an increased risk of preventable asthma-related death.[13]

These observations are further supported by results from the online survey. Among respondents using an inhaler without a dose counter, most stated that they were not sure or did not feel confident about when their inhaler was empty. The survey also highlighted that many respondents only regarded their inhaler as empty when it stopped 'puffing', felt empty on shaking, or when they were no longer receiving any dose or benefit from it. Although most respondents using an inhaler with a dose counter started using a new inhaler when the old one was empty, more than one in five respondents reported that they continued to use it after the counter had reached zero or stopped using it despite not having a new inhaler. This highlights the need for patients to improve their understanding of when their inhaler is running low ahead of time so that they can avoid using it once it has run out. This is particularly concerning because using an inhaler beyond its labelled number of doses may have serious effects on both disease control and patient safety. It has been shown that an important factor responsible for suboptimal treatment in patients with respiratory conditions is running out of medication or using devices beyond their labelled number of actuations, which may result in ineffective dosing of medication, leading to poor clinical outcomes.[13 18]

Almost half of the survey respondents were using pMDIs and one-quarter were using both pMDIs and DPIs. This is consistent with studies reporting that most inhalers prescribed in the UK are pMDIs.[42 43]

Respondents had limited awareness of appropriate disposal mechanisms for inhalers. This may lead to the disposal of inhalers with surplus medication and propellant remaining, with a resulting environmental impact.[28] A common theme among survey respondents was the need for more information about recycling schemes and the lack of knowledge about ways to recycle inhalers. Some respondents reported that they had problems with pharmacies accepting old inhalers. These results are consistent with previous surveys[24 27] and are unsurprising because the UK has limited schemes to collect and recover used and/or unwanted inhalers. Patients may also not be aware that community pharmacies are obliged to accept unwanted medicines from patients for safe disposal, as part of the NHS Community Pharmacy Contractual Framework. This is implemented by the regional NHS England team that makes arrangements for a waste contractor to collect the medicines from pharmacies at regular intervals.[26 28] Despite the lack of awareness around inhaler recycling, feedback from the published Take AIR pilot highlighted a high level of interest in inhaler recycling owing to environmental concerns and the need to make the scheme available nationally across the UK.[28] Future initiatives will require national stakeholders to collaborate in implementing a scheme for HCPs and patients that also reduces carbon emissions.[28]

The availability of population-based inhaler weighing data is a key strength of our analysis; nevertheless, this study does have some limitations. While our findings can provide valuable insights into usage patterns, the use of inhaler return data as a proxy for inhaler use may not accurately represent patient adherence or usage practices. Hence, these data should be interpreted with caution and complemented by direct assessments of patient adherence to obtain a more comprehensive understanding of inhaler use and its implications for health and environmental outcomes. The number of different products that the waste management company collected is limited and is for only one area of the UK, which limits the generalisability of our findings. The small number of LABA and SAMA pMDIs likely reflects the fact that these are not recommended as first line therapy for the management of asthma or COPD, thus the data for these device types may not be generalisable. Some pMDIs have in-use expiry dates and/or a requirement for disposal after being stored for a certain amount of time at room temperature; little information is available about how this may have affected inhaler recycling behaviour in the study. Finally, the online survey includes results from patients using pMDIs and/or DPIs, whereas the inhaler weighing analysis only refers to pMDIs. Therefore, it is possible that some of the results may reflect differences in patient behaviours between device types.

In conclusion, our analysis demonstrated remarkable variability in inhaler disposal behaviours, with a relevant proportion of inhalers not returned empty but either underused or overused, which can negatively affect both disease control and patient safety. This also has an impact on medicine wastage, healthcare-related costs and the environment. Findings from the online survey confirmed that there was a lack of knowledge about the number of therapeutic doses remaining in respondents' inhalers, and a limited awareness of appropriate recycling mechanisms. The presence of dose counters helps patients monitor the remaining doses in their inhalers; however, this does not necessarily mean that they will consistently recognise when the number of doses is running low. Therefore, it is crucial to emphasise the importance of ensuring how to accurately interpret and use dose counters. This includes educating the patients to track the number of doses remaining in inhalers without a dose counter by keeping a written tally and/or calculating the expected duration of an inhaler based on the labelled number of doses. Moreover, medicine wastage occurs when inhalers on a repeat prescription list are automatically ordered but not needed; thus, managing repeat SABA prescribing may also contribute to reducing the environmental impact of inhalers. Overall, our findings highlight that high-quality education, for both patients and HCPs, is required to optimise the management of

respiratory diseases and to reduce the environmental impact of inhalers.

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REFERENCES

1 Usmani OS. Choosing the right inhaler for your asthma or COPD patient. *Ther Clin Risk Manag* 2019;15:461–72.
2 NHS. Asthma - treatment, 2021. Available: https://www.nhs.uk/conditions/asthma/treatment [Accessed Oct 2024].
3 NHS. Chronic obstructive pulmonary disease (COPD) – treatment, 2023. Available: https://www.nhs.uk/conditions/chronic-obstructive-pulmonary-disease-copd/treatment [Accessed Oct 2024].
4 Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention. 2022. Available: https://ginasthma.org/wp-content/uploads/2022/05/GINA-Main-Report-2022-FINAL-22-05-03-WMS.pdf
5 Woodcock A, Beeh KM, Sagara H, *et al*. The environmental impact of inhaled therapy: making informed treatment choices. *Eur Respir J* 2022;60:2102106.
6 NHS. Prescription cost analysis - England - 2022-23, 2023. 2023. Available: https://www.nhsbsa.nhs.uk/statistical-collections/prescription-cost-analysis-england/prescription-cost-analysis-england-2022-2 [Accessed Oct 2024].
7 Emeryk AW, Sosnowski T, Kupczyk M, *et al*. Impact of inhalers used in the treatment of respiratory diseases on global warming. *Adv Respir Med* 2021;89:427–38.
8 O'Byrne PM. Clinical comparisons of inhaler systems: what are the important aspects? *J Aerosol Med* 1995;8 Suppl 3:S39–46; .
9 Usmani OS, Hickey AJ, Guranlioglu D, *et al*. The impact of inhaler device regimen in patients with asthma or COPD. *J Allergy Clin Immunol Pract* 2021;9:3033–40.
10 Munro S. Trends and future challenges in inhaled drug delivery. Life Sciences Knowledge Hub, 2021. Available: https://www.vectura.com/science/trends-and-future-challenges-in-inhaled-drug-delivery/ [Accessed Oct 2024].
11 Sule A, Sule S, Mullington T, *et al*. Comparison of in-vitro performance characteristics of salbutamol pMDI with low GWP propellant (HFA-152a) vs the current propellant (HFA-134a). Available: https://ddl-conference.com/wp-content/uploads/2022/11/21.Sule_.pdf [Accessed Oct 2024].
12 Conner JB, Buck PO. Improving asthma management: the case for mandatory inclusion of dose counters on all rescue bronchodilators. *J Asthma* 2013;50:658–63.
13 Kaur I, Aggarwal B, Gogtay J. Integration of dose counters in pressurized metered-dose inhalers for patients with asthma and chronic obstructive pulmonary disease: review of evidence. *Expert Opin Drug Deliv* 2015;12:1301–10.
14 Price DB, Rigazio A, Buatti Small M, *et al*. Historical cohort study examining comparative effectiveness of albuterol inhalers with and without integrated dose counter for patients with asthma or chronic obstructive pulmonary disease. *J Asthma Allergy* 2016;9:145–54.
15 Fullwood I, Evans T, Davies B, *et al*. Do you know when the inhaler is empty? *Arch Dis Child* 2022;107:902–5.
16 Rubin BK, Durotoye L. How do patients determine that their metered-dose inhaler is empty? *Chest* 2004;126:1134–7.
17 Scullion J. The nurse practitioners' perspective on inhaler education in asthma and chronic obstructive pulmonary disease. *Can Respir J* 2018;2018:2525319.
18 Price DB, Román-Rodríguez M, McQueen RB, *et al*. Inhaler errors in the CRITIKAL study: type, frequency, and association with asthma outcomes. *J Allergy Clin Immunol Pract* 2017;5:1071–81.
19 Schultz RK. Drug delivery characteristics of metered-dose inhalers. *J Allergy Clin Immunol* 1995;96:284–7.
20 Robinson J. Greener inhalers: are we setting the wrong targets. 2021. Available: https://pharmaceutical-journal.com/article/feature/greener-inhalers-are-we-setting-the-wrong-targets [Accessed Oct 2024].
21 Baron C. Is now the time to shake up the pMDI environment? *Pulm Nasal Drug Deliv* 2020;106:10–3.
22 Carroll WD, Gilchrist FJ, Horne R. Saving our planet one puff at a time. *Lancet Respir Med* 2022;10:e44–5.
23 NHS. The NHS long term plan. 2019. Available: https://www.longtermplan.nhs.uk/wp-content/uploads/2019/08/nhs-long-term-plan-version-1.2.pdf [Accessed Oct 2024].
24 Chebbout C, Murphy AC. Inhaler disposal: where do our patients put them when finished. Presented at East Midlands Thoracic Society Conference; 23 September 2021.
25 Roome C, Bush O, Steinbach I, *et al*. Reducing the environmental impact of inhaler use and disposal within paediatrics and the local community. *Arch Dis Child* 2021;106:A1–514.
26 Pharmaceutical Services Negotiating Committee. Disposal of unwanted medicines. 2023. Available: https://psnc.org.uk/services-commissioning/essential-services/disposal-of-unwanted-medicines [Accessed May 2024].
27 Sivarajasingam V. Understanding patients' knowledge of inhaler recycling. BJGP Life; 2021. Available: https://bjgplife.com/understanding-patients-knowledge-of-inhaler-recycling [Accessed Apr 2024].
28 Murphy A, Howlett D, Gowson A, *et al*. Understanding the feasibility and environmental effectiveness of a pilot postal inhaler recovery and recycling scheme. *NPJ Prim Care Respir Med* 2023;33:5.
29 Righton L. Six inhaler sustainability myths - and why they must be busted. 2021. Available: https://www.ondrugdelivery.com/wp-content/uploads/2021/11/126_2021_OctNov_Sustainability_Kindeva.pdf [Accessed Apr 2024].
30 Busse WW, Kraft M. Current unmet needs and potential solutions to uncontrolled asthma. *Eur Respir Rev* 2022;31:210176.

31 Wilkinson A, Menzies-Gow A, Sawyer M, *et al*. S26 An assessment of short-acting β2-agonist (SABA) use and subsequent greenhouse gas (GHG) emissions in five European countries and the consequence of their potential overuse for asthma in the UK. British Thoracic Society Winter Meeting, Wednesday 17 to Friday 19 February 2021, Programme and Abstracts; February 2021:A1–256.
32 Durrant N. Salbutamol: hero or villain? *Paediatr Child Health (Oxford)* 2023;33:97–103.
33 Janson C, Menzies-Gow A, Nan C, *et al*. SABINA: an overview of short-acting β_2-agonist use in asthma in European countries. *Adv Ther* 2020;37:1124–35.
34 Loh ZC, Hussain R, Balan S, *et al*. Perceptions, attitudes, and behaviors of asthma patients towards the use of short-acting β2-agonists: a systematic review. *PLoS One* 2023;18:e0283876.
35 Kaplan A, Mitchell PD, Cave AJ, *et al*. Effective asthma management: is it time to let the AIR out of SABA? *J Clin Med* 2020;9:921.
36 Bloom CI, Cabrera C, Arnetorp S, *et al*. Asthma-related health outcomes associated with short-acting β_2-agonist inhaler use: an observational UK study as part of the SABINA global program. *Adv Ther* 2020;37:4190–208.
37 Suissa S, Ernst P, Benayoun S, *et al*. Low-dose inhaled corticosteroids and the prevention of death from asthma. *N Engl J Med* 2000;343:332–6.
38 O'Byrne PM, Jenkins C, Bateman ED. The paradoxes of asthma management: time for a new approach? *Eur Respir J* 2017;50:1701103.
39 Tennison I, Roschnik S, Ashby B, *et al*. Health care's response to climate change: a carbon footprint assessment of the NHS in England. *Lancet Planet Health* 2021;5:e84–92.
40 Bell J, Ding B, De Nigris E, *et al*. Greenhouse gas emissions associated with copd care in the uk: results from sherlock carbon. ERS International Congress 2021 Abstracts; 5 September 2021.
41 NHS. Annex B – investment and impact fund (IIF): 2021/22 and 2022/23. Available: https://www.england.nhs.uk/wp-content/uploads/2021/08/B0828-iii-annex-b-investment-and-impact-fund-21-22-22-23.pdf [Accessed Mar 2024].
42 Attar-Zadeh D, Lewis H, Orlovic M. Health-care resource requirements and potential financial consequences of an environmentally driven switch in respiratory inhaler use in England. *J Health Econ Outcomes Res* 2021;8:46–54.
43 Lavorini F, Corrigan CJ, Barnes PJ, *et al*. Retail sales of inhalation devices in European countries: so much for a global policy. *Respir Med* 2011;105:1099–103.