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Responsible Prescribing and Dispensing: I. Sustainable COPD Inhalers

The Centre for Sustainable Healthcare

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Executive Summary

Introduction

The National Health Service Commissioning Guides[1] give the population benchmark for the number of people with diagnosed chronic obstructive pulmonary disease (COPD) as 1.6% of those 18 years of age or older. With a population of over 62 million, this puts the likely number of people in the UK with diagnosed COPD at close to 800,000. Over twice this many people are thought to have undiagnosed COPD[2].

COPD is demanding of healthcare resources. It is one of the most common causes of death in England[3] and is the fifth largest cause of emergency hospital admissions - in 2009/10 there were more than 100,000 emergency admissions to hospital in England for exacerbations of COPD. COPD also accounts for more than 750,000 'bed days' each year in hospitals in England[4].

Globally, the World Health Organisation estimates 65 million people have moderate to severe chronic obstructive pulmonary disease and that 5% of all deaths are related to COPD. It is estimated that COPD will become the third leading cause of death worldwide by 2030[5].

Over the next 20 years, medical costs related to COPD will total approximately $832.9 billion in the United States, according to a study presented at the American Thoracic Society International Conference. The study is part of the Burden of Obstructive Lung Disease (BOLD) initiative, which is designed to examine the prevalence and burden of COPD around the world[6].

Respiratory inhalers are a key part of respiratory care. In 2001, for example, the total number of community dispensed prescriptions for inhaled therapy in England was around 33 million, with a net ingredient cost in excess of £442 million [ref]

The market research group Kalorama estimated that, driven by an increased incidence of respiratory disease and an aging population, the world respiratory market was over $44 billion in 2011. Moreover they concluded that about 77% of this market is respiratory inhalers and associated therapeutic pharmaceuticals (see Kalorama Information's latest research report, World Market for Respiratory Devices).

[1] http://publications.nice.org.uk/services-for-people-with-chronic-obstructive-pulmonary-disease-cmg43/commissioning-services-for-people-with-chronic-obstructive-pulmonary-disease

[2] These figures are supported by The Healthcare Commission report 'Clearing the air' which estimated that there are 900,000 people diagnosed with COPD in the UK and 2 million people with undiagnosed COPD.

[3] Office for National Statistics (2009) Statistical Bulletin: Death registrations by cause in England and Wales. Office for National Statistics.

[4] The NHS Information Centre (2010) Hospital episode statistics. Leeds: The NHS Information Centre for health and social care.

[5] http://www.who.int/respiratory/copd/burden/en/index.html

[6] http://www.medicalnewstoday.com/releases/44235.php

Together these figures show that COPD is a major threat to health both nationally and internationally, and that it exerts a major strain on healthcare and social resources. Moreover the inhalers used to treat COPD by the sheer weight of the numbers involved impact on the sustainability of this form of care. As James Smith and Richard Tiner point out in their letter to the Lancet[7]

> ***The propellants used in metered-dose inhalers are hydrofluorocarbons (HFCs). These are potent greenhouse gases with global warming potential of, in many cases, more than 1000 times that of carbon dioxide. (page 982)***

Smith and Tiner go on to conclude that there is "insufficient recognition…of the importance of environmental sustainability when selecting an inhaler device".

The purpose of the present paper is to address the lack of recognition by reviewing the factors influencing sustainability of inhaler use for treating COPD.

[7] Smith J, Tiner R. Aerosol drug delivery: developments in device design and clinical use. The Lancet, Volume 378, Issue 9795, Page 982, 10 September 2011.http://www.thelancet.com/journals/lancet/article/PS0140-6736(11)61445-1/fulltext#bib2

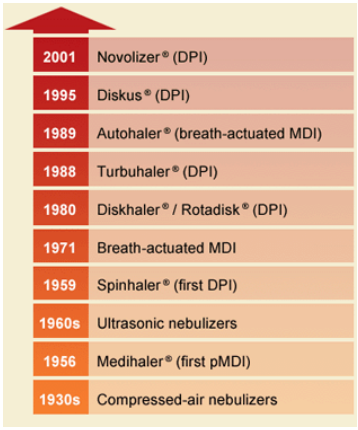
Respiratory Inhalers

The bronchodilators and corticosteroids used in the maintenance therapy of chronic COPD are best delivered through inhalation. Small doses of drugs are delivered direct to their site of action, leading to a rapid onset of action and a low incidence of side effects.

Although a variety of inhalers are on the market, there are 2 main types used with COPD (and asthma). These are:

- pressurized metered-dose inhalers (pMDIs), and
- dry powder inhalers (DPIs),

The advantages and disadvantages of the different varieties of inhaler are listed in Annex 1 (from Newman 2005). The "press-and-breathe" pressurised metered dose inhaler (pMDI) was introduced in 1956 and is generally credited as being the first inhaler device. The drug is dissolved or suspended in the propellant under pressure. When activated, a valve system releases a metered volume of drug and propellant. Spacer chambers can be attached to pMDIs to make them easier to use. Other devices include breath actuated pMDIs (BA-pMDI) such as Autohaler® and Easibreathe®. They enable the patient to prime the inhaler which is then only activated when the patient takes a breath, avoiding the need to coordinate pressing and breathing.



From:http://www.admit-online.info/en/inhalation-systems/development-history/

Dry powder inhalers (DPI) such as Turbohaler®, Diskhaler®, Accuhaler® and Clickhaler® provide an alternative to MDIs. These inhalers are also breath activated: the powdered drug is dispersed into particles by the inhalation.

The DPIs may require some procedure to allow a measured dose of powder to be ready for the patient to take. The medication is commonly held either in a capsule for manual loading or a proprietary form from inside the inhaler. Once loaded or actuated, the operator puts the mouthpiece of the inhaler into their mouth and takes a deep inhalation, holding their breath for 5-10 seconds. The dose that can be delivered is typically less than a few tens of milligrams in a single breath since larger powder doses may lead to coughing.

Most DPIs rely on the force of patient inhalation to entrain powder from the device and subsequently break-up the powder into particles that are small enough to reach the lungs. For this reason, insufficient patient inhalation flow rates may lead to reduced dose delivery and incomplete disaggregation of the powder, leading to unsatisfactory device performance.

Thus, most DPIs have a minimum inspiratory effort that is needed for proper use and it is for this reason that such DPIs are normally used only in older children and adults.

MDI Propellants

The original MDIs contained chlorofluorocarbons (CFCs) as a propellant. With the implementation of the 1987 Montreal Protocol (see sidebar) and the phasing out of CFCs, newer CFC-free inhaler devices using hydrofluorocarbons (HFCs) were developed. The two alternatives to CFC propellants for pharmaceutical aerosols are hydrofluorocarbon (HFC) 134a (also known as hydrofluoroalkane (HFA) 134a or 1,1,1,2-tetrafluoroethane), and HFC-227ea (HFA-227ea or 1,1,1,2,3,3,3- heptafluoropropane). In the view of the International Pharmaceutical Aerosol Consortium (IPAC), HFC-134a and HFC-227ea are the only viable alternatives to CFCs in MDIs (IPAC, 2002).

Montreal Protocol

The Vienna Convention for the Protection of the Ozone Layer and its Montreal Protocol on Substances that Deplete the Ozone Layer are dedicated to the protection of the earth's ozone layer. With 196 parties, they are the most widely ratified treaties in United Nations history, and have, to date, enabled reductions of over 97% of all global consumption of controlled ozone depleting substances.[1]

These hydrofluorocarbons are among the six greenhouse gases to be controlled in the Kyoto Protocol 'basket of gases'. They are produced commercially mainly for use in refrigeration and insulating foam. The Global Warming Potentials of HFC-134a and HFC-227ea are respectively 1300 and 3500 times that of CO2 (http://www.epa.gov/ozone/geninfo/gwps.html).

EC Regulation No 842/2006 on Certain Fluorinated Greenhouse Gases (DEFRA 2006[8])

There has been uncertainty regarding the use of HFCs since the adoption of the Kyoto Protocol. The Government recognises that the successful phaseout of ozone-depleting substances under the Montreal Protocol is being achieved, and accepts that HFCs are necessary to replace ozone-depleting substances in some applications. In view of this, the Government's position on HFCs is as follows:

- HFCs should only be used where other safe, technically feasible, cost effective and more environmentally acceptable alternatives do not exist;
- HFCs are not sustainable in the long term – the Government believes that continued technological developments will mean the HFCs may eventually be able to be replaced in the applications where they are used;
- HFC emission reduction strategies should not undermine commitments to phaseout ozone depleting substances under the Montreal Protocol; and
- HFC emissions will not be allowed to rise unchecked.

[8] http://www.bis.gov.uk/files/file31943.pdf

DEFRA Report: HFC consumption and emissions forecasting

Source:http://archive.defra.gov.uk/environment/quality/air/fgas/documents/fgas-hfc-forecasting.pdf

DEFRA (September 2010) commissioned a report on current levels of HFC consumption and a forecast of consumption to 2050[9]. The forecast included two scenarios: Business as Usual (BaU) and Reduction (Low HFC).. The report addresses all sectors where HFCs are licensed for use, including MDIs for both asthma and COPD care.

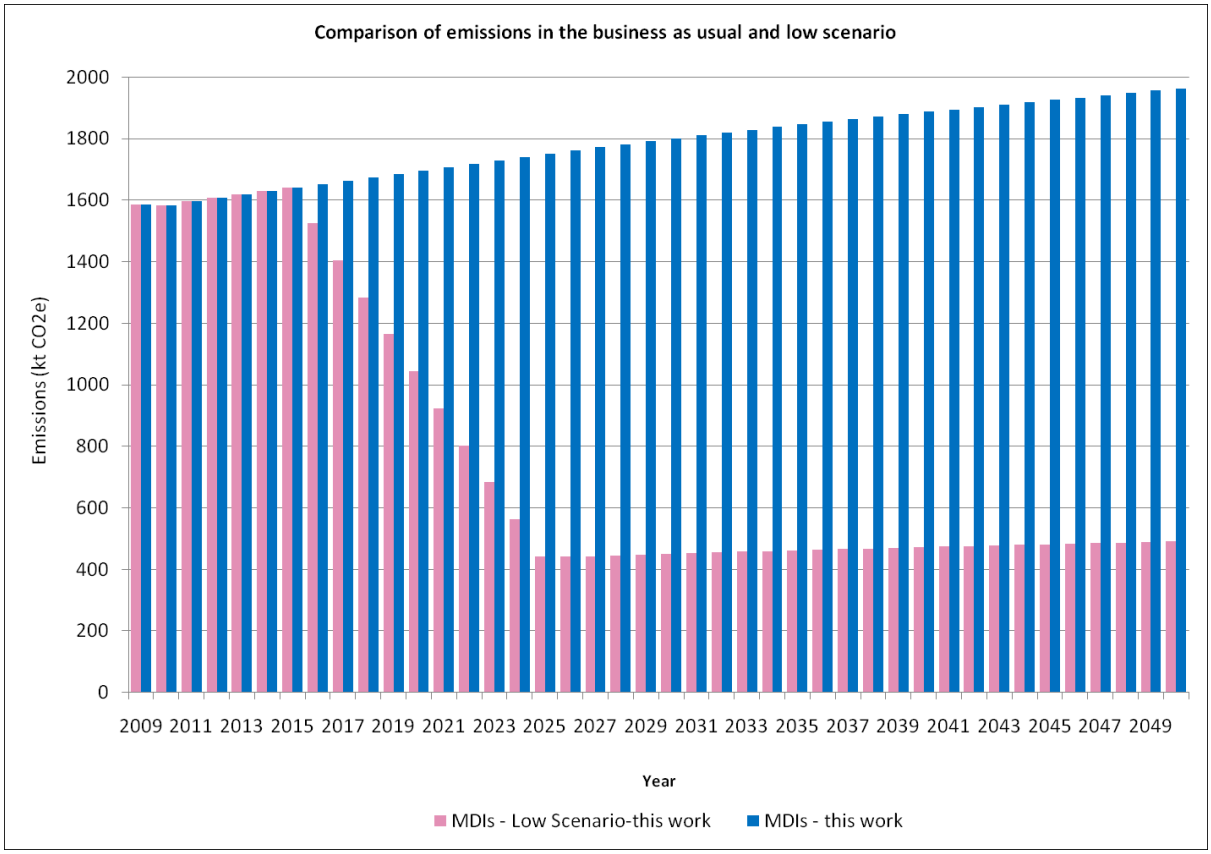
Business as usual scenario (BaU)

The Business as Usual scenario forecasts that HFC emissions from inhalers will increase from 2010 onwards due to the increase in the population in the UK. The report concludes that it is unlikely that alternative MDI propellants will be developed, and that only a move to DPIs or another alternative device would reduce HFC emissions from this sector.

Low HFC emissions scenario (Low HFC)

The "Low HFC" emissions scenario assumes the use of dry powder inhalers (DPIs) increases from 2015 to 2025 linearly. In addition the authors made a conservative assumption that 25% of the population that currently use inhalers will not be suitable for DPIs. Use of DPIs and MDIs are then kept constant from 2025-2050. The increase in emissions from 2025-2050 is due to population increase. Emissions lower by 1,308 kt CO2 eq. (75 %) in 2025 in the "low HFC emissions" scenario relative to the "BaU" scenario (from Table ES1).

[9] Okamura S, Ashford P, Jackson J, Watterson J. HFC consumption and emissions forecasting. Harwell: AEA Technology, 2011. http://archive.defra.gov.uk/environment/quality/air/fgas/documents/fgas-hfc-forecasting.pdf.



The Low-HFC scenario shows what the CO2e emission projections would look like if there was a push for the use of DPIs or the development of other non-HFC alternatives. Below is a list of the assumptions used in the DEFRA Low-HFC model (paraphrased from the report):

- The push for DPIs or other replacements does not impact on the number of MDIs used in the UK until 2015. This takes into account the fact that it will take time to change the prescription behaviour of doctors and for patients to adapt to DPIs.
- The time taken for all patients to make a transition to available alternatives is assumed to be 10 years.
- 25% of the people will remain reliant on the use of MDIs due to no replacement being available since DPIs are an alternative to MDIs not a replacement.

Based on the above assumptions, the emissions in the "low HFC emissions" scenario are lower by 1,308 Mt CO2 eq. (75%) in 2025 compared to the BaU scenario.

As a point of comparison, the estimated carbon footprint of the NHS is 20 million tonnes of CO2e. MDI propellants are the equivalent of 6.5% of the NHS footprint.

COPD HFC consumption and emission forecasting

The DEFRA report included MDI use for both asthma and COPD. In the following analysis we have replicated the DEFRA forecasts using data on COPD alone.

COPD HFC Algorithm

We have used the values in the table below to calculate COPD-specific consumption and emission forecasts. Like DEFRA, we have modelled two scenarios: Business as usual (BaU) and HFC and reduction (Low-HFC).

Parameter	Value	Notes
UK population	62 million	
UK population growth rate	0.6%	Office of Nat'l Stats
COPD Incidence	1.6%	From NICE Guidance
% COPD patients using pMDI inhalers	75%	From sales figures
% Number of pMDI inhalers/patient	12	1 per month on average
No. pMDI inhalers prescribed for COPD	Not yet obtained	Not yet obtained
HFC content per inhaler	17g	From DEFRA report

COPD Business as usual scenario (BaU)

The BaU scenario assumes HFC emissions will increase over time as the population increases. We have used the Office of National Statistics estimate of 0.6% per year population growth for 2010 to 2050 to produce the model. There is also an argument for including an increased incidence of COPD, but we have not included such an assumption in the current scenario. The BAU scenario suggests that by 2030 over 200,000 tonnes of CO2e per year would be attributable to HFC emissions from MDI inhalers used by COPD patients in the UK. By 2050, 250,000 tonnes of CO2e would be attributable to COPD inhalers.

COPD Reduction scenario (Low HFC)

The reduction scenario assumes that it will take 5 years to change UK prescribing patterns from MDs to PDIs. This is shown by the 2012 – 2017 increase in CO2e emissions. From 2018 to 2030 we have modeled a 75% reduction in MDI prescriptions.

Figure 5. HFC emissions using the DEFRA scenario where MDI usage initially goes up with increased incidence in the population, but then the shift from MDIs to DPIs comes into effect. The graph shows the effects of a shift from 75% MDI use to 25% MDI use in 2030. If achieved, this would save almost 1.5 Million tonnes of CO2e (1.5MtCO2e) in the years 2017 to 2030. Across the full range, from 2017 to 2050, over 5 MtCO2e would be saved relative to the business as usual scenario. These figures would be even larger if we could achieve a target of less than 25% for COPD patients using MDI inhalers.

MDIs versus DPIs

Moving patients from MDIs to DPIs is viable only if the quality of patient care is not jeopardised. Here we look at 3 issues that relate to inhaler type and quality of COPD care:

1. Prescribing patterns in Europe as reflected by sales of different inhalation devices across Europe.
2. Clinical effectiveness of the different types of inhalers.
3. Patient compliance and cost-effectiveness of different inhalers.

Sales of Inhalation Devices in Europe

http://www.admit-online.info/fileadmin/materials/pdf/posters/Poster_Lavorini_ERS_2010.pdf

There is considerable variation in the sales and by implication prescribing of pMDI and DPI inhalers across Europe. pMIDs in the UK represented 75% of sales, while in Sweden DPIs predominated with only about 10% of sales from pMDIs (see Figure 1).

It seems likely that the differences in sales between countries are due to differences in in government or insurance group guidance and reimbursement policy, and that there is little difference in the clinical effectiveness of different types of inhalers.

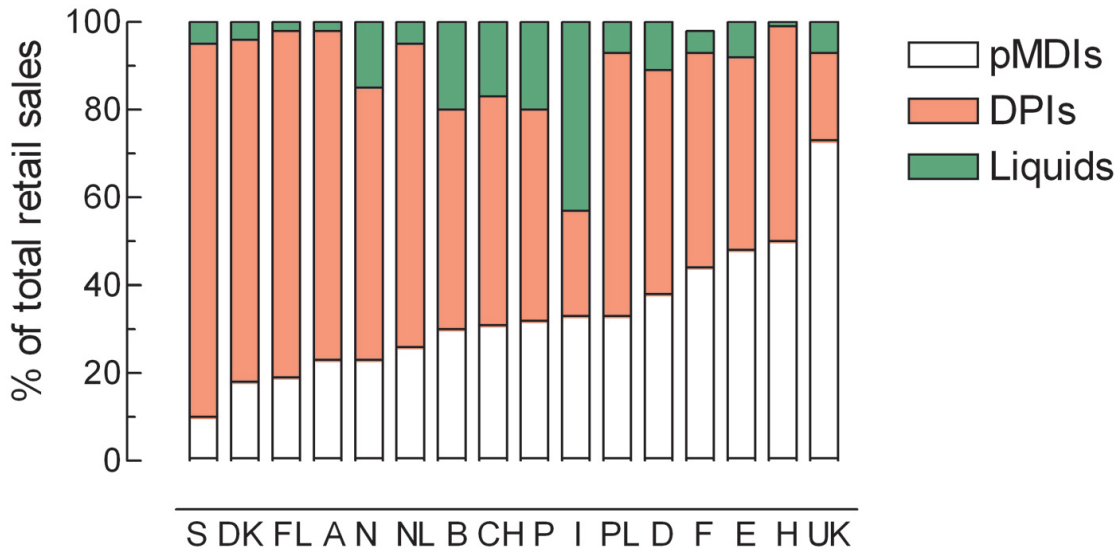
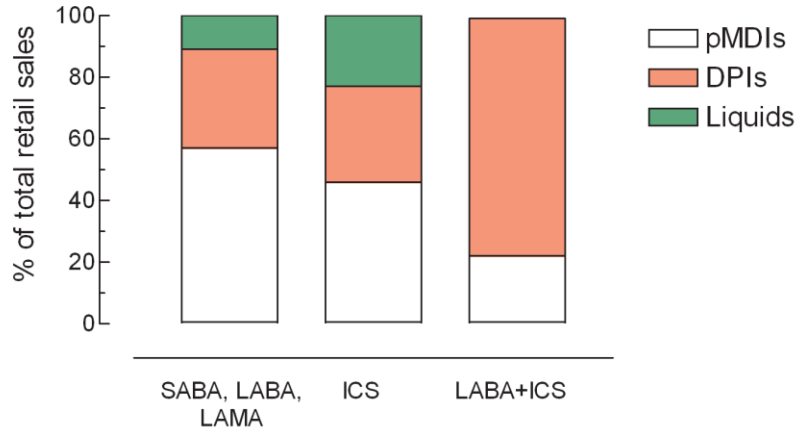


Figure 1. Retail sales of inhalation devices, expressed as percentages of the total retail sales, in 16 European countries in the time period 2002-2008. A, Austria; B, Belgium; CH, Switzerland; DK, Denmark; E, Spain; F, France; F, Finland; H, Hungary; I, Italy; D, Germany; N, Norway; NL, The Netherlands; P, Portugal; PL, Poland; S, Sweden; UK, United Kingdom



In the case of retail sales of inhalation devices delivering bronchodilators, the pMDI is the most frequently used inhaler device. In contrast, retail sales of DPIs are similar to those of pMDIs when considering ICS, or higher in the case of combinations of bronchodilators and ICS (Figure 2).

Clinical effectiveness of DPIs versus MDIs

There have been numerous randomised control trials and several systematic reviews examining the clinical effectiveness of different types of inhalers delivering different types of drugs for different patient groups. The results of these reviews are almost unanimous in concluding that the main inhaler types do not differ and that all are clinically effective.

For example, a review of 394 RCTs assessing inhaled corticosteroid, β_2–agonist, and anticholinergic agents delivered by an MDI, an MDI with a spacer/holding chamber, a nebulizer, or a DPI, for example, concluded

> ***None of the pooled metaanalyses showed a significant difference between devices in any efficacy outcome in any patient group for each of the clinical settings that was investigated. The adverse effects that were reported were minimal and were related to the increased drug dose that was delivered. Each of the delivery devices provided similar outcomes in patients using the correct technique for inhalation.***[10]

Other reviews include:

Shepherd J, Rogers G, Anderson R, Main C, Thompson-Coon J, Hartwell D, Liu Z, Loveman E, Green C, Pitt M, Stein K, Harris P, Frampton GK, Smith M, Takeda A, Price A, Welch K, Somerville M.Systematic review and economic analysis of the comparative effectiveness of different inhaled corticosteroids and their usage with long-acting beta2 agonists for the treatment of chronic asthma in adults and children aged 12 years and over.Health Technol Assess. 2008 May;12(19):iii-iv, 1-360. http://www.ncbi.nlm.nih.gov/pubmed/18485271

A comparison of the costs associated with each combination therapy indicates that at low dose FP/SAL delivered via a pMDI is currently the cheapest combination inhaler but only marginally cheaper than BUD/FF delivered as a DPI. At higher doses, both the FP/SAL combination inhalers (PMDI and DPI) are marginally cheaper than BUD/FF (DPI)

Ram FSF, Brocklebank DDM, Muers M, Wright JJ, Jones P. Pressurised metered-dose inhalers versus all other hand-held inhalers devices to deliver bronchodilators for chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2002, Issue 1. Art. No.: CD002170. DOI: 10.1002/14651858.CD002170.

[10] Dolovich MB, Ahrens RC, Hess RD, Anderson P, Dhand R, Rau JL, Smaldone GC, Guyatt G. Device selection and outcomes of aerosol therapy: evidence-based guidelines. 2005. Chest; 127 (1): 335-37. http://chestjournal.chestpubs.org/content/127/1/335.full.html

Brocklebank D, Ram F, Wright J, Barry P, Cates C, Davies L, *et al*. Comparison of the effectiveness of inhaler devices in asthma and chronic obstructive airways disease: a systematic review of the literature. *Health Technol Assess* 2001;**5**(26).

Gellerv DE. Comparing Clinical Features of the Nebulizer, Metered-Dose Inhaler, and Dry Powder Inhaler. Respir Care 2005;50(10):1313–1321. © 2005 Daedalus Enterprises.

Compliance and cost effectiveness

In most healthcare systems PDIs cost more than MDIs on a per-dose basis (see Annex 3). This cost difference combined with a lack of evidence of a difference in clinical effectiveness has led to recommendations such as that in an influential Health Technlogy Assessment review[11] which concluded that

> ***The 28-day cost of pMDIs is lower than dry powder inhalers and other inhaler devices. Both pMDIs and dry powder inhalers are cheaper than nebulisers. As there are no significant differences in patient outcomes, a stepped approach to treatment would seem justified. pMDIs (with or without a spacer), or the cheapest inhaler device the patient can use adequately, should be prescribed as first-line treatment in all adults and children with stable asthma or COPD requiring inhaled medication.***

However review authors and critics alike point out that clinical trials are unusual situations because participants are given extensive training on the different inhaler devices and in some cases those unable to use the device correctly are excluded from the study. Observational studies suggest that patients often make errors when using inhalers and that some of these errors result in a failure of the inhaler to deliver the drug (see Annex 2).

As the Aerosol Drug Management Improvement Team note on their web site, *the most expensive inhaler is that which is not used correctly*[12]*.* Usage errors raise the possibility that in practice inhalers are not equally effective.

One report on Inhaled Corticosteroids (ICS) for the control of asthma, for example, reviewed over 55,000 cases in the General Practice Research Database and concluded

> ***…for patients initiating ICS, BAIs were more effective than MDIs most of the time, … DPIs were consistently more effective and expensive than MDIs, These findings suggest that the real world effectiveness of ICS inhalers may vary and that the selection of inhaler device for patients with asthma should take into consideration not only initial cost of the device itself but also the subsequent health care resource costs.[13]***

[11] Brocklebank D, Ram F, Wright J, Barry P, Cates C, Davies L, *et al*. Comparison of the effectiveness of inhaler devices in asthma and chronic obstructive airways disease: a systematic review of the literature. *Health Technol Assess* 2001;**5**(26)

[1212] Strapline of the Aerosol Drug Management Improvement Team (ADMIT). http://www.admit-online.info/en/why-admit/

[13] Kemp L, Haughney J, Barnes N, Sims E, et al. Cost-effectiveness analysis of corticosteroid inhaler devices in primary care asthma management: A real world observational study ClinicoEconomics and Outcomes Research 2010:2 75–85. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3116791/

Similarly, a study including 445 asthma patients in the Canadian healthcare system found DPIs to be more cost effective when hospital costs were included in the analysis:

> ***From the analysis, we concluded that the effectiveness of treatment (measured as the number of exacerbations and days with exacerbation) was significantly better for patients treated via Turbuhaler than via a pMDI ($p = 0.03$). Furthermore, the total annual costs of treatment were, on average, $Can331 less ($p < 0.01$) for patients using Turbuhaler than for those using a pMDI (mainly due to lower costs for hospitalisation and medication).[14]***

[14] Liljas B, Ståhl E, Pauwels RA. Cost-effectiveness analysis of a dry powder inhaler (Turbuhaler) versus a pressurised metered dose inhaler in patients with asthma. PharmacoEconomics, 1997; 12(2 Pt 2):267-277.

NICE Guidelines

The National Institute for Health and Clinical Excellence (NICE) provides extensive guidance on the diagnosis and treatment of COPD. NICE Guidelines are not particularly prescriptive when it comes to drug delivery systems for COPD (see text box).

NICE clinical guideline 101: Chronic obstructive pulmonary disease

Delivery systems used to treat patients with stable COPD

Most patients – whatever their age – are able to acquire and maintain adequate inhaler technique given adequate instruction. The exception to this is that those with significant cognitive impairment (as a guideline, those with a Hodkinson Abbreviated Mental Test Score of 4 or less) are unable to use any form of inhaler device. In most patients, however, a pragmatic approach guided by individual patient assessment is needed in choosing a device.

Inhalers

In most cases bronchodilator therapy is best administered using a hand-held inhaler device (including a spacer device if appropriate). [2004]

If the patient is unable to use a particular device satisfactorily, it is not suitable for him or her, and an alternative should be found. [2004]

Inhalers should be prescribed only after patients have received training in the use of the device and have demonstrated satisfactory technique. [2004]

Patients should have their ability to use an inhaler device regularly assessed by a competent healthcare professional and, if necessary, should be re-taught the correct technique. [2004]

Life Cycle of Inhalers

The NHS Sustainable Development Unit is in the process of developing industry standards for assessing life-cycle footprints of pharmaceutical agents[15] Given that the standards have not yet been agreed we thought it inappropriate to attempt a life-cycle analysis of inhalers. We do however recognize that it is useful to separate two basic activities, namely (1) preparation of the active ingredient and (2) the manufacturing and life-cycle of the device used to deliver the agent.

SDU provide a *Sample Process Map for Application Devices (Inhaler)* as part of the consultation document (Figure 4.12 page 87), as well as examples of determining the footprint of the inhaler API salbutamol sulphate (page 40),

Although it may be possible to build up a database of life-cycle footprints of inhalers and their component parts, it is clear for the time-being at least that we will have to rely on the pharmaceutical industry to provide the primary data on APIs and Application devices.

[15] http://www.sdu.nhs.uk/sd_and_the_nhs/Pharmaceuticals-and-Medical-Devices.aspx

Recycling

The “Complete the Cycle” take-back scheme run by GlaxoSmithKline (GSK) in conjunction with Terracycle UK appears to be very successful and the only one of its kind. A recent news piece[16] from 24 April 2012 reported the scheme is operating now in 265 pharmacies in Scotland, England, and all of Wales.

GSK[17] reports that 62,175 inhalers have been recovered since they started to the end of June 2012. Moreover they estimate that based on the average amount of gas left in the cans, the scheme has prevented 436 tonnes of CO2e from being released into the environment. This equates to 76 journeys around the world in a VW Golf with a 1.4 litre engine.

It is estimated that 73 million inhalers were used in the UK in the 12 months to the end of May 2012.

[16] http://www.dumbartonreporter.co.uk/news/thisweek/articles/2012/04/24/427690-inhaler-recycling-scheme-launched/

[17] Personal communication from Mark Rhodes 24 July 2012.

Conclusions and recommendations

Given the evidence reviewed above we conclude that the following are the key actions needed to reduce the negative impact of COPD care.

1. Accelerate the shift from MDI to DPI inhalers

The only viable alternative to perpetuating HFC intensive MDI inhalers is to shift patients to DPI inhalers. Given the global warming potential of MDI propellants the first action recommended by the Sustainable Respiratory Care project is to accelerate the shift from MDI to DPI products. The following projects would support this initiative:

1. Determine the maximum proportion of COPD patients that could be using DPIs. Conversely, for how many competent inhaler users are DPI devices not clinically appropriate?
2. Create a programme to raise awareness among clinicians & patient groups of the carbon impact and global warming potential of using MDI inhalers.
3. Influence guidelines/formularies.
4. Determine the life-cycle carbon footprints of MDI and DPI respiratory inhalers.
5. Model the carbon and monetary cost-benefits of a (X%) shift from MDI to DPIs.

2. Improve inhaler usage technique

Waste is never 'green' and if people do not use inhalers properly there is waste from use of inhaler components and hospital costs more generally.

1. Improve targeting and appropriateness of inhaler prescriptions.
2. Investigate ways of ensuring good inhaler technique.
3. Documenting patient's respond to the potential choice between MDI and PDI given all the information about their impacts.
4. Determine the Carbon and £ impact of good vs poor inhaler technique, regardless of device. The alignment with clinical imperative is that better, more effective care is still better even if patients 'can't' use low carbon technology

3. Increase inhaler recycling

Recycling is something that will engage patients, their families and staff.

1. Develop case study/business case for recycling programmes
2. Engage pharmacies and companies to set up programmes
3. Promote to patients
4. Increase uptake of medicines use reviews in community pharmacy
5. How much propellant remains in the canister when inhalers are thrown away or recycled? Does this differ between inhalers and is this waste a function of inhaler technique?
6. What are the carbon and £ cost-benefits of inhaler recycling programmes?

ANNEX 1. Advantages and disadvantages of different inhaler devices

Adapted from: Newman SP. Inhaler treatment options in COPD. *Eur Respir Rev,* 2005: vol. 14 no. 96; 102-108. doi: 10.1183/09059180.05.00009605.
http://err.ersjournals.com/content/14/96/102.full

Device	Advantages	Disadvantages
"Press and breathe" pMDI	Compact	Contains propellants
	Portable	Not breath-actuated
	100+ doses	Many patients cannot use it correctly (*e.g.* coordination difficulties, "cold Freon" effect)
	Convenient	Usually low lung deposition/high oropharyngeal deposition
	Quick to use	
	Relatively cheap	
	Cannot contaminate contents	
Breath-actuated pMDI	Compact	Contains propellants
	Portable	"Cold Freon" effect
	100+ doses	Usually low lung deposition/high oropharyngeal deposition
	Convenient	
	Quick to use	
	Breath-actuated (no coordination needed)	
	Cannot contaminate contents	
"Press and breathe" pMDI plus spacer	100+ doses	Contains propellants
	Quick to use	Not very portable or convenient
	Easier to coordinate	Not breath-actuated
	Tidal breathing often OK	Plastic spacers may acquire static charge
	Less oropharyngeal deposition	

	Usually higher lung deposition than a pMDI	
DPI	Compact	Work poorly if inhalation is not forceful enough
	Portable	Many patients cannot use them correctly (*e.g.* capsule handling problems for elderly)
	Convenient (multi-dose devices)	Most types are moisture sensitive
	Quick to use	
	Breath-actuated (no coordination needed)	
	Usually higher lung deposition than a pMDI	
	Do not contain propellants	

ANNEX 2. Correct techniques for different types of inhaler and the errors patients are known to make

Adapted from: Newman SP. Inhaler treatment options in COPD. *Eur Respir Rev,* 2005: vol. 14 no. 96; 102-108

Correct techniques for different types of inhaler and the errors patients are known to make

Device	Correct technique	Errors in technique
"Press and breathe" pMDI	Remove mouthpiece cap	Failure to remove mouthpiece cap
	Shake inhaler (suspensions only)	Inhaler not shaken
	Hold inhaler upright	Inhaler upside down*
	Breathe out	No exhalation
	Place mouthpiece between lips	
	Fire while breathing in deeply and slowly	Firing device before start of inhala
		Firing device at or after end of inh
		Inhaling through nose*
	Continue to inhale after firing	Stopping inhalation as device is fir
		Fast inhalation
	Hold breath (10 s)	No/short breath-hold
Breath-actuated pMDI	Remove mouthpiece cap	Failure to remove mouthpiece cap
	Shake inhaler (suspensions only)	Inhaler not shaken
	Hold inhaler upright	Inhaler upside down*
	Prepare device (*e.g.* lift lever)	Failure to prepare device correctly
	Breathe out	No exhalation
	Place mouthpiece between lips	Poor seal around mouthpiece
		Using "open mouth" inhalation te
	Breathe in deeply and slowly	Weak inhalation, failure to trigger
		Inhaling through nose*
	Continue to inhale after firing	Stopping inhalation as device is fir
		Fast inhalation
	Hold breath (10 s)	No/short breath-hold
"Press and breathe" pMDI plus spacer		Inappropriate handling (static cha
	Remove mouthpiece cap	Failure to remove mouthpiece cap
	Shake inhaler (suspensions only)	Inhaler not shaken
	Hold inhaler upright	Inhaler upside down*
	Insert pMDI into spacer	
	Breathe out	No exhalation
	Fire while breathing in deeply and slowly	Long delay before inhalation
		Multiple actuation
		Weak inhalation, failure to open v
		Inhaling through nose*
	Continue to inhale after firing	Stopping inhalation as device is fir
		Fast inhalation
	Hold breath (10 s)	No/short breath-hold
DPIs	Remove cover (device specific)	Failure to remove cover*

	Load dose (device specific)	Incorrect dose loading*
	Pierce capsule (single-dose devices)	Failure to pierce capsule*
	Breathe out	Breathing out into device*
	Place mouthpiece between lips	Inhalation vents blocked¶
		Poor seal round mouthpiece
		Using “open-mouth” inhalation te
	Inhale deeply and quickly	Not inhaling quickly enough*
		Insufficient “acceleration”
		Inhaling through nose*
	Hold breath (10 s)	No/short breath-hold
	Store in cool dry place	Inappropriate storage

*: crucial error, likely to result in zero lung deposition of drug.

ANNEX 3. Range and costs of drugs and devices.

From: Centre for Reviews and Dissemination. Inhaler devices for the management of asthma and COPD. University of York. Effective Health Care 8(1). 2003 http://www.york.ac.uk/inst/crd/EHC/ehc81.pdf

Table 1: Range and costs of drugs and devices[5]

Drug	Device type	Name	Company	Cost
Beclometasone dipropionate	pMDI	non-proprietary		£4.61*
		Becotide® 100	A&H	£5.78*
	pMDI (CFC-Free)	Qvar® 50	3M	£4.41*
	Dry powder	non-proprietary		£5.76*
		Asmabec Clickhaler®	Celltech	£5.91*
		Becodisks®	A&H	£10.17* (refill cost)†
		Becotide Rotahaler®		£8.04* (refill cost)†
	Breath actuated	Aerobec 100 Autohaler®	3M	£7.22*
		Beclozone Easi-breathe®	IVAX	£4.61*
	Breath actuated (CFC-free)	Qvar 50 Autohaler®	3M	£4.41*
Budesonide	pMDI	Pulmicort®	AstraZeneca	£5.32*
	Dry powder	non-proprietry (Cyclohaler)		£9.32*
		Pulmicort Turbohaler®	AstraZeneca	£10.36*
	Nebuliser solution	Pulmicort Respules®		£89.60*††
Fluticasone propionate	pMDI (CFC-free)	Flixotide Evohaler®	A&H	£5.46*
	Dry powder	Flixotide Accuhaler®		£8.96*
		Flixotide Diskhaler®		£12.23* (refill cost)
	Nebuliser solution	Flixotide Nebules®		£56.22*††
Salbutamol	pMDI	non-proprietary		£1.91**
	pMDI (CFC-Free)	non-proprietary		£1.90**
		Airomir®	3M	£1.97**
		Evohaler®	A&H	£2.30**
	Dry powder	non-proprietary		£5.05**
		As Cyclohaler		£4.28* (refill cost)
		Asmasal Clickhaler®	Celltech	£6.32**
		Ventodisks®	A&H	£5.26* (refill cost)
		Ventolin Accuhaler®		£8.33**
		Ventolin Rotahaler®		£4.76** (refill cost)
	Breath actuated	Aerolin Autohaler®	3M	£10.04**
		Salamol Easi-breathe®	IVAX	£6.30**
	Breath actuated (CFC-free)	Airomir Autohaler®	3M	£6.02**
		Salamol Easi-breathe®	IVAX	£6.30**
	Nebuliser solution	non-proprietary		£12.45**
		Ventolin Nebules®	A&H	£16.90**
Terbutaline sulphate	pMDI	Bricanyl®	AstraZeneca	£2.66**
	Dry powder	Bricanyl Turbohaler®		£6.30**
	Nebuliser solution	Bricanyl Respules®		£18.35**
		non-proprietary		£18.35**
Ipratropium bromide	pMDI	Atrovent®	Boehringer Ingelheim	£4.21**
	Dry powder	Atrovent Aerocaps®		£10.53** (refill cost)
	Breath actuated	Arrovent Autohaler®		£9.39**
	Nebuliser solution	Atrovent®		£32.40**
		non-proprietary		£30.10**
		Ipratropium Steri-Neb®	IVAX	£30.70**
		Respontin®	A&H	£27.25**
Oxitropium bromide	pMDI	Oxivent®	Boehringer Ingelheim	£6.69**
	Breath actuated	Oxivent Autohaler®		£15.72**

* Costs based on 28 days treatment with beclometasone dipropionate 200µg twice daily or equivalent. Assumes that fluticasone dipropionate is twice as potent and that qvar (beclometasone CFC-free) can be substituted at half the dose.[5]

** Costs based on 100 'reliefs' i.e. 200µg of salbutamol (two actuations of pMDI or one dry powder)[5]

† Becotide Becodisks® and Rotahaler® probably require twice the dose for equivalent efficacy and as such the higher cost figure would apply.

†† Nebulised doses may not be equivalent to the above assumptions as little information is available as to the equivalence of doses between hand-held inhalers and nebulisers (which in themselves are highly variable).