Working title:

Expert opinion on the impact of inhaler choice on climate change and personalised healthcare

Focus therapy area(s): Inhalers, asthma, COPD

Proposed by:

Omar Usmani, Imperial College London and Royal Brompton Hospital, National Heart and Lung Institute, London, UK and REG

Objective:

This project aims to provide an opinion piece on choice of inhaler delivery method and the impact of on climate change and personalised healthcare. It has the following objectives:

1. Identify experience and preferences of patients and healthcare professionals (HCPs) of inhaler choice/change in relation to climate change and personalized healthcare.
2. Gather expert opinion and consensus on (a) costs to environment (b) impact on personalized healthcare.
3. An extensive literature review covering current discussion on the above topics.

This research will offer expert opinion and consensus of physicians and health care workers on:

- (a) ***Costs to environment***: The impact of inhaler choice and switching inhaler delivery system on climate change, as well as short-term vs long-term solutions for reduction of impact.

The research will also gather information from patients on:

- (b) ***Personal impact:*** The impact of changing medication that has affected their personalized healthcare plan and inhaler use.

Rationale:

Medications for asthma and COPD are mostly administered using inhaler devices. Inhalers are crucial to managing daily symptoms, acute emergencies and chronic disease. Most of the current inhaler devices available provide therapy using one of three drug delivery systems: dry powder inhalers (DPI), metered-dose inhalers (MDIs) and soft mist inhalers (SMIs). DPIs are breath-activated, where the patient requires deep and forceful inhalation, whereas MDIs require patient coordination of inhalation and actuation of the inhaler, and SMIs are propellent free. Until the early 1990s, MDIs contained chlorofluorocarbon (CFC) propellants.

These ozone-depleting substances[1] were phased out under the Montreal Protocol (1987)[2] in a global effort to address climate change. To ensure a seamless transition for patients that were already using MDIs, pharmaceutical companies developed CFC-free MDIs, replacing CFC with hydrofluoroalkane (HFA) propellants: HFA134a and HFA227ea. Although HFCs are not ozone-depleting, they still have a high global warming potential (GWP). As such, the UNEP Kigali Amendment to the Montreal Protocol, introduced the phase-down of HFCs as greenhouse gases[3]. The European Commission has now approved two F-gas regulations, the second one in 2015, granting an exemption for pharmaceutical use[4].
Most recently, the UK government provided a recent directive of the Environmental Audit Committee that stipulated that at least 50% of prescribed inhalers should be of low global warming potential by 2022[5]. The directive has recommended that stable patients using MDIs are switched to DPIs, due to the lower GWP of the latter[5], despite the higher proportion of patients in the UK using MDI inhalers[6]. There is a potentially significant impact on patient outcomes due to switching device[7], as well as an impact on the financial drive to innovate and develop greener or lower carbon MDIs[8].

Although there is currently limited discussion in the literature as to the contribution of inhaler choice to climate change[1,7–13], the potential benefits and drawbacks of the three inhaler delivery systems and their impact on patient care is well documented. Previous publications have considered accessibility of inhaler type to those with mobility issues or lack of understanding of proper inhaler use[14,15]; differences in efficacy between the delivery systems[16]; the impact on adherence of patients switching from one inhaler type to another[17–19]; and costs associated with each delivery method and switching inhaler type have been discussed[1,20–22]. The impact of switching inhaler on tailored and personalised healthcare has also been poorly defined, where the inability to tailor inhaler choice to patient preference[23,24] may have impact on patient understanding[25,26] and technique[27], and therefore patient outcomes[28,29].
There has been limited discussion and expert opinion on the impact of switching inhaler type on inhaler error, adherence; and their cumulative contribution to climate change and effect on patient outcomes. Additionally, there has been little discussion on short- and mid-term solutions to reduce the inhaler effect on climate change, such as avoiding landfills through increased recycling of inhalers and use of reusable inhalers[30–32]; and patient education to reduce the waste of medication through improper inhaler use, non- adherence and excessive use[33].

With public knowledge and discussion being opened up through media coverage of this topic[34], policy change driving and affecting the development and innovation of novel

technologies[13], and the inevitable impact of climate change on exacerbation frequency in sufferers of respiratory diseases[35], now is the ideal time to provide open up the discussion on the consequences of inhaler choice.

This research aims to gather patient-centric expert opinion to deliver consensus on the impact of switching inhaler type on climate change and the suggestion of green alternatives to switching inhaler types; as well as measure the impact of switching on patients and their personalised healthcare plan. Extra focus will be given to switching inhaler type for non-medical reasons (i.e. based on policy change, rather than patient health requirements); and offer perspective on driving inhaler development for carbon reduction. It will also provide an update of the current discussion in the literature on the impact of inhaler choice to provide support to the consensus.

Proposed methodology:

Study design

The study will be carried out in 3 parts:

1) Questionnaires will be distributed to:
    a. health care professionals
    b. patients

    Questionnaires will be distributed electronically, and responses of the questionnaires will be analysed to generate evidence of perspective and impact of switching inhaler.
2) A Delphi study will be developed based on the findings from the questionnaires. The Delphi exercise will be carried out with experts to evaluate the available evidence and reach consensus on inhaler choice and its impact on climate change and personalized healthcare.
3) The results of these two processes will then be used to shape an REG consensus-based opinion piece.

Literature review:

An extensive review of the available literature on MDI, DPI, SMI, and the effects of switching inhaler type in relation to impact on environment and patient health care will also be carried out to inform the design of both questionnaires and Delphi surveys.

Data collection using two questionnaires:

The first questionnaire will be distributed remotely to healthcare professionals (primary and secondary care physicians, nurses, pharmacists and physiotherapists) recruited through the REG extended network (comprised of REG collaborators primarily in Europe and Asia-Pacific).

The aim is to identify key needs, opinions, priorities and values in inhaler choice and associated policy changes and the impact of switching delivery systems on patient care. The healthcare professionals will also be asked about greener alternatives and whether they are or will be used in practice. The scope of questions for the survey will be to gauge opinion on:

- Prioritisation of the environment over clinical need regarding policy on inhaler devices.
- Importance of patient involvement in choosing the right inhaler.
- Concerns/complications/unintended consequences of device switching.
- Importance of device simplicity/continuity to ongoing care of disease.
- The care improvement approach to sustainability.

The second survey will be for patients using inhalers recruited through professional networks and patient associations to participate in the electronic survey using *(a)* Likert-like scale to gauge their opinion on priorities in their care, or *(b)* yes/no questions aiming to gather data on their inhaler switch and its impact. Questions will focus on their difficulties of changing inhaler and will include appropriate questions from the scope outlined above. The study will be exploratory and will involve patients based on the following:

Patient inclusion criteria

- Clinically stable asthma or COPD diagnosis
- Prescribed inhaler medication
- Age >18 years
- Have switched inhaler type in the last 1 year

Exclusion criteria

- Unable to access questionnaire
- Unable to understand the electronic questionnaire process
- Using a non-MDI/DPI/SMI device

Data analysis:

Descriptive statistics will be used to identify the strength of opinion/knowledge of healthcare workers and patients. Subgroup analysis will be used, as appropriate, between healthcare worker types and differences in patient age, time since inhaler switch, demographic, number of exacerbations, and whether the patient is diagnosed with asthma or COPD. These results will inform the survey design for the Delphi study

Delphi exercise

For the first round of Delphi, experts will be contacted remotely using the REG extended network for participation. Countries of participation will be defined by the authors. A survey will be designed based on the results from the HCP/patient questionnaires and sent to participants to identify and prioritise key issues in inhaler choice in personalised health care, changing delivery systems and development of green alternatives. Focus will be directed to raising key themes and questions of the impact of inhaler choice on climate change and patient care.

The second round of the Delphi exercise will aim to reach consensus on the needs identified in phase I Delphi and evidence provided by the survey responses. The process will gather information from panellists in three email rounds, moving from open-ended free text questions, to rating of themes, to finally scoring of statements on the impact of inhaler switching on climate change and patient outcomes. Evidence from the surveys will be reviewed and interpreted, and priorities among the groups will be compared, identifying common priorities and commenting on any discrepancies.

Outputs from the research:

The final output of this study will be a structured expert consensus/opinion piece which offers a clear concise statement on the impact of inhaler choice/switch and policy on both the environment and patient care and potential alternative solutions to balancing the needs of the patient and the needs to reduce environmental cost in short- and mid-term vs long-term. The consensus will include recommendations for quality improvement driving carbon reduction and development of low carbon propellants to avoid policy-based inhaler switch as opposed to patient needs.

Dissemination of research:

Results of this study will be submitted to present at an international respiratory congress (e.g. the European Respiratory Society, American Thoracic Society or similar), followed by two manuscripts (one for the patient/HCP questionnaires and one for the Delphi study) submitted to an appropriate peer-reviewed scientific journal within 12 months of completion of each phase of the study.

Proposed funding strategy:

The total budget will be divided equally across four involved companies (AstraZeneca, Boehringer Ingelheim, Chiesi and Kindeva).

References

1 Braggins R, Steinbach I, Smith J, *et al.* Costs of switching to low global warming potential inhalers . An economic and carbon footprint analysis of NHS prescription data in England. *BMJ Open* 2019; **9**: 1–8.

2 The United Nations. MULTILATERAL Montreal Protocol on Substances that Deplete the Ozone Layer (with annex). Concluded at Montreal on 16 Sep tember 1987. 1987; **1522**.

3 UNEP. The Kigali Amendment to the Montreal Protocol: HFC Phase-down. *OzonAction Fact Sheet* 2016; : 1–7.

4 European Commission. EU legislation to control F-gases | Climate Action. 2015. https://ec.europa.eu/clima/policies/f-gas/legislation_en (accessed June 4, 2020).

5 House of Commons Environmental Audit Committee. UK Progress on reducing F-gas emissions. 2018.

6 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.

7 Usmani OS, Scullion J, Keeley D. Our planet or our patients—is the sky the limit for inhaler choice? *Lancet Respir Med* 2019; **7**: 11–3.

8 Janson C, Henderson R, Löfdahl M, *et al.* Carbon footprint impact of the choice of inhalers for asthma and COPD. *Thorax* 2020; **75**: 82–4.

9 Hillman T, Mortimer F, Hopkinson NS. Inhaled drugs and global warming: Time to shift to dry powder inhalers. *BMJ* 2013; **346**: 10–1.

10 Hänsel M, Bambach T, Wachtel H. Reduced Environmental Impact of the Reusable Respimat® Soft Mist™ Inhaler Compared with Pressurised Metered-Dose Inhalers. *Adv Ther* 2019; **36**: 2487–92.

11 Ortsäter G, Borgström F, Soulard S, Miltenburger C. A Budget Impact Model to Estimate the Environmental Impact of Adopting RESPIMAT® Re-usable in the Nordics and Benelux. *Adv Ther* 2019; **36**: 3435–45.

12 Lehtimäki L, Björnsdóttir U, Janson C, Haahtela T. Minimising the environmental impact of inhaled therapies. Eur. Respir. J. 2020; **55**. DOI:10.1183/13993003.00721-2020.

13 Keeley D, Scullion JE, Usmani OS. Minimising the environmental impact of inhaled therapies: Problems with policy on low carbon inhalers. Eur. Respir. J. 2020; **55**. DOI:10.1183/13993003.00048-2020.

14 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**: 1071-1081.e9.

15 Usmani OS, Lavorini F, Marshall J, *et al.* Critical inhaler errors in asthma and COPD: A systematic review of impact on health outcomes. *Respir Res* 2018; **19**: 9–12.

16 Ibrahim M, Verma R, Garcia-Contreras L. Inhalation drug delivery devices: Technology update. *Med Devices Evid Res* 2015; **8**: 131–9.

17 Park H-SS, Yoon D, Lee HY, *et al.* Real-life effectiveness of inhaler device switch from dry powder inhalers to pressurized metred-dose inhalers in patients with asthma treated with ICS/LABA. *Respirology* 2019; **2019**: 1–8.

18 Rhee CK, van Boven JFMM, Yau Ming SW, *et al.* Does Changing Inhaler Device Impact Real-Life Asthma Outcomes? Clinical and Economic Evaluation. *J Allergy Clin Immunol Pract* 2019; **7**: 934–42.

19 Miravitlles M, Montero-Caballero J, Richard F, *et al.* A cross-sectional study to assess inhalation device handling and patient satisfaction in COPD. *Int J Chron Obstruct Pulmon Dis* 2016; **11**: 407–15.

20 Kemp L, Haughney J, Barnes N, *et al.* Cost-effectiveness analysis of corticosteroid inhaler devices in primary care asthma management: A real world observational study. *Clin Outcomes Res* 2010; **2**: 75–85.

21 Forster R, Ratcliffe A, Lewis M, Crossley A, Bastida JL, Dunlop WCN. Cost–utility analysis of an intervention designed to reduce the critical handling error of insufficient inspiratory effort. *Eur J Heal Econ* 2018; **19**: 1303–18.

22 Bloom CI, Douglas I, Olney J, D'Ancona G, Smeeth L, Quint JK. Cost saving of switching to equivalent inhalers and its effect on health outcomes. *Thorax* 2019; : thoraxjnl-2018-212957.

23 Dekhuijzen PNR, Lavorini F, Usmani OS. Patients' perspectives and preferences in the choice of

inhalers: The case for Respimat® or HandiHaler®. Patient Prefer. Adherence. 2016; **10**: 1561–72.
24 Usmani OS. Choosing the right inhaler for your asthma or COPD patient . *Ther Clin Risk Manag* 2019; **Volume 15**: 461–72.
25 Press VG, Arora VM, Shah LM, *et al.* Teaching the use of respiratory inhalers to hospitalized patients with asthma or COPD: a randomized trial. *J Gen Intern Med* 2012; **27**: 1317–25.
26 Lavorini F, Usmani OS. Correct inhalation technique is critical in achieving good asthma control. Prim. Care Respir. J. 2013; **22**: 385–6.
27 Chorao P, Pereira AM, Fonseca JA. Inhaler devices in asthma and COPD--an assessment of inhaler technique and patient preferences. *Respir Med* 2014; **108**: 968–75.
28 Scichilone N. Asthma Control: The Right Inhaler for the Right Patient. Adv. Ther. 2015; **32**: 285–92.
29 Bosnic-Anticevich S, Chrystyn H, Costello RW, *et al.* The use of multiple respiratory inhalers requiring different inhalation techniques has an adverse effect on COPD outcomes. *Int J COPD* 2017; **12**: 59–71.
30 Hänsel M, Bambach T, Wachtel H. Reduced environmental impact of a reusable soft mist inhaler. In: European Respiratory Journal. European Respiratory Society (ERS), 2018: PA1021.
31 Macdonald G, Mikolasch TA, Stadler CI, Macdonald G. Our prescription for climate change: Reduce and recycle inhalers! *Br J Gen Pract* 2020; **70**: 168.
32 Ortsäter G, Borgström F, Baldwin M, Miltenburger C. Incorporating the Environmental Impact into a Budget Impact Analysis: The Example of Adopting RESPIMAT® Re-usable Inhaler. *Appl Health Econ Health Policy* 2020; **18**: 433–42.
33 Dipper A, Anning L, Zorzi A, *et al.* Reducing plastic waste, carbon footprint and cost: inhaler recycling at Musgrove Park Hospital. In: European Respiratory Journal. European Respiratory Society (ERS), 2018: PA3158.
34 McNulty W, Usmani OS. Asthma carbon footprint 'as big as eating meat'. BBC News. 2019; **1**: 25898.
35 Ayres JG, Forsberg B, Annesi-Maesano I, *et al.* Climate change and respiratory disease: European Respiratory Society position statement. *Eur Respir J* 2008; **34**: 295–302.