Adv Ther (2022) 39:2270–2280
https://doi.org/10.1007/s12325-022-02076-7

STUDY PROTOCOL

Environmental Sustainability in Respiratory Care: An Overview of the healthCARe-Based envirONmental Cost of Treatment (CARBON) Programme

Alex Wilkinson · Ekaterina Maslova · Christer Janson · Yang Xu · John Haughney · Jennifer K. Quint · Nigel Budgen · Andrew Menzies-Gow · John Bell · Michael G. Crooks

Received: December 10, 2021 / Accepted: February 4, 2022 / Published online: March 13, 2022

ABSTRACT

Introduction: Faced with the challenges of climate change, countries are seeking to decarbonise their economies. A greater understanding of what comprises the carbon footprint of care in healthcare systems will identify potential strategies for reduction of greenhouse gas (GHG) emissions. In respiratory care, the focus has been on preventer inhalers, thereby omitting contributions from other aspects such as healthcare resource utilisation (HCRU) and reliever inhaler use. The healthCARe-Based envirONmental cost of treatment (CARBON) programme aims to provide a broader understanding of the carbon footprint associated with respiratory care.

Methods: CARBON will quantify the carbon footprint of medications and HCRU among approximately 2.5 million patients with respiratory diseases from seven ongoing studies spanning more than 40 countries. Across studies, to obtain the carbon footprint of all inhaled, oral, and injectable medications, SimaPro life cycle assessment software modelling resource and energy consumption data, in addition to Ecoinvent® data sets and certified published studies, will be used. The carbon footprint of HCRU in the United Kingdom will be estimated by applying the methodology and data obtained from the Sustainable Healthcare Coalition Care Pathway Guidance.

Planned Outcomes: In asthma, CARBON studies will quantify GHG emissions associated with well-controlled versus not well-controlled asthma, the contribution of short-acting β_2-agonist (SABA) reliever inhalers (and their potential overuse) to the carbon footprint of care, and how implementation of treatment guidelines can drive improved outcomes and footprint reduction. In chronic obstructive pulmonary disease (COPD), CARBON studies will assess the

A. Wilkinson (✉)
Respiratory Department, Lister Hospital, East and North Hertfordshire NHS Trust, Coreys Mill Lane, Stevenage, Hertfordshire SG1 4AB, UK
e-mail: alex.wilkinson2@nhs.net

E. Maslova · Y. Xu · J. Bell
AstraZeneca, Cambridge, UK

C. Janson
Department of Medical Sciences, Respiratory, Allergy and Sleep Research, Uppsala University, Uppsala, Sweden

J. Haughney
Queen Elizabeth University Hospital, Glasgow, UK

J. K. Quint
National Heart and Lung Institute, Imperial College London, London, UK

N. Budgen
AstraZeneca, Macclesfield, UK

A. Menzies-Gow
Royal Brompton Hospital, London, UK

M. G. Crooks
Hull York Medical School, Hull, UK

impact of exacerbation history on GHG emissions associated with HCRU and SABA use in subsequent years and estimate the carbon footprint associated with all aspects of COPD care.

Conclusion: CARBON aims to show that the principle of evidence-led care focused on improvement of clinical outcomes has the potential to benefit patients and the environment.

Keywords: Asthma; Carbon footprint; COPD; Greenhouse gas emissions

Key Summary Points

Why carry out this study?

The healthcare sector is one of the largest public sector emitters of carbon globally and will need to achieve significant reductions to achieve net zero carbon targets.

Within the respiratory community, this focus has been on the carbon footprint of preventer pressurised metered-dose inhalers, omitting other relevant factors such as reliever medication and healthcare resource utilisation (HCRU).

The CARBON programme aims to quantify the carbon contribution of these additional aspects of respiratory care in asthma and chronic obstructive pulmonary disease (COPD).

A more holistic understanding as to how respiratory care contributes to greenhouse gas emissions will help identify opportunities for reduction without the potential harm to patients from non-clinically led switching of therapy (for "environmental" reasons).

What was learned from this study?

CARBON is an ongoing programme and is the first to quantify the carbon footprint of care of a disease.

Comprising approximately 2.5 million patients from seven studies in more than 40 countries, CARBON aims to calculate the impact of poor disease control and disease progression on the carbon footprint of respiratory care and demonstrate how guideline implementation can improve outcomes and reduce the carbon footprint.

CARBON will help determine whether patients with well-managed disease are likely to have a lower carbon impact overall through reduced requirement for HCRU and lower short-acting β_2-agonist use in order to identify tangible solutions for how a focus on an outcomes-improvement approach in respiratory diseases such as asthma and COPD can help achieve carbon targets.

INTRODUCTION

Climate change is the defining challenge of the twenty-first century and is associated with extreme weather events, food scarcity, and worsening of chronic and infectious conditions [1–3]. Based on an urgent need for countries to take concrete steps against this climate emergency, the Paris Agreement, a legally binding international treaty on climate change, was adopted by 196 countries in 2015 [4]. It commits signatories to reduce global warming by limiting the rise in average global temperatures this century to less than 2 °C. Signatories will thus need to undertake efforts to limit greenhouse gas (GHG) emissions and become carbon neutral by mid-century.

The healthcare sector is one of the largest public sector contributors of GHGs in many countries, accounting for 10% of the total national emissions in the United States of America (USA) in 2013 [5] and 7% in Australia in 2014–2015 [6]. In Canada, from 2009 to 2015, the healthcare system generated 33 million tonnes of CO_2 equivalents (CO_2e) (primarily from hospitals, pharmaceuticals, and physician services) and over 200,000 tonnes of

other pollutant emissions [7]. Health damages from healthcare-generated emissions in Canada equated to an estimated 23,000 disability-adjusted life years (DALYs) lost annually, with a range of 4500–610,000 DALYs, reflecting potential uncertainty at each step. In the USA, assessment of a broad sample of emergency medical services agencies in 2011 identified GHG emissions of 660,000–1.6 million tonnes CO_2e/year, with diesel and gasoline consumption accounting for 71.6% of emergency services–related emissions [8]. In England, the carbon footprint from health and social care was 27.12 million tonnes CO_2e in 2017, of which medical instruments/equipment were the largest contributors (13.2%) [9].

Healthcare systems will thus need to achieve substantial reductions in GHG emissions as societies look to decarbonise. The National Health Service (NHS) in the United Kingdom (UK) is the first health service to set emissions targets, aiming to achieve net zero emissions by 2045, with an ambition to reach an 80% reduction by 2036–2039 [10]. Key to this is the ability to quantify the carbon footprint of healthcare practices in a standardised manner. The UK has standardised and validated methodology for quantifying CO_2e for pharmaceuticals and interventions [11] and has also carbon footprinted components of healthcare resource utilisation (HCRU) [12].

Inhaled corticosteroids (ICS) and bronchodilators are the mainstay of treatment for airway diseases and many are delivered via pressurised metered-dose inhalers (MDIs) [13]. MDIs contain hydrofluorocarbon propellants that have high global warming potential (GWP) [14]. As a result, the environmental impact of preventer MDIs has received attention [13, 15]. The development of a next-generation of MDIs that contain propellants with 90–99% less GWP is also underway [16] with the expectation that they will have an impact on reducing total GHG emissions from inhalers from 2025. With more than 500 million people worldwide currently living with asthma and chronic obstructive pulmonary disease (COPD) [17], examining the impact of respiratory care on the environment may provide insights into whether, and how, better management of chronic diseases can lead to greater environmental sustainability. However, the focus on preventer inhalers without considering the contributions made by HCRU, short-acting β_2-agonist (SABA) reliever use, and other medications to the carbon footprint provides an incomplete picture of the carbon impact of respiratory care. Many patients with asthma and COPD remain poorly managed and uncontrolled [18, 19] because of multifactorial reasons, including lack of implementation of treatment guidelines into standard of care [20, 21]. This is exemplified by the widespread overuse of SABA in asthma globally, which in itself is associated with increased risk of exacerbations and hospitalisations [22–24]. Poorly controlled disease and progression will drive increased demand for HCRU [25, 26], and, intuitively, this will carry a higher carbon footprint compared with patients whose disease is well controlled. Conversely, better disease management may reduce reliever use and HCRU and lower the carbon footprint. Thus, attempts to decarbonise respiratory care by focusing on preventer inhalers alone are likely to fall short as they account for only one component of care. Furthermore, there is conflicting evidence of therapeutic equivalence between different inhaler devices with the same active compounds [27, 28], emphasising the requirement for treatment to be personalised to patient needs with the aim of improving outcomes. Non-consensual switching has been associated with worsened asthma control, increased HCRU, and wasted medication [29, 30], which in turn may increase the carbon footprint. Hence, switching of inhalers should only be done as part of a clinical consultation and based on clinical need or patient preference.

The healthCARe-Based envirONmental cost of treatment (CARBON) programme was designed to broaden the understanding of the carbon footprint of respiratory care. This programme aims to quantify the total carbon footprint of care, identify how poor disease management contributes to a larger carbon footprint, and examine whether targeting improvement of care reduces the carbon footprint without compromising patient outcomes.

METHODS

Design of the CARBON Programme

CARBON will quantify the carbon footprint of medications and HCRU among respiratory patients using a combination of certified published studies and methodologies.

Quantification of GHG emissions will be based on the quantity and type of medications sold or prescribed/possessed (as a surrogate for use) and the CO_2e emission value of each asthma treatment. To obtain the carbon footprint of all inhaled, including SABA and ICS treatments, as well as oral and injectable medications, SimaPro life cycle assessment software modelling resource and energy consumption data, in addition to Ecoinvent® data sets and certified published studies [31, 32], will be used. To obtain the carbon footprint of HCRU in the UK, emissions data from the Sustainable Healthcare Coalition (SHC) [12] will be used for all healthcare visit types, including travel by the patient and healthcare professional. The carbon footprint of HCRU is currently not available for other countries.

CARBON will use data from seven ongoing studies spanning more than 40 countries and involving approximately 2.5 million patients (Table 1). SABINA CARBON UK will draw from the SABA use IN Asthma (SABINA) UK study [22], with the aim of quantifying GHG emissions associated with asthma care of patients (at least 12 years of age) with well-controlled and not well-controlled asthma. Similar analyses evaluating the carbon footprint associated with poor asthma control are planned in separate studies in the USA (SABA CARBON USA) and Canada (as part of SABA CARBON Europe-Canada).

A second set of studies will use SABA prescription/possession data from SABINA studies as well as inhaler sales data to evaluate emissions linked to SABA use versus all inhaler use, and that of SABA overuse in asthma. The analyses on SABA overuse will be conducted in patients (at least 12 years of age) as part of the SABINA studies [22, 23, 33] in Europe and Canada (SABA CARBON Europe-Canada), USA (SABA CARBON USA) and in other mostly low- and middle-income countries outside of Europe (SABA CARBON International).

In COPD, prior exacerbations are linked to increased likelihood of future exacerbations [26]. The Study of HEalthcare Resource utiLisation related to exacerbatiOns in patients with COPD (SHERLOCK) CARBON, an observational cohort study conducted in UK patients (over 40 years of age), will quantify the impact of prior exacerbations on GHG emissions associated with HCRU and SABA use in subsequent years. EXACerbations and their OutcomeS (EXACOS) CARBON, an observational cohort study, will take this a step further by examining the carbon footprint associated with all aspects of COPD care as well as the influence of disease severity and comorbidities.

Lastly, SABA rEductioN Through ImpleMeNting Hull asthma guidELines (SENTINEL), a quality improvement programme including UK patients (at least 18 years of age) with asthma across six primary care networks in Hull and East Yorkshire, will evaluate the environmental impact associated with system-wide implementation of evidence-based asthma treatment guidelines focused on the use of maintenance and reliever therapy. SENTINEL aims to improve asthma outcomes and reduce SABA overuse through supported guideline implementation and, as a consequence, reduce the environmental impact of asthma treatment.

Ethics and Dissemination

All studies in this programme will be conducted in accordance with the ethical principles consistent with the International Conference on Harmonisation (ICH) guideline for Good Clinical Practice and the Declaration of Helsinki, and all applicable legislation on non-interventional studies and/or observational studies of the countries where the research is conducted.

DISCUSSION

Societies will have to decarbonise all aspects of their economies in the coming years, including healthcare, if nations are to meet their climate

Table 1 Summaries of CARBON studies

Programme	SABINA CARBON UK	SHERLOCK CARBON	EXACOS CARBON	SENTINEL	SABA CARBON Europe-Canada	SABA CARBON International	SABA CARBON USA
CARBON objectives	To quantify GHG emissions associated with asthma care, with a focus on the environmental cost of asthma that is not well controlled	To evaluate the impact of exacerbation history on GHG emissions associated with HCRU and SABA use[a] in COPD in subsequent years	To evaluate the carbon footprint associated with COPD care and the effect of disease severity and cardiovascular comorbidities on the carbon footprint	To evaluate GHG emissions associated with changes in prescribing practice and HCRU after system-wide implementation of The Hull University Teaching Hospitals NHS Trust Guideline for the Treatment of Adult Asthma in patients at risk of poor clinical outcomes due to high SABA use[a]	To evaluate the volume and carbon footprint of SABA use[a] (versus total inhaler use) in all respiratory conditions and GHG emissions associated with potential SABA overuse in asthma To evaluate the environmental cost of asthma that is not well controlled using the SABINA Canada data set	To evaluate the volume and carbon footprint of SABA use[a] (versus total inhaler use) in all respiratory conditions, and GHG emissions associated with SABA overuse in asthma	To evaluate GHG emissions linked with SABA inhaler use (and overuse in asthma) versus total inhaler use in all respiratory conditions To quantify the GHG emissions associated with asthma care, with a focus on the environmental cost of asthma that is not well controlled
Study design	Observational open-cohort study	Observational cohort study	Observational cohort study	Non-randomised, stepped-wedge design quality improvement programme	Observational cross-sectional and cohort study	Observational cross-sectional study	Observational cross-sectional and cohort study
Study period	2008–2019	2013–2016	2010–2018	2021–2022	09/2018–09/2019 (sales data); 2006–2019 (SABINA I and II data)	09/2018–09/2019 (sales data); 2019–2020 (SABINA III data)	09/2018–09/2019 (sales data); 2010–2017 (IBM MarketScan®)

Table 1 continued

Programme	SABINA CARBON UK	SHERLOCK CARBON	EXACOS CARBON	SENTINEL	SABA CARBON Europe-Canada	SABA CARBON International	SABA CARBON USA
Respiratory indication	Asthma	COPD	COPD	Asthma	All respiratory uses and asthma	All respiratory uses and asthma	All respiratory uses and asthma
Participating countries	UK	UK	UK	UK (6 primary care networks in Hull and the East Riding of Yorkshire healthcare regions)	Bulgaria, Canada, Croatia, Czech Republic, Denmark, France, Finland, Germany, Greece, Hungary, Ireland, Italy, Netherlands, Norway, Poland, Romania, Sweden, Spain, Switzerland, and UK	Algeria, Argentina, Australia, Brazil, Chile, China, Colombia, Costa Rica, Egypt, Hong Kong, India, Indonesia, Japan, Kenya, Kazakhstan, Kuwait, Malaysia, Mexico, New Zealand, Oman, Peru, Philippines, Russia, Saudi Arabia, Singapore, South Africa, South Korea, Taiwan, Thailand, Turkey, United Arab Emirates, and Vietnam	USA
Number of patients	236,506	22,462	340,515	20,000 (estimated)	1,131,416	8351	725,499
Age	≥ 12 years	≥ 40 years	≥ 40 years	≥ 18 years	≥ 12 years (SABINA data)	≥ 12 years (SABINA data)	≥ 12 years (SABINA data)

Table 1 continued

Programme	SABINA CARBON UK	SHERLOCK CARBON	EXACOS CARBON	SENTINEL	SABA CARBON Europe-Canada	SABA CARBON International	SABA CARBON USA
Data source	CPRD GOLD, HES, and ONS mortality data	NHS Greater Glasgow and Clyde Health Board Safe Haven database	CPRD Aurum and HES	NHS and SUS data sets	IQVIA™ sales data[b] and SABINA I and II data	IQVIA™ sales data[b] and SABINA III data	IQVIA™ sales data[b] and IBM MarketScan® Commercial, Medicare Supplemental, and Multistate Medicaid Research databases

CARBON healthCARe-Based carbON cost of treatment, *COPD* chronic obstructive pulmonary disease, *CPRD* Clinical Practice Research Datalink, *EXACOS* Exacerbations and Their Outcomes, *GHG* greenhouse gas, *HCRU* healthcare resource utilisation, *HES* Hospital Episode Statistics, *NHS* National Health Service, *ONS* Office for National Statistics, *SABA* short-acting β2-agonist, *SABINA* SABA use IN Asthma, *SENTINEL* SABA rEductioN Through ImplemeNting Hull asthma guidELines, *SHERLOCK* Study of HEalthcare Resource utiLisation related to exacerbatiOns in patients with COPD, *SUS* Secondary Uses Services, *UK* United Kingdom, *USA* United States of America

[a]Prescription/possession data are used as a surrogate for medication use

[b]IQVIA™ Quarterly MIDAS database Q3 2019

change commitments. CARBON, to our knowledge, will be the first programme to systematically quantify the carbon footprint of respiratory care globally to better understand its potentially modifiable contribution to global GHG emissions. Findings from CARBON will help reveal what comprises the carbon footprint of respiratory healthcare, how it is impacted by poor disease control or progression, and how optimal treatments and guideline implementation can drive carbon reduction.

Although reducing carbon emissions is important, it must be achieved without putting patients at risk. Patients with well-managed disease are likely to have a lower carbon impact overall through reduced requirements for HCRU and lower SABA use. CARBON aims to highlight that optimising care through implementation of quality standards and clinical guidelines targeting reductions in SABA use and exacerbation frequency could benefit patients by improving disease control, while at the same time reducing carbon emissions associated with all elements of their care.

Strengths and Limitations of the Programme

Strengths of this programme include the following. All CARBON studies use standardised methodology to evaluate the carbon footprint of medications globally. In addition, in the UK, the carbon footprint of HCRU is estimated applying the methodology and data obtained from the SHC guidance enabling quantification of the sustainability performance of care pathways in a consistent and transparent manner. Overall, results from this programme have the potential to promote the development and implementation of effective treatment strategies that will improve patient outcomes, whilst also reducing the carbon footprint of asthma and COPD care. Moreover, once established, the principle of prioritising improvements in patient outcomes, which in turn may elicit environmental benefits, could be applied to other common progressive diseases such as diabetes and chronic kidney disease [34, 35].

A potential limitation of the CARBON programme is that medication prescription and/or sales data are used across studies as a surrogate for actual use. Additionally, only CARBON studies conducted in the UK will initially quantify the carbon footprint of HCRU because of the lack of care pathway guidance in other countries. Lastly, GHG estimates were quantified on the basis of published guidelines and estimates but are subject to some uncertainty. To account for this potential variability, where possible, sensitivity analyses will be conducted using one-tenth to tenfold of recommended HCRU CO_2e values.

CONCLUSIONS

In CARBON, a detailed mapping of the carbon footprint associated with healthcare will enable a thorough assessment of the environmental impact of treatment and management of respiratory diseases. Output from CARBON has the potential to generate awareness among policy and healthcare decision makers of the carbon footprint of poor care and accelerate innovations to make respiratory care both patient-centric and carbon conscious.

ACKNOWLEDGEMENTS

Funding. The CARBON programme is funded by AstraZeneca. AstraZeneca was involved in designing the studies, developing the study protocols, conducting the studies and performing the analyses. AstraZeneca was given the opportunity to review the manuscript before submission. AstraZeneca funded the journal's Rapid Service and Open Access Fees.

Medical Writing, Editorial, and Other Assistance. Editorial support was provided by Roopashri Holehonnur Sudarshanprasad, PhD, and Michelle Rebello, PhD, of Cactus Life Sciences (part of Cactus Communications) and funded by AstraZeneca.

Authorship. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

Author Contributions. Ekaterina Maslova and John Bell contributed to the programme conception. All authors contributed to the design and data collection/analysis/interpretation of CARBON studies. All authors participated in editing and reviewing the drafts of the manuscript and all read and approved the final manuscript.

Disclosures. Alex Wilkinson has made unpaid contributions to publications on the carbon footprint of inhalers and respiratory treatment, which were sponsored by GSK and AstraZeneca; Christer Janson has received payments for educational activities from AstraZeneca, BI, Chiesi, GSK, Novartis, and Teva and has served on advisory boards arranged by AstraZeneca, BI, Chiesi, GSK, Novartis, and Teva; Michael G. Crooks has received honoraria, fees for advisory boards, and non-financial support from AstraZeneca, BI, Chiesi, GSK, Novartis, and Pfizer and grants from AstraZeneca, BI, Chiesi, and Pfizer; Jennifer K Quint has received grants from The Health Foundation, MRC, GSK, Bayer, BI, British Lung Foundation, IQVIA, Chiesi, Insmed, and Asthma UK and personal fees for advisory board participation or speakers' fees from GSK, BI, AstraZeneca, and Bayer; Andrew Menzies Gow has attended advisory boards for AstraZeneca, GSK, Novartis, Sanofi, and Teva; received speakers' fees from AstraZeneca, Novartis, Sanofi, and Teva; participated in research with AstraZeneca, for which his institution has been remunerated; attended international conferences with Teva; and made consultancy agreements with AstraZeneca and Sanofi; John Haughney has received personal fees from AstraZeneca, BI, Chiesi, Cipla, and Teva; Ekaterina Maslova, Yang Xu, Nigel Budgen, and John Bell are employees of AstraZeneca.

Compliance with Ethics Guidelines. All studies in this programme will be conducted in accordance with the ethical principles consistent with the International Conference on Harmonisation (ICH) guideline for Good Clinical Practice and the Declaration of Helsinki, and all applicable legislation on non-interventional studies and/or observational studies of the countries where the research is conducted.

Prior Presentation. An overview of the CARBON programme has been previously presented at the 10th International Primary Care Respiratory Group World Conference (IPCRG 2021) and encored at the 33rd Annual Conference of the International Society for Environmental Epidemiology (ISEE 2021).

Data Availability. Data sharing is not applicable to this article as it describes the design of a programme and no data sets were generated or analysed.

REFERENCES

1. Xu R, Yu P, Abramson MJ, et al. Wildfires, global climate change, and human health. New Engl J Med. 2020;383:2173–81.

2. Patz JA, Campbell-Lendrum D, Holloway T, Foley JA. Impact of regional climate change on human health. Nature. 2005;438:310–7.

3. Hoegh-Guldberg O, Jacob D, Taylor M, et al. Impacts of 1.5°C global warming on natural and human systems. In: Global warming of 1.5°C. An IPCC Special Report. IPCC; 2018. https://www.ipcc.ch/sr15/chapter/chapter-3/. Accessed Feb 2022.

4. United Nations. Paris Agreement. https://unfccc.int/sites/default/files/english_paris_agreement.pdf. 2015. Accessed Oct 2021.

5. Eckelman MJ, Sherman J. Environmental impacts of the U.S. health care system and effects on public health. PLoS ONE. 2016;11: e0157014.

6. Malik A, Lenzen M, McAlister S, McGain F. The carbon footprint of Australian health care. Lancet Planet Health. 2018;2:e27–35.

7. Eckelman MJ, Sherman JD, MacNeill AJ. Life cycle environmental emissions and health damages from the Canadian healthcare system: an economic-environmental-epidemiological analysis. PLoS Med. 2018;15:e1002623.

8. Blanchard IE, Brown LH, North American EMS Emissions Study Group. Carbon footprinting of North American emergency medical services systems. Prehosp Emerg Care. 2011;15:23–9.

9. National Health Service (NHS) Sustainable Development Unit. Reducing the use of natural resources in health and social care. https://networks.sustainablehealthcare.org.uk/sites/default/files/resources/20180912_Health_and_Social_Care_NRF_web.pdf. 2018. Accessed Feb 2022.

10. National Health Service (NHS). Delivering a 'net zero' National Health Service. https://www.england.nhs.uk/greenernhs/wp-content/uploads/sites/51/2020/10/delivering-a-net-zero-national-health-service.pdf. 2020. Accessed Oct 2021.

11. National Health Services (NHS). Greenhouse gas accounting sector guidance for pharmaceutical products and medical devices. https://ghgprotocol.org/sites/default/files/Summary-Document_Pharmaceutical-Product-and-Medical-Device-GHG-Accounting_November-2012_0.pdf. 2012. Accessed Oct 2021.

12. Sustainable Healthcare Coalition. Sustainable care pathways guidance. https://shcoalition.org/sustainable-care-pathways-guidance/accessed. Accessed Oct 2021.

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

14. Ko MK, Sze ND, Molnar G, Prather MJ. Global warming from chlorofluorocarbons and their alternatives: time scales of chemistry and climate. Atmos Environ Part A. 1993;27:581–7.

15. United Nations Industrial Development Organisation (UNIDO). UNIDO brochure: HFC phase-down. https://www.unido.org/sites/default/files/files/2020-04/UNIDO-brochure_HFC-Phase_Down-Complete.pdf. 2017. Accessed Oct 2021.

16. AstraZeneca [Press release]. AstraZeneca's 'Ambition Zero Carbon' strategy to eliminate emissions by 2025 and be carbon negative across the entire value chain by 2030. https://www.astrazeneca.com/media-centre/press-releases/2020/astrazenecas-ambition-zero-carbon-strategy-to-eliminate-emissions-by-2025-and-be-carbon-negative-across-the-entire-value-chain-by-2030-22012020.html. Accessed Oct 2021.

17. Soriano JB, Kendrick PJ, Paulson KR, et al. Prevalence and attributable health burden of chronic respiratory diseases, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet Respir Med. 2020;8:585–96.

18. Price D, Fletcher M, Van Der Molen T. Asthma control and management in 8000 European patients: the REcognise Asthma and LInk to Symptoms and Experience (REALISE) survey. NPJ Prim Care Respir Med. 2014;24:1–10.

19. Quaderi S, Hurst J. The unmet global burden of COPD. Glob Health Epidemiol Genom. 2018;3:e4.

20. Sehl J, O'Doherty J, O'Connor R, O'Sullivan B, O'Regan A. Adherence to COPD management guidelines in general practice? A review of the literature. Ir J Med Sci. 2018;187:403–7.

21. Cloutier MM, Salo PM, Akinbami LJ, et al. Clinician agreement, self-efficacy, and adherence with the guidelines for the diagnosis and management of asthma. J Allergy Clin Immunol Pract. 2018;6:886–94 (**e884**).

22. Bloom CI, Cabrera C, Arnetorp S, et al. Asthma-related health outcomes associated with short-acting beta2-agonist inhaler use: an observational UK study as part of the SABINA global program. Adv Ther. 2020;37:4190–208.

23. Janson C, Menzies-Gow A, Nan C, et al. SABINA: an overview of short-acting beta2-agonist use in asthma in European countries. Adv Ther. 2020;37:1124–35.

24. Nwaru BI, Ekstrom M, Hasvold P, et al. Overuse of short-acting beta2-agonists in asthma is associated with increased risk of exacerbation and mortality: a nationwide cohort study of the global SABINA programme. Eur Respir J. 2020;55:1901872.

25. Pavord ID, Mathieson N, Scowcroft A, et al. The impact of poor asthma control among asthma patients treated with inhaled corticosteroids plus long-acting β2-agonists in the United Kingdom: a cross-sectional analysis. NPJ Prim Care Respir Med. 2017;27:1–8.

26. Haughney J, Lee AJ, Nath M, et al. The long-term clinical and economic impact of COPD exacerbations: an observational study (SHERLOCK). Eur Respir J. 2020;56:4910.

27. Thomas M, Williams AE. Are outcomes the same with all dry powder inhalers? Int J Clin Pract Suppl. 2005;59:33–5.

28. Ram FS. Clinical efficacy of inhaler devices containing β2-agonist bronchodilators in the treatment of asthma. Am J Respir Med. 2003;2:349–65.

29. Doyle S, Lloyd A, Williams A, et al. What happens to patients who have their asthma device switched without their consent? Prim Care Respir J. 2010;19:131–9.

30. Thomas M, Price D, Chrystyn H, et al. Inhaled corticosteroids for asthma: impact of practice level device switching on asthma control. BMC Pulm Med. 2009;9:1.

31. Panigone S, Sandri F, Ferri R, et al. Environmental impact of inhalers for respiratory diseases: decreasing the carbon footprint while preserving patient-tailored treatment. BMJ Open Respir Res. 2020;7:e000571.

32. Wilkinson AJK, Braggins R, Steinbach I, Smith J. 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:e028763.

33. Bateman ED, Price DB, Wang H-C, et al. Short-acting β2-agonist prescriptions are associated with poor clinical outcomes of asthma: the multi-country, cross-sectional SABINA III study. Eur Respir J. 2021. https://doi.org/10.1183/13993003.01402-2021.

34. Connor A, Lillywhite R, Cooke MW. The carbon footprints of home and in-center maintenance hemodialysis in the United Kingdom. Hemodial Int. 2011;15:39–51.

35. Fordham R, Dhatariya K, Stancliffe R, et al. Effective diabetes complication management is a step toward a carbon-efficient planet: an economic modeling study. BMJ Open Diabetes Res Care. 2020;8:e001017.