To the Editor:

Climate change represents a global challenge and nations are increasingly looking to decarbonise their economies by developing roadmaps for reducing greenhouse gas (GHG) emissions in accordance with international treaties, such as the Paris Agreement [1]. As the healthcare sector remains a key contributor to GHG emissions [2], an examination of the global carbon footprint of its operations and treatment pathways is essential to identify targets for decarbonisation.

In respiratory treatment, the environmental impact of controller inhalers has received considerable attention due to the hydrofluorocarbon propellants used in metered-dose inhalers (MDIs), which have global warming potential [3]. In the United Kingdom (UK), where MDIs represented \(\sim 3\%\) of health and social care system carbon emissions [4] and 13.1% of emissions related to the delivery of care in 2019 [2], targets are in place to reduce total emissions by 80% by 2036–2039, including those from MDIs [5]. However, the focus on controller inhalers omits other contributors, such as the impact of short-acting \(\beta_2\)-agonists (SABAs), presenting an incomplete picture of the carbon footprint of respiratory treatments for both asthma and COPD.

Patients with mild asthma, who represent approximately half of the European asthma population [6], are commonly prescribed SABA-only treatment [7], placing them at increased risk of poor outcomes [8]. Additionally, findings from the real-world SABA use IN Asthma (SABINA) programme revealed that approximately one-third of patients with asthma across Europe overuse SABA (prescription/dispensing of three or more canisters per year) [9], which is associated with an increased risk of exacerbations and healthcare resource use [10, 11]. Moreover, increased healthcare resource use in respiratory treatment, whether associated with poor disease control of asthma [12] or progression of COPD [13], carries an additional carbon burden [14].

We considered that suboptimal care of patients with asthma or COPD may drive a higher, yet potentially modifiable, contribution to global GHG emissions, and developed the healthCARe-Based carbON cost of treatment (CARBON) programme, an evolving healthcare sustainability programme to better understand the carbon footprint of respiratory disease control and progression [15]. As part of the CARBON programme, the SABA CARBON Europe and Canada observational cohort study quantified the carbon footprint associated with 1) the use of both reliever and controller inhalers in 20 European countries and in Canada and 2) SABA overuse (prescription/dispensing of three or more canisters per year) in five European countries and two Canadian provinces (Alberta and Nova Scotia) from the SABINA programme.

Inhaler sales data, as a surrogate for inhaler use, for SABA and controller medications (MDIs and dry powder inhalers (DPIs)), across all respiratory uses, were obtained from the IQVIA quarterly MIDAS database Q3 2019 (September 2018 to September 2019), accessed and analysed via the AstraZeneca in-house STAR system. This analysis included patients treated for any respiratory condition. Controller treatments included inhaled corticosteroid-containing drugs, long-acting \(\beta_2\)-agonists (LABA), long-acting muscarinic antagonists (LAMA) and LAMA/LABA combinations.
SABA overuse in patients with asthma (aged \(\geq 12\) years) of any severity was assessed using prescription/dispensing data from the SABINA programme (2006–2019) [10, 16–19].

Data were compared by dose, preventing confounding from inhaler actuation count differences. A 1:1 equivalence of actuation and dose was assumed for SABAs and controller medication delivered via a DPI, whereas a 2:1 ratio for actuation to dose was assumed for controller medication delivered via a MDI. Both analyses were descriptive in nature and annual GHG emissions were expressed as carbon dioxide equivalent (CO\(_2\)e) and quantified using published data [3, 20] and internal AstraZeneca estimates. Per capita inhaler usage and associated carbon footprint were calculated using the national population for IQVIA sales data and using the study populations for the SABINA data.

SABA use was common across 20 countries in Europe and in Canada (table 1). Although SABAs were mostly administered via MDIs, this varied across countries, ranging from 28.2% in Sweden to 100% in Italy. Per capita SABA use ranged from 98 770 (Poland) to 1 033 535 (UK) doses per 10 000 persons per year. Compared with SABA use, per capita controller medication use was lower, ranging from 58 506 (Romania) to 437 945 (UK) doses per 10 000 persons per year.

As a proportion of total inhaler use, SABA inhalers ranged from 33% (Belgium) to 71% (Canada and Ireland), with SABA GHG emissions ranging from 47% (Netherlands and Sweden) to 80% (Romania). Compared with per capita GHG emissions from SABA, which ranged from 12 (Sweden) to 134 (UK) tonnes CO\(_2\)e per 10 000 persons per year, per capita GHG emissions from controller medication use were lower and ranged from 4 (Romania) to 65 (UK) tonnes CO\(_2\)e per 10 000 persons per year. Total GHG emissions from the use of SABA and controller medications were approximately 2 and 1 million tonnes CO\(_2\)e, respectively, with SABA use accounting for 66% of the total GHG emissions from inhalers.

Across the seven SABINA datasets comprising 1 131 416 patients with asthma (table 1), most SABA prescriptions were received by patients who were overusing SABA (three or more canisters per year), ranging from 69% (Italy and Sweden) to 94% (Canada (Nova Scotia)). SABA overuse contributed to excess per capita GHG emissions, ranging from 78 (Sweden) to 864 (Canada (Nova Scotia)) tonnes CO\(_2\)e per 10 000 persons per year. Per capita GHG emissions from SABA overuse in Canada (Nova Scotia) were 1.6- to 11.1-fold higher versus the UK and Sweden, respectively. As an example, SABA overuse when scaled to the national asthma population of \(\sim\)5.4 million in the UK translated to an excess carbon footprint of 293 227 tonnes CO\(_2\)e. Across the two Canadian provinces, both SABA overuse and the associated per capita emissions were higher in Nova Scotia compared with Alberta.

Although inhaler sales and prescriptions/dispensing data may not reflect actual medication use and final disposal (together accounting for \(\sim\)90% of the GHG emissions) [3], this study provides an understanding of how high SABA use, a marker of poor disease control and suboptimal disease management [8], drives the associated carbon footprint of respiratory treatment.

Overall, our findings reveal that suboptimal respiratory treatment, in the form of high SABA use across Europe and Canada, remains widespread, representing approximately two-thirds of total GHG emissions. These findings highlight the importance of assessing the contribution of SABAs to the carbon footprint of respiratory treatment, which in many countries were commonly used and administered by MDIs, thereby explaining higher GHG emissions associated with SABA versus controller inhaler use. Furthermore, an analysis of SABINA datasets demonstrated that SABA overuse, as defined by the threshold of three or more canisters per year [8], drives the majority of SABA prescriptions/dispensing in asthma, suggesting suboptimal disease management in a high proportion of patients who are at increased risk of asthma exacerbations and exacerbation-related healthcare resource use, thereby further contributing to the total carbon footprint.

In most countries, SABAs represented the majority of respiratory-related inhaler use, indicating suboptimal disease control in these populations. The highest per capita use of both SABA and controller inhalers was observed in the UK. SABA overuse in asthma was prevalent despite the different healthcare and reimbursement policies of each country, a finding consistent with previous studies [9–11, 17, 18, 21, 22]. Across all SABINA datasets, SABA prescribing/dispensing was primarily driven by patients who were potentially overusing SABA relievers. However, these findings should be interpreted in light of diverse asthma management practices and differences in healthcare delivery systems and socioeconomic status across the individual datasets, particularly in relation to access to medications [19]. For example, in Germany and Sweden, SABA is a prescription-only medicine [9], while in Italy, SABA is available without a prescription [17]. Thus, actual SABA use in Italy may have been higher than observed.
### TABLE 1. Greenhouse gas (GHG) emissions related to short-acting β2-agonist (SABAs) versus controller medication in 21 countries (IQVIA dataset), and SABA overuse among patients with asthma from the seven SABA use IN Asthma (SABINA) datasets and associated GHG emissions.

| Country        | IQVIA dataset | SABINA dataset |
|----------------|---------------|----------------|
|                | Per capita SABA use, doses per 10 000 persons per year | Per capita controller medication use, doses per 10 000 persons per year |
| Belgium        | 131 047 | 267 567 |
| Bulgaria       | 125 630 | 141 248 |
| Canada         | 543 796 | 224 999 |
| Czech Republic | 125 088 | 210 556 |
| Denmark        | 281 377 | 284 622 |
| Croatia        | 126 186 | 111 056 |
| Croatia        | 126 186 | 111 056 |
| Greece         | 237 510 | 288 218 |
| Hungary        | 182 449 | 144 174 |
| Ireland        | 743 424 | 300 928 |
| Italy          | 125 516 | 144 659 |
| Belgian        | 256 961 | 288 783 |
| Norwegian      | 285 983 | 279 637 |
| Poland12       | 98 770 | 166 863 |
| Romania        | 126 896 | 58 506 |
| Portuguese     | 318 751 | 222 311 |
| Sweden13       | 238 512 | 349 211 |
| Switzerland    | 154 456 | 150 331 |
| United Kingdom | 1 033 535 | 437 945 |

|                | Per capita GHG emissions from SABA, tonnes CO2e per 10 000 persons per year | Per capita GHG emissions from controller medication, tonnes CO2e per 10 000 persons per year |
|----------------|---------------------------------------------------------------------------|-------------------------------------------|
| Belgium        | 19 672                                                                     | 17 422                                   |
| Bulgaria       | 11 959                                                                     | 9 640                                    |
| Canada         | 193 356                                                                    | 73 898                                   |
| Czech Republic | 10 889                                                                     | 8 017                                    |
| Croatia        | 725 38                                                                   | 417 57                                  |
| Denmark        | 10 963                                                                    | 11 563                                   |
| Croatia        | 63 725                                                                    | 417 57                                  |
| Greece         | 10 889                                                                    | 8 017                                    |
| Hungary        | 22 957                                                                    | 12 560                                   |
| Ireland        | 48 986                                                                    | 16 762                                   |
| Italy          | 104 503                                                                   | 86 040                                   |
| Belgian        | 46 559                                                                    | 52 922                                   |
| Norwegian      | 14 776                                                                    | 10 188                                   |
| Polish12       | 49 893                                                                    | 43 738                                   |
| Romania        | 36 749                                                                    | 93 731                                   |
| Portuguese     | 195 771                                                                   | 86 977                                   |
| Sweden13       | 11 632                                                                    | 12 895                                   |
| Switzerland    | 16 067                                                                    | 61 741                                   |
| United Kingdom | 862 685                                                                   | 415 345                                   |

|                | GHG emissions associated with medication use were quantified using SimaPro life cycle assessment software modelling resource and energy consumption data, in addition to Ecoinvent datasets and certified published studies. Per capita GHG emissions were calculated to allow comparisons across countries/datasets. CO2e: carbon dioxide equivalent; GINA: Global Initiative for Asthma. # : data from Alberta and Nova Scotia from the SABINA datasets were analysed separately to compare SABA overuse and associated emissions across the two provinces; ¶ : in the SABINA dataset, patients from Poland with zero SABA use could not be categorised across GINA steps; + : in the SABINA dataset, 8061 patients from Sweden could not be categorised according to GINA steps. |
SABA prescribing/dispensing patterns in Poland may be attributable to underfunding of the healthcare system, leading to relatively high out-of-pocket spending [23]. Variations in SABA overuse between the two Canadian provinces may be due, in part, to differences in socioeconomic status [24] that may have influenced access to recommended asthma medications. However, further research is needed to verify these findings.

Although global asthma guidelines no longer recommend as-needed SABA use alone due to safety concerns [8] and an inconsistent evidence base, asthma management practices have not yet caught up with current evidence-based recommendations, and SABA overuse therefore continues to drive the majority of GHG emissions across countries. Consequently, implementation of clinical guidelines, adherence to asthma action plans, and delivery of personalised care along with a focus on the management of modifiable risk factors for poor disease control, such as SABA overuse, poor medication adherence and incorrect inhaler technique should be prioritised to improve patient outcomes [8]. This approach will subsequently reduce SABA reliever use and additional healthcare resource use, thereby benefiting patients and realising carbon savings that go beyond the reduction in SABA use alone. As suboptimal disease management continues to be an unacceptable unmet need in respiratory treatment, this is a call to action for healthcare professionals and policymakers to ensure that treatment-related decisions are guided by current evidence-based recommendations and tailored to patient needs, thereby reducing SABA use and associated carbon emissions in respiratory treatment, without risking improvements in patient outcomes or causing harm.

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