Reductions in inhaler greenhouse gas emissions by addressing care gaps in asthma and chronic obstructive pulmonary disease: an analysis

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ABSTRACT

Introduction Climate change from greenhouse gas (GHG) emissions represents one of the greatest public health threats of our time. Inhalers (and particularly metered-dose inhalers (MDIs)) used for asthma and chronic obstructive pulmonary disease (COPD), constitute an important source of GHGs. In this analysis, we aimed to estimate the carbon footprint impact of improving three distinct aspects of respiratory care that drive avoidable inhaler use in Canada.

Methods We used published data to estimate the prevalence of misdiagnosed disease, existing inhaler use patterns, medication class distributions, inhaler type distributions and GHGs associated with inhaler actuations, to quantify annual GHG emissions in Canada:

1. attributable to asthma and COPD misdiagnosis;
2. attributable to overuse of rescue inhalers due to suboptimally controlled symptoms; and
3. avoidable by switching 25% of patients with existing asthma and COPD to an otherwise comparable therapeutic option with a lower GHG footprint.

Results We identified the following avoidable annual GHG emissions:

1. ~49 100 GHG metric tons (MTs) due to misdiagnosed disease;
2. ~143 000 GHG MTs due to suboptimal symptom control; and
3. ~262 100 GHG MTs due to preferential prescription of strategies featuring MDIs over lower-GHG-emitting options (when 25% of patients are switched to lower GHG alternatives).

Conclusions Our analysis shows that the carbon savings from addressing misdiagnosis and suboptimal disease control are comparable to those achievable by switching one in four patients to lower GHG-emitting therapeutic strategies. Behaviour change strategies required to achieve and sustain delivery of evidence-based real-world care are complex, but the added identified incentive of carbon footprint reduction may in itself prove to be a powerful motivator for change among providers and patients. This additional benefit can be leveraged in future behaviour change interventions.

INTRODUCTION

Human-induced climate change resulting from greenhouse gas (GHG) emissions poses one of the greatest public health threats of the 21st century. In Canada, healthcare accounts for 4.6% of GHG emissions, ranking second in health systems worldwide, with an increasing trend. Most health system GHG emissions occur during manufacture of pharmaceuticals and medical equipment, and in the actual delivery of care. An example of the latter is the metered-dose inhaler (MDI), which is used commonly in the two most prevalent chronic respiratory diseases—asthma and chronic obstructive pulmonary disease (COPD)—and accounts for 3.5% of the UK National Health Service carbon footprint. To generate aerosol
clouds, MDIs use various hydrofluorocarbons (HFCs) as propellants, which are potent GHGs. While the carbon footprint of MDIs depends on the type and amount of propellant used, the production, use and disposal of a single canister of the most commonly prescribed MDI release an amount of GHGs that is equivalent to a 110-km car journey. Although they also have important lifecycle environmental impacts through their production, use and disposal, newer inhalation devices such as dry powder inhaler (DPIs), which do not require a propellant, have an overall carbon footprint that is 8–12 times lower than that of MDIs.

Ironically, it is the very patients who use these GHG-emitting devices for respiratory diseases who bear a disproportionate burden of the harmful health effects of climate change. Climate change drives heat waves and increases in particulate matter (including through forest fires) both of which are associated with increased symptoms, exacerbations and healthcare usage in asthma and COPD. Similarly, gradual tropicalisation of temperate latitudes has led to higher pollen concentrations and longer pollen seasons, resulting in worsening symptoms and increased exacerbations.

At the same time, evidence suggests that most MDI use for asthma and COPD may be avoidable. In fact, three key evidence-to-practice gaps contribute to avoidable inhaler use in asthma and COPD: misdiagnosis, leading to inhaler use in those who do not actually have the condition; suboptimal disease control, leading to excess use of rescue inhalers; and prescription patterns favouring high GHG-emitting options, despite equivalent or similar therapeutic options with lower global warming potential that might be considered with careful patient discussion and education. In this paper, we aimed to calculate the magnitude of annual GHG emission reductions that could be achieved by bridging these three existing practice gaps in Canada.

**METHODS**

We calculated the carbon footprint impact of addressing these three care gaps based on the following conditions derived from published literature. For each analysis, we considered a Canadian prevalence of 3.8 million people with a clinical diagnosis of asthma, and of 2.0 million people with a clinical diagnosis of COPD (clinical diagnosis is often made on the basis of symptoms alone, as opposed to an objective diagnosis through pulmonary function testing).

**Avoidable GHG emissions from misdiagnosed asthma and COPD**

To calculate avoidable GHG emissions from misdiagnosed disease, we estimated: the proportion of prevalent patients carrying a diagnosis of asthma or COPD who were misdiagnosed; the proportion of these misdiagnosed people who use inhalers (see ‘A’ below); the predicted distributions of medication classes and inhaler device types in each class (see ‘B’) along with the number of actuations from each device type per year in this population (see ‘C’). Finally, we multiplied the calculated number of inhaler actuations in misdiagnosed people over a year (see ‘D’) by the corresponding carbon footprint of each actuation (see ‘E’).

**Population sizes and inhaler use among misdiagnosed people**

We applied data from a prospective, multisite, population-based study which determined that 33% of Canadian adults with physician-diagnosed asthma did not have the diagnosis when tested objectively. Of these patients without current asthma, 79% used asthma medications. Similarly, in COPD, we applied findings of a retrospective practice-based analysis showing that 44% of those with a label of COPD did not actually have the disease when tested objectively, and 67% of these patients were on COPD medications.

**Inhaler medication class distributions**

We derived data on inhaler class distributions from clinical studies reporting controller and rescue medication use in asthma and COPD populations. We assumed that: all people with misdiagnosed asthma using medications (corresponding to 990,660 people, see ‘A’ above), had a short-acting beta₂-agonist (SABA) rescue inhaler; and that 33% (or 326,918 people) had either an inhaled corticosteroid (ICS) or an ICS-long-acting beta₂-agonist (LABA) combination controller inhaler. In COPD, among the 589,600 misdiagnosed patients using medications (see ‘A’), we assumed that 95% (560,120 people) were using a SABA, 5% (29,480 people) a short-acting muscarinic antagonist (SAMA), 6% (35,376 people) a LABA, 54% (318,384 people) either a long-acting muscarinic antagonist (LAMA) or a combined LABA-LAMA inhaler, 40% (235,840 people) an ICS-LABA inhaler and 0.04% (23,584 people) a combined LABA-LAMA-ICS inhaler.

**Inhaler device-type distributions**

We applied market sales data to determine the proportion of inhalers that were MDIs versus DPIs in each medication class (note that these inhaler device distributions were used in all analyses). In asthma, we assumed that MDIs comprised 94% of SABA agents, 56% of ICS agents and 47% of combined ICS-LABA agents. Among ICS MDIs, 88% were HFC-134a-containing MDIs and 12% HFC-227ea-containing MDIs (HFC-134a and HFC-227ea are two different propellants, each with distinct GHG emission footprints). In COPD, we assumed that MDIs comprised 95% of SABA agents and 47% of ICS-LABA agents. Concordant with market availability, all SAMA inhalers were treated as MDIs, and LABA and combined LAMA-LABA-ICS inhalers were treated as DPIs. LAMA and combined LAMA-LABA inhalers were also treated as DPIs, though some formulations are also available as soft mist inhalers (these are propellant-free MDIs with a comparably low carbon footprint).
Inhaler actuations
We conservatively assumed that people with misdiagnosed asthma or COPD using medication(s) regularly use only a single dose of rescue inhaler per week.\textsuperscript{24, 25} Note that a single dose of rescue medication translates to two medication actuations for a SABA MDI and one medication actuation for a SABA DPI (based on product monographs). For controllers, considering that this analysis focused on misdiagnosed patients reportedly using medications, we further assumed that: (1) patients with asthma were using one dose (two actuations) of ICS or two doses (four actuations) of ICS-LABA per day (for COPD, please refer to online supplemental file 1). (2) We then subtracted 20% of actuations from the total yearly actuations, to account for inadvertent missed doses among patients otherwise reporting regular medication use.\textsuperscript{26}

Carbon footprint of each actuation
We applied the following widely-used life-cycle carbon footprint impacts from each inhaler actuation: 0.3485 kg of CO\textsubscript{2} equivalent (CO\textsubscript{2}e)/actuation for MDIs using HFC-227ea as a propellant; 0.1315 kg of CO\textsubscript{2}e/actuation for MDIs using HFC-134a as a propellant; 0.0475 kg of CO\textsubscript{2}e/actuation for MDIs using a combination of HFC-134a and oleic acid as a propellant (used in some SABA MDIs); and 0.009 kg of CO\textsubscript{2}e/actuation kg for DPIs.\textsuperscript{27} These numbers were used in all analyses.

Patient and public involvement
Patients or the public were not involved in the design, or conduct, or reporting of this research but will be involved in its dissemination, through engagement with asthma and COPD patient organisations, who can present our results to their members and the broader public.

Avoidable GHG emissions from excess use of rescue therapy in asthma and COPD
To calculate avoidable GHG emissions from excess use of rescue therapy in asthma and COPD, we estimated: the proportion of prevalent patients carrying a diagnosis of asthma or COPD who overuse their rescue MDI or DPI, and the extent of rescue overuse by disease severity (see ‘A’ below). We then applied the above-described predicted distributions of rescue inhaler device types in each class, in each disease and multiplied excess rescue actuations from each device type over a year by the corresponding carbon footprint of each actuation.

Population sizes and excess rescue inhaler actuations among rescue inhaler ‘overusers’
Asthma guidelines have defined well-controlled disease as requiring no more than two doses of SABA per week.\textsuperscript{24, 25} Here, we conservatively considered an average use of no more than three rescue SABA doses per week (~150 doses per year) to be acceptable. As in prior studies, in COPD, we defined ‘acceptable’ rescue therapy use as no more than four doses of a short-acting reliever per day.\textsuperscript{28, 29} Note that we also assumed that patients with mild disease (as defined by Canadian Thoracic Society guidelines)\textsuperscript{30} do not overuse rescue therapy by this definition. Accordingly, we calculated the benefits of eliminating usage beyond the third dose used in a week (beyond the 150th dose used in a year) in asthma, and beyond the fourth dose each day in moderate-to-severe COPD. In asthma, based on a recent population-based cohort study,\textsuperscript{31} we assumed that 21% of prevalent patients (corresponding to 798 000 Canadians) used >150–375 excess doses of rescue inhaler over a year (‘mild’ overuse category); 7% (266 000 Canadians) used >375–750 excess doses per year (‘moderate’ overuse); and 2% (76 000 Canadians) used >750 doses per year (‘severe’ overuse).\textsuperscript{31} In calculating excess dose actuations, we used the mid-point estimate of these ranges in mild and moderate overuse categories, and the low-point estimate for the severe overuse category (we subtracted the acceptable 150 doses per year before calculating overuse in each category). In COPD, based on a prospective cohort study of patients with COPD monitoring daily SABA use with a portable electronic inhaler sensor,\textsuperscript{28} we assumed that: 28% of patients with moderate-to-severe COPD (227 405 Canadians) exceeded ‘acceptable’ use on half or less days in each year (‘mild’ overuse category) (translating to an average of 0.6 excess MDI actuations); and 19% (151 603 Canadians) exceeded this use on more than half the days in each year (‘severe’ overuse) (translating to an average of 5.8 excess MDI actuations per day).

Avoidable GHG emissions from switching therapeutic options in asthma and COPD
In calculating avoidable GHG emissions from switching therapeutic options, we explored three different approaches, each time modelling for a conservative 25% of patients to switch therapies: (1) switching from MDIs used in asthma and COPD to DPIs, within the same molecule; (2) switching from ICS therapy with as-needed SABA (a regimen usually involving at least one MDI) to as-needed ICS/LABA DPI (budesonide-formoterol) in people aged ≥12 years with mild asthma,\textsuperscript{24, 25} and switching from separate LAMA and ICS/LABA inhalers (a regimen often involving at least one MDI) to a single triple therapy DPI inhaler in people with COPD; and (3) switching MDI prescriptions from the highest to the lowest available carbon footprint MDI (within the same drug class), in each disease.

For each analysis, we considered the entire population of patients carrying a diagnosis of asthma or COPD (including people with misdiagnosed disease and those who overuse rescue therapies). Based on population distributions of different levels of disease severity, we derived the number of actuations from each device type per year (after also accounting for reported non-adherence) (see ‘A’ below). We then applied the above-described predicted distributions of inhaler device use only a single dose of rescue inhaler per week.\textsuperscript{24, 25}
types in each medication class, estimated the existing and expected number of inhaler actuations over a year, multiplied these numbers by the corresponding carbon footprint of each actuation and calculated the expected reduction in GHG emissions with each strategy.

Population sizes and inhaler use among patients with prevalent asthma and COPD

Based on a population distribution of different levels of asthma severity, we assumed that 63% of patients had mild asthma and were on an ICS as controller inhaler (along with a SABA as rescue inhaler). For ICS controller inhalers, we assumed that patients were using two actuations per day (based on recommended dosing regimens), but conservatively applied a 12% adherence rate over a year (to reflect real-world usage). In patients considered to have moderate-to-severe asthma, we assumed that 37% were considered to be on an ICS-LABA as controller inhaler (along with a SABA as rescue inhaler). We assumed that these patients were using four actuations of their controller inhaler per day, and had a higher adherence rate of 43%. We also conservatively considered that 70% of these patients used an average of one rescue dose per week (others were assumed to use their rescue inhaler as defined in ‘Avoidable GHG emissions from excess use of rescue therapy in asthma and COPD above, based on a real-world study).

In COPD, we applied a population distribution across the Global Initiative for Chronic Obstructive Lung Disease (GOLD) A–D stages derived from Le et al., whereby we assumed that 28% of patients had GOLD A disease, 52% GOLD B, 3% GOLD C and 20% GOLD D. Patients in the GOLD A group were assumed to be on either a SABA, LAMA, LABA and/or SAMA inhaler. Patients in the GOLD B group were assumed to be on either a LAMA, LABA-LABA, LAMA-ICS or LAMA-LABA-ICS inhaler. Patients in the GOLD C group were assumed to be on a LAMA inhaler, and patients in the GOLD D group on either a LAMA-LABA, ICS-LABA or LAMA-LABA-ICS inhaler. Recommended dosing regimens were used to derive the number of doses per day for each drug class. We applied a real-world controller therapy adherence of 37% for regimens comprising of multiple separate inhalers and of 43% for single-inhaler regimens. We further assumed that 53% of patients with COPD used four doses of rescue inhaler per week, while others were assumed to use their rescue inhaler as defined in ‘Avoidable GHG emissions from excess use of rescue therapy in asthma and COPD above.

RESULTS

Avoidable GHG emissions from misdiagnosed asthma and COPD

In table 1, we show that addressing asthma misdiagnosis and eliminating the associated unnecessary inhaler use would reduce GHG emissions by ~35900 metric tons of CO_2e (MT CO_2e) annually.

Although as noted, certain COPD drug classes are available exclusively as DPIs, eliminating COPD misdiagnosis would still save ~13200 MT CO_2e annually in Canada (table 2).

The combined impact of addressing misdiagnosis in asthma and COPD would be an emission reduction of ~49100 MT CO_2e annually, comparable to taking 10900 vehicles off the road each year (figure 1A).

AVOIDABLE GHG EMISSIONS FROM EXCESS USE OF RESCUE THERAPY IN ASTHMA AND COPD

Even applying a conservative estimate eliminating doses beyond an average of three weekly doses, addressing SABA overuse could avert the release of ~6700 MT CO2e a year in asthma (table 3). Although eliminating this excess SABA use may require additional controller prescriptions, we found that sizeable GHG emission savings remain after accounting for additional emissions from new controller MDIs (online supplemental material 1, appendix B, table S2, S3). Similarly, even when people with misdiagnosed asthma are not included in this calculation, large carbon savings remain from eliminating excess SABA use (online supplemental material 1, appendix B, table S4).

In COPD, addressing excess rescue therapy (rescue doses in excess of our times a day) use could save ~82300 MT CO_2e in a single year (table 4). As with asthma, carbon savings remain large even when excluding people with misdiagnosed disease (online supplemental material 1, appendix B, table S6).

When combined, eliminating excess use of rescue therapy in asthma and COPD could reduce emissions by ~143000 MT CO_2e, similar to taking 31800 passenger vehicles off the roads each year (figure 1B).

Avoidable GHG emissions from switching therapeutic options in asthma and COPD

In asthma, based on current use of inhaled therapies, switching even 25% of MDI prescriptions to DPIs (within the same drug class) would save ~75400 MT CO_2 equivalent (figure 1C). Switching 25% of patients with mild asthma from an ICS+SABA regimen to as-needed budesonide-formoterol would further reduce GHGs by ~10700 MT CO_2e each year (figure 1D). Finally, switching 25% of patients with asthma to a lower carbon footprint MDI could save ~63600 MT CO_2e annually (figure 1E).

In COPD, switching 25% of MDI prescriptions to DPIs (in drug classes where both devices are available) would cut ~95200 MT CO_2e (figure 1C). Furthermore, switching 25% of LAMA and ICS/LABA prescriptions (in two separate inhalers) to a LAMA/LABA/ICS inhaler could save ~80000 MT CO_2e, even after accounting for the increased adherence anticipated with monotherapy (figure 1D). Finally, switching 25% of patients to a lower carbon footprint MDI within the same class would save ~106200 MT CO_2e (figure 1E).
Detailed calculations and supportive information are presented in online supplemental material 1, appendix C, table S1, S2 (asthma), and in online supplemental material 1, appendix C, table S6, S7 (COPD).

Herein, we illustrate the anticipated GHG emission reductions achievable through switching 25% of patients with mild asthma from an ICS+SABA regimen to as-needed budesonide-formoterol and 25% of patients receiving a prescription for a LAMA and an ICS/LABA (in two separate inhalers) to a LAMA/LABA/ICS inhaler.

Detailed calculations and supportive information are presented in online supplemental material 1, appendix C, table S3 (asthma), and in online supplemental material 1, appendix C, table S8 (COPD).

Even after accounting for the overlap in carbon savings achieved through these three outlined strategies, the total impact of these changes would be an emission reduction by ~91 900 MT CO₂e in asthma (online supplemental material 1, appendix D, table S1) and ~1 70 200 MT CO₂e in COPD (online supplemental material 1, appendix D, table S2)—the combined equivalent of taking 58 300 passenger vehicles off the roads each year.

Expected carbon savings from each of the described strategies are outlined in figure 2.

When calculating carbon savings from ‘switching 25% of patients to therapeutic options with lower global warming potential,’ we accounted for overlapping carbon savings from the three outlined strategies: (1) switching MDIs to DPIs; (2) switching separate inhalers to combination inhalers; and (3) switching from high to lower global warming potential MDIs.

Detailed calculations and supportive information are presented in online supplemental material 1, appendix D, table S1 (asthma), S2 (COPD).

**DISCUSSION**

Our analysis shows that considerable carbon savings can be achieved by addressing three major aspects of care in asthma and COPD: misdiagnosis, suboptimal symptom control, and prominent use of strategies featuring MDI prescriptions.

Given that only 48% and 36% of patients with a clinical diagnosis of asthma or COPD, respectively, are sent for rescue inhalers: SABA, Rescue inhalers: MDI.

Table 2 | Carbon footprint associated with misdiagnosis of asthma in Canada

<table>
<thead>
<tr>
<th>A</th>
<th>Prevalence of clinically-diagnosed asthma</th>
<th>3 800 000 people</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>Number of people in ‘A’ who do not have objective evidence of disease</td>
<td>1 254 000 people</td>
</tr>
<tr>
<td>C</td>
<td>Number of people in ‘B’ who are using asthma medications</td>
<td>990 660 people</td>
</tr>
<tr>
<td>D</td>
<td>Number of people in ‘C’ who are using a SABA MDI</td>
<td>931 220 people</td>
</tr>
<tr>
<td>E</td>
<td>Carbon footprint associated with SABA MDI use in people in ‘D’</td>
<td>12 735 MT CO₂e</td>
</tr>
<tr>
<td>F</td>
<td>Number of people in ‘C’ who are using an ICS MDI</td>
<td>76 891 people</td>
</tr>
<tr>
<td>G</td>
<td>Carbon footprint associated with ICS MDI use in people in ‘F’</td>
<td>5 905 MT CO₂e</td>
</tr>
<tr>
<td>H</td>
<td>Number of people in ‘C’ who are using an ICS/LABA MDI</td>
<td>16 866 MT CO₂e</td>
</tr>
<tr>
<td>I</td>
<td>Carbon footprint associated with ICS/LABA MDI use in people in ‘H’</td>
<td>8 911 18 people</td>
</tr>
<tr>
<td>J</td>
<td>Carbon footprint of MDIs in misdiagnosed patients</td>
<td>35 039 MT CO₂e</td>
</tr>
<tr>
<td>K</td>
<td>Carbon footprint of DPIs in misdiagnosed patients – online supplemental appendix, table S1</td>
<td>8 14 MT CO₂e</td>
</tr>
<tr>
<td>L</td>
<td><strong>Total inhaler carbon footprint due to misdiagnosed patients</strong></td>
<td>35 852 MT CO₂e</td>
</tr>
</tbody>
</table>

Detailed calculations, supportive information, and additional data on DPIs are presented in online supplemental material 1, appendix C, table S1.

DPI, dry powder inhaler; ICS, inhaled corticosteroid; LABA, long-acting beta₂-agonist; MDI, metered-dose inhaler; MT CO₂e, metric tons of CO₂ equivalent; SABA, short-acting beta₂-agonist.
confirmatory objective testing,38 39 many patients carrying this label do not in fact have the disease. In addition to the substantial carbon savings that we have demonstrated, addressing this misdiagnosis in asthma and COPD will benefit health systems and patients alike by decreasing unnecessary medication use and corresponding costs and side-effects, and by reducing delays in identifying the actual diagnosis in misdiagnosed patients.40 Although carbon savings achieved by addressing misdiagnosis have been considered in other diseases,41 we are not aware of comparable analyses in airways diseases. However, we do note that significant ‘underdiagnosis’ also exists, with 20–70% of patients with asthma42 and up to 70% of patients with COPD in the community being undiagnosed.43 Accordingly, approaches to improve availability and uptake of objective testing will also likely drive increased appropriate diagnoses and corresponding treatment. Although this will improve patient outcomes, it will decrease carbon savings achieved through reduced misdiagnosis. However, if previously undiagnosed patients are managed according to guideline criteria to achieve good disease control and are preferentially prescribed DPI inhalers (the other two analysed strategies), the environmental impact of new diagnoses will be minimal.

Over half of patients with asthma44–46 and COPD47 do not meet guideline criteria for well-controlled disease. Multiple criteria are considered when defining disease control.29 48 In asthma, the most common reason for a poor control status is a high acute symptom burden requiring frequent rescue therapy,25 while in COPD, exertional dyspnoea and overall disability seem to drive overuse.28 In addition to expected improvements in health and healthcare system burden, our analysis demonstrates that improving disease control reduces the carbon footprint associated with both asthma and COPD.49 Previous authors have suggested comparable carbon savings with such an approach using European market share data.5 50 Ultimately, markets in which MDIs dominate SABA prescriptions, such as the US,18 the UK19 and Canada,20 or where SABA excess use is more prevalent51 will realise the greatest GHG emission reductions from therapeutic optimisation. Although escalation of controller therapy will be required to achieve control in most patients, non-pharmacological interventions remain an underused but important aspect of care that will also reduce rescue inhaler use and corresponding GHG emissions (see Solutions, below). It is also of note that in improving disease control, not only would emissions from day-to-day rescue inhaler use be reduced, but also those associated with exacerbation care (estimated at ~700 000 MT CO₂e a year in the UK alone).19

<table>
<thead>
<tr>
<th>Table 2 Carbon footprint associated with misdiagnosis of COPD in Canada</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A</strong> Prevalence of clinically-diagnosed COPD</td>
</tr>
<tr>
<td><strong>B</strong> Number of people in ‘A’ who do not have objective evidence of disease</td>
</tr>
<tr>
<td><strong>C</strong> Number of people in ‘C’ who are using COPD medications</td>
</tr>
<tr>
<td><strong>D</strong> Number of people in ‘C’ who are using a SABA MDI</td>
</tr>
<tr>
<td><strong>E</strong> Carbon footprint associated with SABA MDI use in people in ‘D’</td>
</tr>
<tr>
<td><strong>F</strong> Number of people in ‘C’ who are using a SAMA MDI</td>
</tr>
<tr>
<td><strong>G</strong> Carbon footprint associated with SAMA MDI use in people in ‘F’</td>
</tr>
<tr>
<td><strong>H</strong> Number of people in ‘C’ who are using an ICS/LABA MDI</td>
</tr>
<tr>
<td><strong>I</strong> Carbon footprint associated with ICS/LABA MDI in people in ‘H’</td>
</tr>
<tr>
<td><strong>J</strong> Carbon footprint of MDIs in misdiagnosed patients</td>
</tr>
<tr>
<td><strong>K</strong> Carbon footprint of DPIs in misdiagnosed patients – online supplemental appendix A, table S2</td>
</tr>
<tr>
<td><strong>L</strong> Total inhaler carbon footprint due to misdiagnosed patients</td>
</tr>
</tbody>
</table>

Detailed calculations and additional data on DPIs are presented in online supplemental material 1, appendix A, table S2.

COPD, chronic obstructive pulmonary disease; DPI, dry powder inhaler; ICS, inhaled corticosteroid; LABA, long-acting β₂-agonist; MDI, metered-dose inhaler; MT CO₂e, metric tons of CO₂ equivalent; SABA, short-acting β₂-agonist; SAMA, short-acting muscarinic antagonist.
Over the years, despite the availability of propellant-free devices (eg, DPIs), MDIs have remained the most widely used delivery system for short-acting relievers (>90% of inhalers sold), as well as for ICSs and ICS/LABAs (about half of inhalers sold), despite multiple DPI options in these classes. Our study expands on previous findings suggesting that switching MDIs to DPIs could offer attractive carbon savings in asthma and COPD. Janson et al reported that switching 80% of Salbutamol MDIs to DPIs would save 550,000 MT CO₂e annually in the UK. Although we used a more conservative 25% estimate, per capita GHG savings estimates were similar in our study. It is of note, however, that this benefit will be attenuated in markets where DPIs already have a larger market share (eg, Sweden). Although concerns arise about higher costs of DPIs, Wilkinson et al showed that drug costs can actually decrease when selecting the lowest cost DPI within the same drug class. In a global analysis, Kponee-Shovein et al calculated that substituting 2–5% of MDIs with DPIs annually would result in inhaler GHG emission reductions by 38–58% over 50 years, with only slightly increased costs. While the impact of switching devices on asthma control might also be of concern for clinicians, one study showed that changing prescriptions from MDIs to DPIs for the same molecule succeeded in significantly reducing the carbon footprint associated with therapy without loss of control. We also show that favouring budesonide/formoterol DPI rescue and maintenance therapy in mild asthma and combining separate inhalers into a single triple therapy combination inhaler in some patients can drive further GHG emission reductions. Each of these approaches is preferred by patients and increases adherence. Finally, even switching within MDIs can sometimes be beneficial. Controller MDIs using an HFC-227ea propellant carry a global warming potential that is 2.65 times higher than those using an HFC-134a propellant. Similarly, some SABA MDIs use ethanol and/or oleic acid to reduce the amount of propellant required, providing a lower GHG-emitting option within the SABA MDI class. Given that about 5% of patients struggle to use DPIs and that some prefer MDIs, we identified sizeable carbon savings achievable simply by switching some patients to lower GHG-emitting MDIs. Of note, HFC-152a—a new propellant expected to enter the market in 2025—may enable a 90% emission reduction in each actuation (as compared...
with HFC-134a, used in most MDIs), highlighting that future innovations present opportunities for even greater impact.

**Solutions**

Several strategies can be implemented to address the three analysed aspects of care responsible for avoidable GHG emissions in asthma and COPD.

**Improving diagnosis**

Addressing misdiagnosis in asthma and COPD requires increased use of objective pulmonary function testing, particularly in primary care, where the majority of such patients are managed. A recent systematic review applied the Theoretical Domains Framework to identify barriers and enablers to use of spirometry in suspected asthma and/or COPD in primary care settings. Matching these determinants to corresponding behaviour change techniques, they suggested that interventions with the following components could be effective in this setting: electronic-medical record-embedded prompts for objective testing; improved remuneration for spirometry performance and interpretation in office settings; improved access (decreased wait times and travel distances) to spirometry in laboratory settings; audit and feedback on provider performance; and provider education regarding the inaccuracy of clinical diagnosis. The carbon footprint savings identified in our analysis could also be included in such educational content, as environmental stewardship is a potent motivator for change in primary care practice.

**Improving symptom control**

Improvements in symptom control in order to reduce rescue inhaler use may be achieved through both provider-facing and patient-facing interventions. Studies show that primary care providers do not routinely assess their patients’ asthma control, leading to under-recognition of poor control and corresponding under-prescription of controller medications. Over two-thirds of patients with poorly controlled asthma have not been prescribed first-line or second-line controller therapies, and when they do escalate therapy, providers do not follow guideline recommendations in a majority of cases. In COPD, assessments of dyspnoea, impact of symptoms on daily life and risk of future acute exacerbations—which should guide pharmacotherapy—are seldom performed in practice, leading to both

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**Table 3** Carbon footprint associated with excess SABA inhaler use in asthma

<table>
<thead>
<tr>
<th></th>
<th>Prevalence of clinically-diagnosed asthma</th>
<th>3 800 000 people</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Mild overuse: &gt;150 to 375 uses (doses) of SABA per year*</td>
<td>750 120 people</td>
</tr>
<tr>
<td>B</td>
<td>Number of people in ‘A’ who use a SABA MDI &gt;150 to 375 times per year</td>
<td>22 194 MT CO₂e</td>
</tr>
<tr>
<td>C</td>
<td>Carbon footprint associated with excess SABA MDI use in people in ‘B’</td>
<td>27 126 MT CO₂e</td>
</tr>
<tr>
<td>D</td>
<td>Number of people in ‘A’ who use a SABA MDI &gt;375 to 750 times per year</td>
<td>2 500 40 people</td>
</tr>
<tr>
<td>E</td>
<td>Carbon footprint associated with excess SABA MDI use in people in ‘D’</td>
<td>11 273 MT CO₂e</td>
</tr>
<tr>
<td>F</td>
<td>Number of people in ‘A’ who use a SABA MDI &gt;750 times per year</td>
<td>7 144 0 people</td>
</tr>
<tr>
<td>G</td>
<td>Carbon footprint associated with excess SABA MDI use in people in ‘F’</td>
<td>132 MT CO₂e</td>
</tr>
<tr>
<td>H</td>
<td>Total carbon footprint of SABA MDI overuse</td>
<td>60 594 MT CO₂e</td>
</tr>
<tr>
<td>I</td>
<td>Carbon footprint of SABA DPI overuse – online supplemental appendix B, table S1</td>
<td>132 MT CO₂e</td>
</tr>
<tr>
<td>J</td>
<td>Total carbon footprint of SABA inhaler overuse</td>
<td>60 726 MT CO₂e</td>
</tr>
</tbody>
</table>

Detailed calculations, supportive information and additional data on DPIs are presented in online supplemental material 1, appendix B, table S1.

*Overuse is defined as requiring >150 uses (doses) of a SABA over a year. This reflects a conservative definition, given that guidelines define well-controlled asthma as no more than two uses (doses) of SABA per week. Note that a typical use (dose) of a SABA MDI consists of two medication actuations, and of a SABA DPI consists of one medication actuation). Categories of people overusing SABA are derived from Nwaru, Ekstrom. We calculated the mid-point estimate for mild and moderate SABA overuse categories, and the low-point estimate for the severe overuse category. We did not count the first 150 uses (doses) in any category, as those doses are considered within the acceptable limit for good asthma control.

DPI, dry powder inhaler; MDI, metered-dose inhaler; MT CO₂e, metric tons of CO₂ equivalent; SABA, short-acting beta₂-agonist.
under-prescription of long-acting bronchodilators and over-prescription of ICSs. In both diseases, lack of symptom assessment also results in missed opportunities for therapeutic de-escalation in well-controlled patients (which in some cases, would reduce GHG emissions). These gaps are driven by multiple barriers including a lack of knowledge of disease control parameters, lack of time to assess control, and lack of familiarity with what is often rapidly changing guidance. Accordingly, strategies to improve treatment will be necessarily complex and multifaceted. Recently, a technology-based intervention that includes a patient-facing questionnaire linked

Table 4  Carbon footprint associated with excess short-acting bronchodilator use in COPD

| A | Prevalence of clinically-diagnosed COPD (after subtracting people with misdiagnosed COPD – table 2) 2000000 people |
| B | Number of people in ‘A’ who have moderate to severe disease 1440000 people |
| C | Number of people in ‘B’ with mild rescue overuse and who are using a SABA MDI 362629 people |
| D | Carbon footprint of people in ‘C’ 10443 MT CO₂e |
| E | Number of people in ‘B’ with mild rescue overuse and who are using a SAMA MDI 20304 people |
| F | Carbon footprint of people in ‘E’ 585 MT CO₂e |
| G | Number of people in ‘B’ with severe rescue overuse and who are using a SABA MDI 241753 people |
| H | Carbon footprint of people in ‘G’ 67301 MT CO₂e |
| I | Number of people in ‘B’ with severe rescue overuse and who are using a SAMA MDI 13536 people |
| J | Carbon footprint of people in ‘I’ 3768 MT CO₂e |
| K | Carbon footprint of MDI overuse 82097 MT CO₂e |
| L | Carbon footprint of DPI overuse – online supplemental appendix B, table S5 162 MT CO₂e |
| M | Total carbon footprint of inhaler overuse 82259 MT CO₂e |

Detailed calculations, supportive information and additional data on DPIs are presented in online supplemental material 1, appendix B, table S5.

COPD, chronic obstructive pulmonary disease; MDI, metered-dose inhaler; MT CO₂e, metric tons of CO₂ equivalent; SABA, short-acting beta₂-agonist; SAMA, short-acting antimuscarinic agents.

Figure 2  Percentage of total anticipated carbon savings resulting from improving each aspect of care that contributes to avoidable use of inhalers in asthma and COPD. COPD, chronic obstructive pulmonary disease.
to a computerised decision support system for primary care providers improved both assessment of control and prescription of controller therapies. Successful strategies such as this require adaptation for COPD and scaling across health systems.

Even when providers prescribe appropriate controller therapies, patient disease management knowledge and treatment adherence remain low. Self-management interventions including education, regular practitioner review and a written self-management action plan, as well as patient decision aids, have been shown to improve adherence, leading to reduced requirements for rescue therapy in asthma and COPD. Effective delivery of such educational interventions across health systems will require a commitment to train and fund multidisciplinary personnel with required expertise.

**Optimising therapeutic choice**

Carbon savings through preferential use of DPIs (or lower GHG-emitting MDIs) over conventional MDIs can be realised by selecting the preferred device at the time of initial prescription, through strategies such as provider education and default choices in electronic medical record systems. Although switching patients on established therapy to new devices may also be considered, this may affect medication self-efficacy and adherence, and increases the risk of administration errors and loss of symptom control, paradoxically increasing emissions due to acute care events (which are highly carbon-intensive). Accordingly, therapeutic switches must be paired with proper device education. Here, pharmacist-led education has been shown to improve technique, and new device technologies providing real-time patient feedback present a promising adjunct. It is of note, however, that about 5% of patients demonstrate insufficient inspiratory effort to adequately use a DPI (note that in some reports up to one-third of patients did not adequately use an MDI). Also, DPIs require coordination of respiratory efforts that may be challenging for children aged 6 or under, and many patients simply prefer MDIs. Accordingly, device selection should be individualised. Although unconceived switches should not be considered, in patients who want to discuss different inhaler options, clinicians could present a range of options along with information about their differing environmental impacts (an aspect that >80% of patients value) in order to reach a shared treatment decision.

The same approaches could be used to drive use of therapeutic strategies featuring combination inhalers rather than separate inhalers, also driving carbon savings. In fact, decision aids addressing some of these shared decisions already exist. The British National Institute for Health and Care Excellence produced a decision aid that compares inhalation manoeuvre requirements and carbon footprint between MDI and DPI devices. In mild asthma, an electronic decision aid and conversation aid address the choice between (separate) ICS+SABA inhalers and as-needed budesonide/formoterol DPI. Herein, we present a one-page conversation aid for choosing a reliever inhaler in patients with mild asthma, adding to existing tools by including comparisons between high-GHG-emitting and low-GHG-emitting MDI devices, treatment costs and device disposal considerations (figure 3) (also see online supplemental material S2).

This conversation aid can be used to arrive at a shared decision between patients and providers surrounding selection of a rescue inhaler device.

**Limitations**

Our analysis has several limitations. First, in our calculations, we used life-cycle assessment GHG emissions that are comprised of emissions from the production, use and the end-of-life disposal of the device, and emissions from the propellant (for MDIs). However, our calculations do not consider emissions associated with the active pharmaceutical ingredient in each device, whereby actual inhaler GHG emissions for all devices are higher than reported. Second, avoidable GHG emissions from misdiagnosis may be slightly overestimated due to the fact that a small proportion of patients misdiagnosed with asthma could in fact have COPD, and vice-versa. Third, carbon savings achieved by the three main approaches suggested are not necessarily additive. For example, reductions in MDI use through improved diagnosis and disease control would limit additional emission reductions achievable through MDI to DPI substitutions. We attempted to account for this by considering carbon savings from only 25% of devices being substituted. Similarly, if patients with mild asthma preferentially receive as-needed budesonide/formoterol DPI rather than ICS+SABA therapy, GHG emission reductions that would otherwise have been achieved through improved diagnosis and disease control would be reduced. A similar effect would be seen if there was broad use of maintenance and reliever therapy with budesonide/formoterol DPI in moderate or severe asthma. We also note that our analysis of GHG emission reductions achieved through improved diagnosis and disease management did not consider possible further reductions realised through averted exacerbations and hospitalisations as well as the carbon footprint of treating patients in intensive care units, which are all major contributors to healthcare emissions.

Finally, although this paper focuses on carbon footprint due to the urgent need to reduce GHG emissions by 2030, other environmental impacts of all inhaled devices may include water eutrophication and ecotoxicity but require further study. In the coming years, with advancement of: strategies to improve recycling and/or incineration of MDIs (allowing for recovery/disposal of unused propellant); propellant-free, reusable MDIs; newer MDIs that use less propellant; and MDIs that use new (lower global warming potential) propellants (eg, HFC-152a or HFC-1234ze), the balance of environmental impacts between MDIs and DPIs may shift in the
medium-to-long term, stressing the importance of improving diagnosis and control to reduce overall inhaler use, rather than focusing primarily on switching from MDIs to DPIs.

Conclusions

Our analysis of the environmental impact of inhalers in asthma and COPD concludes that addressing misdiagnosis, reducing excess rescue inhaler use due to suboptimal baseline control and switching patients to lower global warming potential devices and/or regimens could result in GHG emission reductions of ~454,200 metric tons per year in Canada. This would be the equivalent to taking ~101,100 gasoline-powered passenger vehicles off Canadian roads each year. As these gaps and patterns of care are common across countries, our findings should apply to other jurisdictions, though quantitative benefits will depend on local differences in the magnitude of care gaps and the existing balance between MDI and DPI use. Although previous literature has mostly focused on estimating the environmental impact of switching from MDI to DPI devices, our analysis shows that bridging fundamental care gaps with respect to misdiagnosis and optimal care could also have a dramatic carbon footprint impact. Accordingly, efforts to address GHG emissions from inhalers should focus on interventions to improve quality of care rather than solely on strategies to promote device substitution, given that the former will also improve patient outcomes. Although strategies to achieve the required changes in behaviour by both providers and patients are complex and multifold, the added incentive of these identified environmental benefits may provide a powerful additional motivator for change.

Contributors

MG and SGu wrote the initial draft. AK and SGr revised it for important intellectual content. All authors gave final approval of the version to be submitted. SGu is the guarantor of the clinical content of this submission.

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Table: Which Inhaler Device Should Your Patient Use for Symptom Relief? A Conversation Aid (for Canadians aged 12 and over with mild asthma)

<table>
<thead>
<tr>
<th>Your inhaler options:</th>
<th>Metered-Dose Inhaler</th>
<th>Dry-Powder Inhaler</th>
<th>Controller + Reliever*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reliever only</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acomir 200 (100 mcg, 2 puffs/dose)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventolin HFA 200 (100 mcg, 2 puffs/dose)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Releaser only</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventolin Diskus 60 (200 mcg, 1 puff/dose)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bricanyl Turbuhaler 100 (0.5 mg, 1 puff/dose)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Controller + Reliever</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symbicort Turbuhaler 120 (200/6 mcg, 1 puff/dose)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Annual Use†</th>
<th>1 inhaler/year</th>
<th>1 inhaler/year</th>
<th>2 inhalers/year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disposal</td>
<td>Return to pharmacy for recycling/incineration‡</td>
<td>Return to pharmacy for recycling/incineration‡</td>
<td>Return to pharmacy for safe disposal</td>
</tr>
<tr>
<td>Carbon footprint of 100 doses§</td>
<td>Equivalent to a 40 km car journey</td>
<td>Equivalent to a 110 km car journey</td>
<td>Equivalent to a 4 km car journey</td>
</tr>
<tr>
<td>Cost per 100 doses</td>
<td>$19 (plus $44-52 for a steroid inhaler)</td>
<td>$20 (plus $44-52 for a steroid inhaler)</td>
<td>$42 (plus $44-52 for a steroid inhaler)</td>
</tr>
<tr>
<td></td>
<td>$42 (plus $44-52 for a steroid inhaler)</td>
<td>$23 (plus $44-52 for a steroid inhaler)</td>
<td>$104 (plus $0 for a steroid inhaler)</td>
</tr>
</tbody>
</table>

*Only if people using Symbicort® as monotherapy. †Based on an average use of 2 doses/week (reflecting optimal symptom control). ‡Returning the inhaler to the pharmacy allows for propellant recycling and/or incineration (a process which degrades leftover greenhouse gases). §Based on the carbon footprint of each individual agent.

Figure 3 An in-office conversation aid to support patients with mild asthma in choosing their rescue inhaler.
REFERENCES

38. Sokal KC, Sharma G, Lin YL, et al. Choosing wisely: adherence by physicians to recommended use of Spirometry in the diagnosis and