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Early View

Original research article

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ORIGINAL RESEARCH

Janson et al

Reducing carbon footprint by switching to reusable soft mist inhalers

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ABSTRACT (250 words)

Objective

Inhalation therapy is the cornerstone of chronic obstructive pulmonary disease, together with non-pharmacological treatments. Long-acting muscarinic antagonists (LAMAs), alone or in combination with long-acting beta agonists (LABAs), are commonly used. Pressurised metered-dose inhalers (pMDIs), dry powder inhalers (DPIs), and soft mist inhalers (SMIs) are used, each with different carbon footprints. This study aimed to assess the carbon footprint of hypothetically replacing LAMA or LAMA/LABA inhalers with an SMI, Respimat Reusable, within the same therapeutic class.

Methods

An environmental impact model was established to assess the change in carbon footprint of replacing pMDIs/DPIs with Respimat Reusable within the same therapeutic class (LAMA or LAMA/LABA), across 12 European countries and the United States over 5 years. Inhaler use for country and disease-specific populations was derived from international prescribing data and the associated carbon footprint (CO_2 equivalents) were identified from published sources.

Results

Over 5 years and across all countries, replacing LAMA inhalers with Spiriva Respimat Reusable reduced CO_2e emissions by 13.3–50.9%, saving 93–6,228 tonnes of CO_2e in the different countries studied. Replacing LAMA/LABA inhalers with Spiolto Respimat Reusable reduced CO_2e emissions by 9.5–92.6%, saving 31–50,843 tonnes of CO_2e. In scenario analyses, which included total replacement of DPIs/pMDIs, consistent CO_2e savings were estimated. Sensitivity analyses showed that results were sensitive to changes in several parameters including varying assumptions around re-usability of inhalers and potential CO_2e impact.

Conclusion

Replacement of pMDIs and DPIs with Respimat Reusable within the same therapeutic class, would result in substantial reductions in CO_2e emissions.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) and asthma are chronic respiratory conditions, with increasing global prevalence.[1, 2] Currently, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) [3] recommend the use of inhaled therapies such as long-acting muscarinic antagonists (LAMAs), alone or in combination with long-acting beta agonists (LABAs) as maintenance treatment for the majority of COPD patients.[3]

Three types of inhalation devices can be used to administer LAMA and LAMA/LABA therapy: pressurised metered-dose inhalers (pMDIs), dry powder inhalers (DPIs), and soft mist inhalers (SMIs).[4] The carbon footprint, expressed in carbon dioxide equivalents (CO_2e), of these three devices differs, with pMDIs being higher than DPIs or SMIs due to use of hydrofluorocarbon (HFC) propellants. The use of HFC is currently being phased down under the Kigali Amendment to the Montreal Protocol, 2016.[5] This stimulus to switch away from HFC pMDIs has prompted innovation of inhaler design, including reusable inhalers and SMIs, with potential to further reduce the carbon footprint.[6] Several global and regional organisations and governments have started to design and implement measures to reduce emissions in the healthcare sector, including the Netherlands [7] and the NHS in the United Kingdom (UK), as outlined in its Long Term Plan, 2019.[8] Furthermore, British Thoracic Society's national guidance has recommended offering patients low carbon alternatives to pMDI, where clinically appropriate.[9]

To exemplify the high carbon footprint of pMDIs, it was estimated that using 50% of inhaler devices with a low carbon footprint, such as DPIs, would save the equivalent of 288,000 tonnes of CO_2e every year, equivalent to taking more than 61,000 cars off the road.[10] No such comparison has been made regarding the carbon footprint of switching pMDIs or DPIs for SMIs, with one study grouping DPIs and SMIs together for analysis.[11] As the carbon footprint is different for every inhaler, robust quantification is needed to assess the current impact of the three types of inhaler devices. This study aimed to compare the carbon footprint, measured in terms of CO_2e emissions, of switching the COPD patient population to the SMI, Respimat Reusable. The main analysis focused on switching within the same therapeutic class, and additional scenarios were conducted to complement the main analysis.

METHODS

Model design

An environmental impact model was developed to assess the change in carbon footprint of 47 different inhalers, including all inhaled treatment classes used in COPD and asthma across 13 countries in Europe and the United States (US). The carbon footprint of replacing DPIs and pMDIs with Respimat Reusable within the same therapeutic class, over a time horizon of five years (2021–2025) in Europe and US was calculated (Figure 1). This hypothetical replacement did not consider further treatment settings and excluded short-acting beta-agonists (SABAs). The model was developed in accordance with ISPOR best practice guidelines for budget impact modelling.[12]

The geographic scope of this study was 13 countries spanning Europe (Belgium, Denmark, France, Germany, Greece, Italy, Netherlands, Norway, Portugal, Spain, Sweden, UK) and the US. These countries were grouped according to the United Nations geoscheme: Northern Europe (Denmark, Norway, Sweden, UK), Southern Europe (Greece, Italy, Spain, Portugal), Western Europe (Belgium, Germany, Netherlands, France), and US.[13]

Patient population

In the model, the eligible population was adults with COPD and asthma on maintenance inhaled therapies. Volumes (number of units) and market shares for each product were derived from IQVIA MIDAS® international data (2021) (Supplementary Table 1). In the model, market share data was not altered over the time horizon of 2021–2025 and no population growth was applied. For each country, the size of the eligible population was estimated as the sold yearly dosages based on market share data.

Main analysis and scenario analyses

The main analysis assessed the carbon footprint of replacing DPI and pMDI with Spiriva Respimat Reusable within the LAMA treatment class and replacing DPI and pMDI with Spiolto Respimat Reusable within the LAMA/LABA treatment class. Additional scenario analyses were conducted for replacing clinically relevant therapeutic class or DPIs/pMDIs with Respimat Reusable over five years (2021–2025). A total of five scenario analyses were conducted, as outlined in Table 1.

Carbon footprint

A targeted literature review was undertaken to estimate the carbon footprint of DPIs, pMDIs and Respimat Reusable. Searches were run using key search terms for disease, intervention, and outcomes on the PubMed database. Inclusion criteria included full text studies published from the year 2000 onwards reporting data on carbon footprint and greenhouse gases, environmental or global warming impact of DPIs, pMDIs, or SMIs for use in COPD, asthma, or other respiratory diseases. Where necessary, outcomes were converted to annual CO_2e based on recommended administration frequency. Hand searching of relevant websites and databases (Google Scholar, National Health Service (NHS), United Nations, World Health Organization, and the European Union) was also conducted for carbon emissions, carbon footprint, and climate change of DPIs or pMDIs, along with data on inhalers and sustainable prescribing.

At the time of the literature review, published estimates on carbon footprint were available for Ellipta, Breezhaler, Accuhaler, Nexthaler, Evohaler, Foster, and Flutiform (Table 1). The carbon footprint of Respimat Reusable has been previously reported by Hänsel et al. (2019).[14] Spiolto Respimat Reusable and Spiriva Respimat Reusable have equivalent carbon footprints.

To estimate the carbon footprint of inhalers with no available data, an average, by inhaler type, was taken between the available estimates and attributed to those inhalers (Table 2). As previously reported by Janson et al. (2020),[15] and Hänsel et al. (2019) [14], 17% of total carbon footprint was attributed to refill based on the proportion of active pharmaceutical ingredients and distribution. A weighted average by therapeutic class/inhaler class was calculated based on the units sold and the associated carbon footprint. The carbon footprint of DPIs was split between the inhaler device and the refill-package.

Inhaler use

Annual use of disposable and reusable DPIs and disposable pMDIs was estimated based on the following assumptions: each patient must cover their annual drug consumption either by using inhalers or refills and each device (inhaler or refill) is assumed to cover one month of drug consumption. It was assumed that each patient on disposable pMDI devices used 12 units per year,

those prescribed Respimat Reusable used 2 inhalers and 12 refills per patient per annum, and IQVIA MIDAS® data on refill rates were used to calculate the average number of DPIs per country. The average number of inhalers used per year and patient by therapeutic and inhaler class was calculated based on these assumptions (Supplementary Table 2). This average was weighted by the number of sold units of each product, in each country.

Sensitivity analyses

The robustness of the results was assessed by carrying out several sensitivity analyses. These included varying assumptions around the extent of inhaler reuse in practice, changing the carbon footprint per inhaler, market shares for devices and therapeutic classes, and the extent of switching from 100% in the base case to alternative switching assumptions.

RESULTS

Main analyses

Replacement of LAMA inhalers with Spiriva Respimat Reusable

Over five years, inhalers used in the LAMA class (a combination of pMDI, DPI, SMI) were estimated to contribute 0.05 mega tonnes of CO_2e emissions across all countries (Table 3). A hypothetical replacement of DPIs and pMDIs in the LAMA class with Spiriva Respimat Reusable could reduce CO_2e emissions by 37.2%, over five years. These reductions varied by country, due to device ratio differences and ranged between 13.3% and 50.9%, saving between 93 and 6,228 tonnes of CO_2e emissions (Figure 2). In Northern Europe, CO_2e emissions were reduced by 33.9% (3,450 tonnes), in Southern Europe, CO_2e emissions were reduced by 42.2% (5,692 tonnes), in Western Europe, CO_2e emissions were reduced by 23.1% (2,374 tonnes), and in the US, CO_2e emissions were reduced by 45.3% (6,228 tonnes) when replaced with Spiriva Respimat Reusable.

Replacement of LAMA/LABA inhalers with Spiolto Respimat Reusable

Over five years, inhalers as used in the LAMA/LABA class (combination of pMDI, DPI and SMI; ratios differ per country) were estimated to contribute 0.08 mega tonnes of CO_2e emissions across all countries (Table 3). A hypothetical replacement of LAMA/LABA inhalers with Spiolto Respimat Reusable could reduce CO_2e emissions by 77.8%, over five years. These reductions varied by country, due to device ratio differences and ranged between 9.5–92.6%, saving between 31 and 50,843 tonnes of CO_2e emissions (Figure 3). In Northern Europe, CO_2e emissions were reduced by 64.4% (5,223 tonnes), in Southern Europe, CO_2e emissions were reduced by 28.7% (1,598 tonnes), in Western Europe, CO_2e emissions were reduced by 42.6% (5,179 tonnes), and in the US, CO_2e emissions were reduced by 92.6% (50,843 tonnes) when replaced with Spiolto Respimat Reusable.

Scenario analyses

1. Replacement of LABA/ICS inhalers with Spiolto Respimat Reusable

Over five years, LABA/ICS inhalers were estimated to contribute 2.0 mega tonnes of CO_2e emissions across all countries (Supplementary Table 3). A hypothetical switch from these devices to Respimat Reusable could reduce this emission by 93.5% (to 0.1 mega tonnes). Due to device ratio differences

per countries, these results vary between 71.8% and 95.3% reduction in the countries studied, saving between 7,683 and 807,077 tonnes of CO_2e (Supplementary Figure 1).

2. Replacement of triple fixed dose combination inhalers with Spiolto Respimat Reusable

Over five years, triple therapy with LAMA/LABA/ICS through FDC inhalers were estimated to contribute 0.3 mega tonnes of CO_2e emissions across all countries (Supplementary Table 3). A hypothetical switch from these devices to Respimat Reusable could reduce this emission by 95.9% (to 0.01 mega tonnes). Due to device ratio differences per countries, these results vary between 70.7 and 98.4%, saving between 277 and 118,079 tonnes of CO_2e in the countries included in the analysis (Supplementary Figure 2).

3. Replacement of DPI with Respimat Reusable

Over five years, DPI were estimated to contribute 0.4 mega tonnes of CO_2e emissions across all countries (Supplementary Table 4). A hypothetical replacement of DPIs with Respimat Reusable could reduce this emission by 64.7% (to 0.1 mega tonnes). Due to device ratio differences per countries, these results vary between 59.4 and 69.2%, saving between 2,207 and 66,334 tonnes of CO_2e (Supplementary Figure 3).

4. Replacement of pMDIs with Respimat Reusable

Over five years, pMDI were estimated to contribute 2.1 mega tonnes of CO_2e emissions across all countries (Supplementary Table 4). A hypothetical replacement of pMDIs with Respimat Reusable, could reduce this emission by 97.1% (to <0.1 mega tonnes). Due to device ratio differences per countries, these results vary between 94.3% and 98.3%, saving between 7,729.3 and 847,218.4 tonnes of CO_2e (Supplementary Figure 4).

5. Replacement of DPIs and pMDIs with Respimat Reusable

Over five years, both pMDIs and DPIs were estimated to contribute 2.5 mega tonnes CO_2e emissions across all countries (Supplementary Table 4). A hypothetical replacement of pMDIs and DPIs with Respimat Reusable could reduce this emission by 92.2% (to 0.2 mega tonnes). Due to device ratio differences per countries, these results vary between 75.9% and 94.5%, saving between 13,136.4 and 913,548.3 tonnes of CO_2e (Supplementary Figure 5). Figure 4 summarises the absolute and annual per patient CO_2e savings across the different countries if all DPIs and pMDIs were switched to Respimat Reusable.

Sensitivity analyses

The details of the sensitivity analyses for the main and scenario analyses are shown in Supplementary Table 5–17. Data show that the main analyses were most sensitive to changes in number of Respimat Reusable inhalers reused. The scenario analyses were most sensitive to changes to the extent of switching and the reusability of the different inhalers.

DISCUSSION

The objective of this study was to assess the carbon footprint of adopting SMIs (Respimat Reusable) across 13 countries in Europe and the US instead of DPIs and pMDIs. This study shows that Respimat Reusable offers considerable environmental benefits in terms of decreased CO_2e emissions when replacing disposable and reusable DPIs and pMDIs of the same therapeutic class. These data extend the previous findings of Hänsel et al. (2019),[14], Ortsäter et al. (2019),[16] Janson et al. (2020),[15], and Wachtel et al. (2020),[17] which show the environmental benefits of switching from pMDIs to devices with a lower carbon footprint and a reusable option. In a study by Pernigotti et al (2021), replacing pMDIs with DPIs/SMIs (classed as a single group), resulted in a 68% reduction in the carbon footprint across the UK, Italy, France, Germany, and Spain when 80% of pMDIs were substituted with DPI or SMIs by 2030.[11] While Pernigotti et al (2021),[11] assessed a total replacement of pMDIs, our study focused on the replacement of pMDIs and DPIs within the same therapeutic class, making the findings applicable in clinical practice. Over five years, replacing alternative LAMA DPIs and pMDIs with Spiriva Respimat Reusable saved 0.02 mega tonnes of CO_2e, equivalent to the annual carbon footprint of 2,648 EU citizens. Similarly, replacing alternative LAMA/LABA DPIs and pMDIs with Spiolto Respimat Reusable saved 0.06 mega tonnes of CO_2e, equivalent to the annual carbon footprint of 9,380 EU citizens. These data show that substantial CO_2e savings can be made with the clinically relevant replacement of inhaler devices.

Based on data from this study, the countries that would benefit most from implementing changes to inhaler use based on CO_2e emissions are the UK, US, and Germany, which is aligned with these countries having the highest prevalence of COPD and the highest ratio of pMDI prescribed. Environmental pressures have prompted governments to introduce targets to reduce the use of inhalers with a high carbon footprint, including the UK Government's Environmental Audit Committee setting the NHS the challenge of reducing the carbon footprint of inhaler use by 50% before 2028.[18] Consequently, NICE (UK) published a Patient Decision Aid on asthma inhalers in 2019 that highlights carbon footprint as a factor in inhaler choice, favouring a switch to DPIs or reusable SMIs.[19] In the UK, pMDIs account for a higher proportion of inhaler use (>50%) compared with other European countries and the US (<50%), as shown by both the market shares used in this study and the high carbon footprint of pMDIs, as shown in scenario analyses performed. Prescribing data from England show that the usage of pMDIs has remained consistent at around 55% since 2021 [20]. Earlier estimates of pMDI use in the UK were 70% in 2011,[21] suggesting that implementation of these NHS policies and efforts to limit CO_2 are working. NHS England are reported to be on track to hit the first year carbon reduction target, though what impact pMDI replacement played in this success is unclear.[22] While successes in the UK have been gained, this continued variation in pMDI prescribing practices between the UK and other countries suggests that there is still room for a reduction in the use of pMDI in the UK. Nonetheless, the implementation of the UK-like policies elsewhere could potentially reduce carbon footprint in the healthcare sector overall.

This study was a theoretical exercise, and while it is a clinically relevant replacement, an indiscriminate replacement of the entire patient population using LAMA or LAMA/LABA DPIs and pMDIs to Respimat Reusable is not feasible as not all patients would be eligible. In our analyses of additional scenarios, we also analysed the carbon footprint of switching to LAMA/LABA administered by SMI from ICS/LABA or ICS/LABA/LAMA therapy. As with the main analyses, the scenario analyses present an ideal scenario where all patients are eligible to switch, and in clinical practice some patients will benefit from ICS. Sensitivity analysis showed that when 50% of the population in each scenario were switched to Respimat Reusable, there was a minimum of a 47.1% decrease in carbon footprint after switch. Switching all COPD patients to SMIs is not clinically appropriate as some COPD

patients, those with high blood eosinophils and a history of exacerbations,[3] are recommended to be treated with ICS, which is not available in an SMI. Similarly, there are limited asthma maintenance treatments available in SMI. However, several studies have shown that overuse of ICS-containing treatment in COPD is common [23, 24] and studies have shown that withdrawal of ICS in many COPD patients can be done without negative clinical consequences.[25, 26] Our results show that the benefits of replacing ICS-containing therapy with LAMA/LABA in COPD patients inappropriately treated with ICS could be two-fold, reducing the risk of side-effects like pneumonia, alongside a reduced carbon footprint.

Nevertheless, the use of DPI and pMDI will continue based on clinical need and as per ERS recommendations, patients should not be switched between devices purely for environmental reasons.[27] It is also important to note that some DPI devices assessed in the environmental impact model are single dose reusable DPIs, with similar carbon footprints to Respimat Reusable and provide comparable environmental benefits. The GOLD group advocate choosing a tailored and personalised approach in clinical practice and choosing the most appropriate inhaler to meet individual patient needs.[3] When considering a switch for clinical need, patient engagement and preference is essential. Durability, ergonomics and ease of use are attributes that influence patient satisfaction and outcome and should be criterion to factor into switching.[4, 28, 29] Reusability and carbon footprint of the device are strong drivers of patient preference,[30, 31] and when patients are made aware of the carbon footprint of their inhalers, many are willing to try a more environmentally friendly device.[32] Patient education of carbon footprint must also be coupled with that of education of clinicians, where it has been shown that few understand the carbon footprint of devices and the presence or absence of propellants.[33] Ultimately, the greenest inhaler is a clinically appropriate device, that gives patients clinical benefit.[34]

Strengths and limitations

A key strength of this study is that it evaluated several scenarios across 13 different countries using up-to-date prescribing data. It spans across all therapeutic classes of inhaler used in COPD treatment. A key limitation to acknowledge is that the base case presents an optimistic scenario, in which all patients are switched to a reusable SMI with optimal use of devices (2 inhalers and 12 refills per patient per annum). In the USA, where Respimat is not available in a reusable format, switching all LAMA and all LAMA-LABA patients to Respimat would still save 28,857 tonnes of CO_2e, mainly due to the current significant use of LAMA-LABA pMDI. Switching inhaler types depends on the clinical need of patients, preferences for inhaler technique, and the availability of the inhaled drugs as an SMI. For this reason, fewer patients will be eligible to switch to SMI, and the maximum hypothetical carbon footprint reduction with switching to SMI is actually lower. However, both the eligibility and optimal use of devices have been accounted for in a sensitivity analysis, in which the eligible population was reduced to 50% and the number of devices were increased from two to six and 12. Second, the sensitivity analysis demonstrated uncertainty around the magnitude of the carbon footprint due to several assumptions. For example, if the reuse of inhalers (refill ratios) is overestimated, then potential CO_2e reduction when switching from a disposable to a reusable device will be lower than reported. However, overall, the sensitivity analysis demonstrated the robustness of the results showing the reduction in carbon footprint when replacing DPIs and pMDIs with SMIs. Third, our analysis is based on carbon footprint data published at the time the environmental impact model was built. In this respect, the model does not consider any newer or forthcoming devices such as pMDIs with low global warming potential or new carbon footprint data published after conducting the literature review, for example for DPIs such as Breezhaler [35] or Easyhaler.[36] Equally, should current market shares change, for example, an increase in use of LAMA-LABA pMDI,

then the switch to Respimat would provide additional carbon footprint savings. While SABAs were also not included in the model, their availability in Respimat device is limited to very few countries. Any switch from SABA pMDIs to Respimat device may provide further environmental savings. Lastly, the analysed prescribing data does not distinguish between COPD and asthma.

Conclusions

This study shows that replacement of LAMA or LAMA/LABA pMDIs and DPIs with an SMI, Respimat Reusable, could result in substantial reductions in CO_2e emissions. A step-change in COPD management and carbon footprint could be delivered through a collaborative partnership between clinicians and patients. This partnership would be driven primarily by patient characteristics and needs, followed by consideration of the carbon footprint of the inhalers.

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Conflict of interest statement

CJ has received honoraria for educational activities and lectures from AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Novartis, Orion and TEVA, and has served on advisory boards arranged by AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Novartis, Orion, Sanofi, and TEVA. LN and SL received consulting fees from Boehringer Ingelheim. JHP, SS, and ESHG are employees of Boehringer Ingelheim. The authors did not receive payment related to the development of the manuscript.

Author contributions

JHP, SS, and ESHG were responsible for developing the initial research question and design and development of the model. LN conducted the analyses. LN and SL drafted the manuscript. All authors were responsible for the interpretation of the data, revising the manuscript for important intellectual content and approving the final version for publication. All author(s) meet criteria for authorship as recommended by the International Committee of Medical Journal Editors (ICMJE). Boehringer Ingelheim was given the opportunity to review the manuscript for medical and scientific accuracy as well as intellectual property considerations.

Data availability statement

The data that support the findings of this study are available from IQVIA. Restrictions apply to the availability of these data, which were used under license for this study. Data are available from the corresponding author, Lindsay Nicholson, with the permission of IQVIA.

Table 1. Main analyses and scenario analyses

Main scenario: replace DPI and pMDI with Respimat Reusable within the same class (LAMA and LAMA/LABA only)	
Main scenario	Within the LAMA treatment class: replacing DPI and pMDI with Spiriva Respimat Reusable Within the LAMA/LABA treatment class: replacing DPI and pMDI with Spiolto Respimat Reusable
Scenario analysis: replace any DPI and pMDI with Spiolto Respimat Reusable	
Scenario 1	Replacing LABA/ICS inhalers with Spiolto Respimat Reusable
Scenario 2	Replacing LAMA/LABA/ICS triple FDC* inhalers with Spiolto Respimat Reusable
Scenario 3	Replacing DPIs from any class with Respimat Reusable
Scenario 4	Replacing pMDIs from any class with Respimat Reusable
Scenario 5	Replacing DPIs and pMDIs from any class with Respimat Reusable

*FDC, LAMA/LABA/ICS. DPI, dry powder inhaler; FDC, fixed dose combination; ICS, inhaled corticosteroid; LABA; long-acting beta-agonists; LAMA, long-acting muscarinic antagonist; pMDI, pressurised metered dose inhaler; SMI, soft mist inhaler.

Table 2. Carbon footprint of the different types and classes of inhaler used as model inputs

Device Type	Class	Product	Reusable?	CF-Inhaler[*,†]	CF-Refill[*,†]	Reference
pMDI	LABA/ICS	Symbicort	No	25.3		Janson et al. (2020); Panigone et al. (2020); Wilkinson et al. (2019), NICE (2020)
		Crivanil Plus	No	25.3		Janson et al. (2020); Panigone et al. (2020); Wilkinson et al. (2019), NICE (2020)
		Seretide	No	25.3		Janson et al. (2020); Panigone et al. (2020); Wilkinson et al. (2019), NICE (2020)
		Sirdupla	No	25.3		Janson et al. (2020); Panigone et al. (2020); Wilkinson et al. (2019), NICE (2020)
		Aliflus	No	25.3		Janson et al. (2020); Panigone et al. (2020); Wilkinson et al. (2019), NICE (2020)
		Dulera	No	25.3		Janson et al. (2020); Panigone et al. (2020); Wilkinson et al. (2019), NICE (2020)
		Foster	No	11.5		Panigone et al. (2020)
		Flutiform	No	35.9		Wilkinson et al. (2019)
	LAMA/LABA	Bevespi Aerosphere	No	25.3		Janson et al. (2020); Panigone et al. (2020); Wilkinson et al. (2019), NICE (2020)
	Triple FDC	Trimbow	No	14.5		Panigone et al. (2020)
		Breztri Aerosphere	No	25.3		Janson et al. (2020); Panigone et al. (2020); Wilkinson et al. (2019), NICE (2020)
DPI	LABA/ICS	Symbicort	No	0.9		Janson et al. (2020)
		Breo Ellipta	No	0.8		Janson et al. (2020)
		Revinty Ellipta	No	0.8		Janson et al. (2020)
		Seretide	No	0.9		Janson et al. (2020)
		Aliflus	No	0.9		Janson et al. (2020)
		Crivanil Plus	No	0.8		Janson et al. (2020); Panigone et al. (2020); Novartis (2021)
		Duoresp	No	0.8		Janson et al. (2020); Panigone et al. (2020); Novartis (2021)
		Gibiter	No	0.8		Janson et al. (2020); Panigone et al. (2020); Novartis (2021)
		Bufomix Easyhaler	No	0.8		Janson et al. (2020); Panigone et al. (2020); Novartis (2021)
		Rolenium	Yes	0.6	0.1	Janson et al. (2020); Panigone et al. (2020); Novartis (2021)
		Pulmoton	Yes	0.6	0.1	Janson et al. (2020); Panigone et al. (2020); Novartis (2021)

		Flutic/Salmet Pras	Yes	0.6	0.1	Janson et al. (2020); Panigone et al. (2020); Novartis (2021)
		Foster	No	0.9		Panigone et al. (2020)
	LAMA/LABA	Anoro Ellipta	No	0.8		Janson et al. (2020)
		Laventair	No	0.8		Janson et al. (2020)
		Duaklir Genuair	No	0.8		Janson et al. (2020); Panigone et al. (2020); Novartis (2021)
		Brimica Genuair	No	0.8		Janson et al. (2020); Panigone et al. (2020); Novartis (2021)
		Ultibro	Yes	0.4	0.1	Novartis (2021)
		Xoterna Breezhaler	Yes	0.4	0.1	Novartis (2021)
		Ulunar Breezhaler	Yes	0.4	0.1	Novartis (2021)
	LAMA	Incruse Ellipta	No	0.8		Janson et al. (2020)
		Rolufta	No	0.8		Janson et al. (2020)
		Spiriva	Yes	0.6	0.1	Janson et al. (2020); Panigone et al. (2020); Novartis (2021)
		Braltus	Yes	0.6	0.1	Janson et al. (2020); Panigone et al. (2020); Novartis (2021)
		Bretaris Genuair	No	0.8		Janson et al. (2020); Panigone et al. (2020); Novartis (2021)
		Eklira Genuair	No	0.8		Janson et al. (2020); Panigone et al. (2020); Novartis (2021)
		Tiotropium br vtrs	Yes	0.6	0.1	Janson et al. (2020); Panigone et al. (2020); Novartis (2021)
		Gregal	Yes	0.6	0.1	Janson et al. (2020); Panigone et al. (2020); Novartis (2021)
		Seebri	Yes	0.4	0.1	Novartis (2021)
		Tovanor Breezhaler	Yes	0.4	0.1	Novartis (2021)
		Enurev Breezhaler	Yes	0.4	0.1	Novartis (2021)
	Triple FDC	Trelegy Ellipta	No	0.8		Janson et al. (2020)
		Elebrato Ellipta	No	0.8		Janson et al. (2020)
		Enerzair	Yes	0.4	0.1	Novartis (2021)

SMI	LAMA/LABA	Spiolto Respimat Reusable	Yes	0.7	0.1	Hänsel et al. (2019)
	LAMA	Spiriva Respimat Reusable	Yes	0.7	0.1	Hänsel et al. (2019)

*The proportion of CF (~17%) attributed to the refill was based on the proportion of active pharmaceutical ingredients and distribution as the total carbon footprint per package in Janson et al.(2020) [15] with the exception of SMIs (in which case Hänsel et al. 2019 [14] provided this data); † for products/inhalers with no available CF-estimate, an average of all available evidence was used. CF, carbon footprint; DPI, dry powder inhaler; FDC, fixed dose combination; ICS, inhaled corticosteroid; LABA; long-acting beta-agonists; LAMA, long-acting muscarinic antagonist; pMDI, pressurised metered dose inhaler; SMI, soft mist inhaler.

Table 3. Reduction in carbon footprint when replacing either inhalers as used in the LAMA or LAMA/LABA class to Spiriva Respimat Reusable and Spiolto Respimat Reusable, respectively, over five years (2021–2025)

	LAMA				LAMA/LABA			
	Before Spiriva Respimat Reusable switch	After Spiriva Respimat Reusable switch			Before Spiolto Respimat Reusable switch	After Spiolto Respimat Reusable switch		
	Cumulative CO_2e emissions (tonnes)	Cumulative CO_2e emissions (tonnes)	Difference in CO_2e emissions (tonnes)	Decrease in carbon footprint after switch (%)	Cumulative CO_2e emissions (tonnes)	Cumulative CO_2e emissions (tonnes)	Difference in CO_2e emissions (tonnes)	Decrease in carbon footprint after switch (%)
Belgium	394.2	281.1	-113.1	**28.7**	321.9	291.2	-30.7	**9.5**
Denmark	345.9	252.8	-93.1	**26.9**	803.7	296.6	-507.1	**63.1**
France	3,582.6	2,742.8	-839.8	**23.4**	2,496.5	2,202.3	-294.2	**11.8**
Germany	5,042.2	3,788.6	-1,253.6	**24.9**	8,560.3	4,241.4	-4,318.8	**50.5**
Greece	1,022.7	574.5	-448.2	**43.8**	782.2	502.7	-279.6	**35.7**
Italy	7,850.9	3,852.0	-3,999.0	**50.9**	1,474.2	819.6	-654.6	**44.4**
Netherlands	1,260.2	1,093.1	-167.1	**13.3**	773.7	238.0	-535.6	**69.2**
Norway	296.4	192.5	-103.9	**35.1**	1,009.5	183.6	-825.8	**81.8**
Portugal	466.7	362.1	-104.6	**22.4**	706.9	493.6	-213.3	**30.2**
Spain	4,163.0	3,023.0	-1,140.0	**27.4**	2,607.9	2,157.5	-450.4	**17.3**
Sweden	713.1	507.5	-205.6	**28.8**	448.8	182.0	-266.8	**59.4**
United Kingdom	8,835.1	5,788.2	-3,046.9	**34.5**	5,853.3	2,229.6	-3,623.7	**61.9**
United States	13,743.6	7,515.3	-6,228.2	**45.3**	54,929.8	4,087.2	-50,842.6	**92.6**
Total	47,716.6	29,973.5	-17,743.1	**37.2**	80,768.6	17,925.4	-62,843.3	**77.8**

CO_2e, carbon dioxide equivalent; LABA; long-acting beta-agonists; LAMA, long-acting muscarinic antagonist

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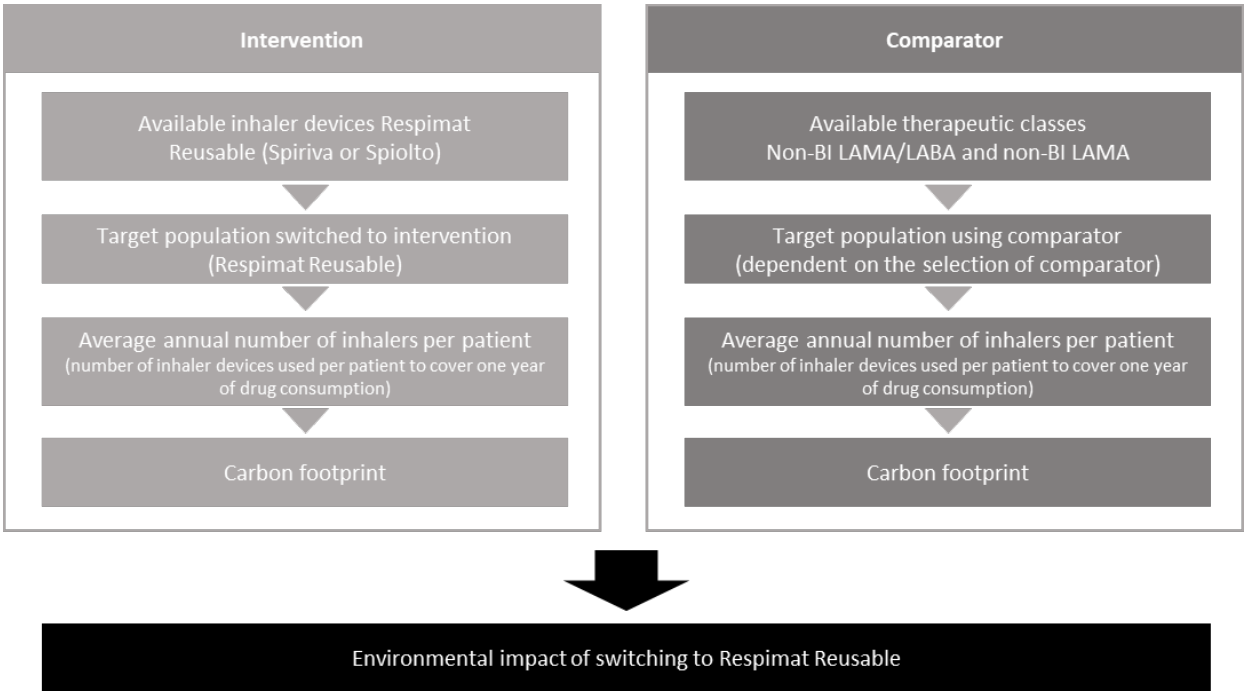
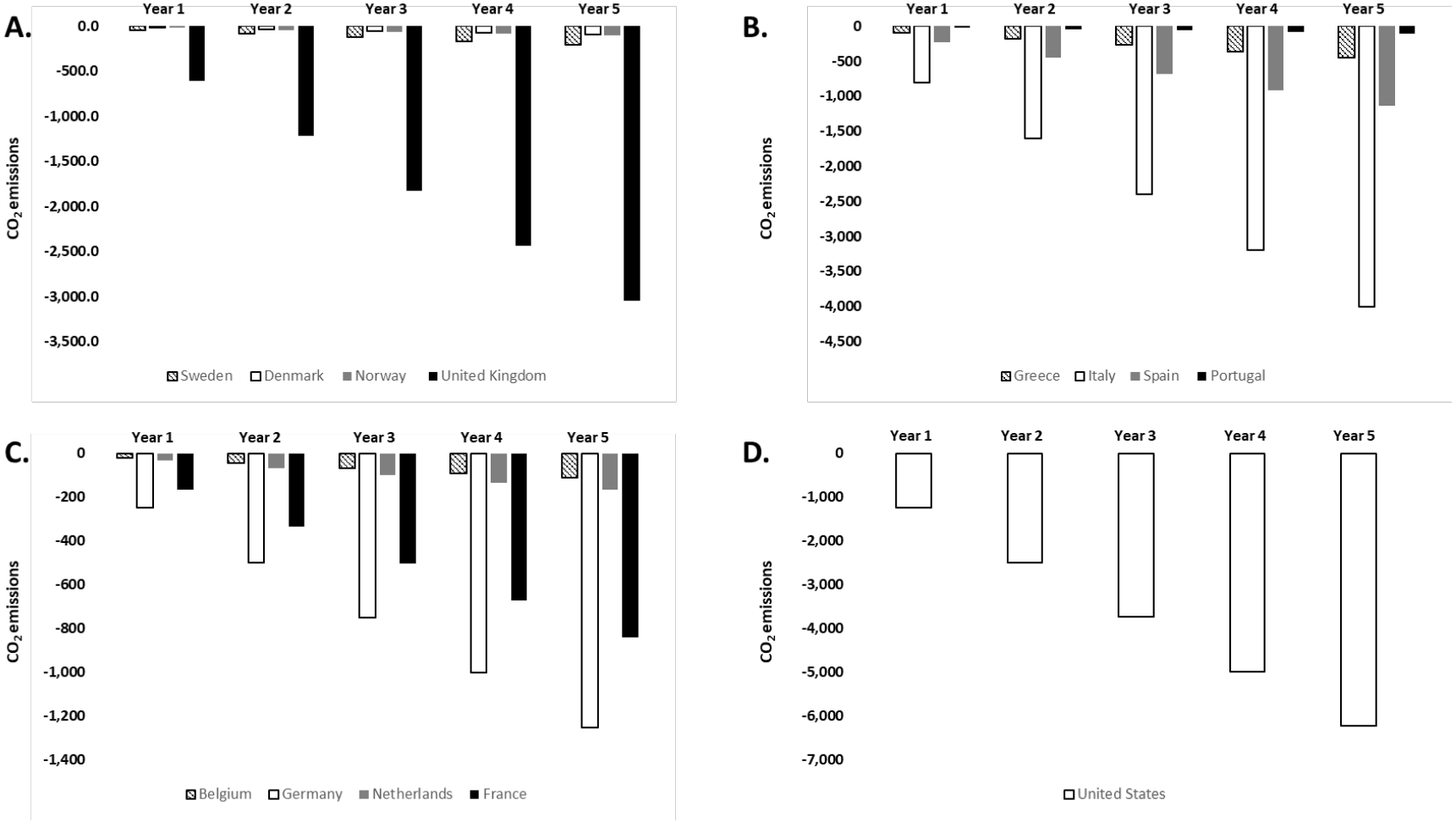
Figure 1. Model design for primary analysis



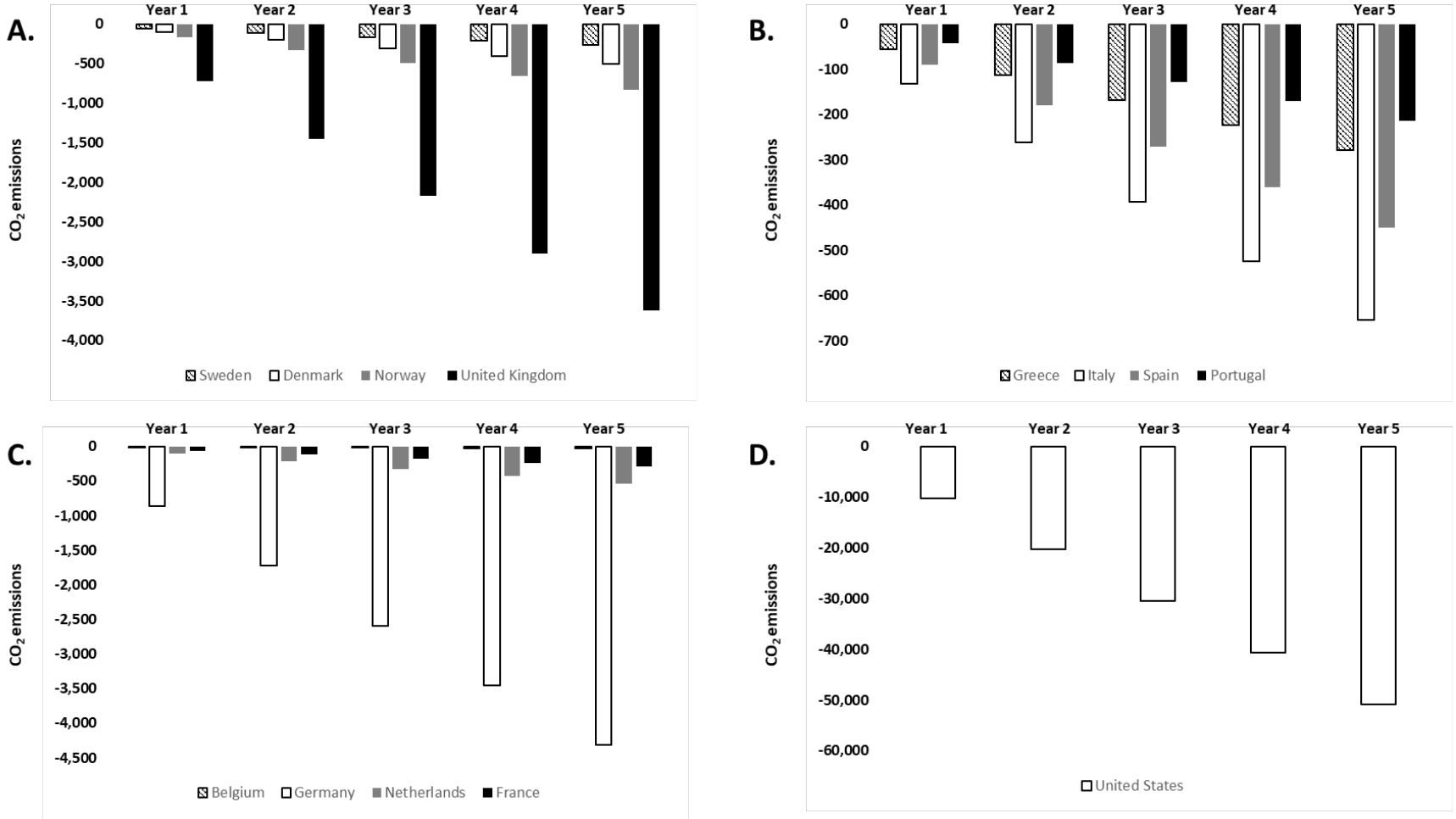
BI, Boehringer Ingelheim; LABA, long-acting beta-agonist; LAMA, long-acting muscarinic antagonist.

Figure 2. Cumulative reduction in CO_2e emissions over five years using Spiriva Respimat Reusable over alternative inhalers used in the LAMA class in Northern Europe (A), Southern Europe (B), Western Europe (C), and United States (D)



LAMA, long-acting muscarinic antagonist. A. Northern Europe: Denmark, Norway, Sweden, and United Kingdom; B. Southern Europe: Greece, Italy, Portugal, and Spain; C. Western Europe: Belgium, France, Germany, the Netherlands; D. United States.

Figure 3. Cumulative reduction in CO_2e emissions over five years using Spiolto Respimat Reusable over alternative inhalers used in the LAMA/LABA class in Northern Europe (A), Southern Europe (B), Western Europe (C), and United States (D)



CO_2e, carbon dioxide equivalents; LABA; long-acting beta-agonists; LAMA, long-acting muscarinic antagonist. A. Northern Europe: Denmark, Norway, Sweden, and United Kingdom; B. Southern Europe: Greece, Italy, Portugal, and Spain; C. Western Europe: Belgium, France, Germany, the Netherlands; D. United States.

Figure 4. Five-year absolute and per patient CO_2e savings across the different countries if all DPIs and pMDIs were switched to Respimat Reusable

	US	UK	Portugal	Spain	France	Germany	Italy	Greece	Belgium	Netherlands	Denmark	Norway	Sweden
ABSOLUTE CO_2e SAVINGS (tonnes)	913,548.3	624,836.5	29,189.9	129,380.6	97,313.6	246,696.6	108,599.5	13,126.4	27,923.1	38,344.2	18,215.5	20,053.2	16,060.9
ANNUAL CO_2e SAVINGS PER PATIENT (kg)	44.3		32.4	21.4	13.2	26.5	18.5	8.5	19.4	19.0	29.4	28.5	16.2

Shading in figure represents absolute CO_2e savings (tonnes).

SUPPLEMENTARY MATERIAL

Reducing carbon footprint by replacing dry powder inhalers and pressurised metered-dose inhalers with reusable soft mist inhalers

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Country	Patients per inhaler type (% of total*)		Patients per therapeutic class (% of total)			
	DPI	pMDI	LAMA*	LAMA/LABA*	LABA/ICS	Triple FDC†

Supplementary Table 1. Market shares based on total number of patients on inhaler device or therapeutic class of inhaler in 2020

Belgium	240,838 (83.5%)	47,422 (16.5%)	20,744 (7.2%)	21,492 (7.5%)	224,053 (77.7%)	21,970 (7.6%)
Denmark	96,836 (78.2%)	27,004 (21.8%)	18,658 (15.1%)	21,887 (17.7%)	70,219 (56.7%)	13,076 (10.6%)
France	1,210,475 (81.9%)	267,892 (18.1%)	202,422 (13.7%)	162,533 (11.0%)	1,046,010 (70.8%)	67,401 (4.6%)
Germany	1,364,761 (73.4%)	495,250 (26.6%)	279,599 (15.0%)	313,021 (16.8%)	1,159,052 (62.3%)	108,339 (5.8%)
Greece	272,622 (88.8%)	34,540 (11.2%)	42,399 (13.8%)	37,099 (12.1%)	222,594 (72.5%)	5,070 (1.7%)
Italy	880,952 (75.2%)	290,861 (24.8%)	284,278 (24.3%)	60,490 (5.2%)	781,588 (66.7%)	45,458 (3.9%)
Netherlands	259,638 (64.4%)	143,743 (35.6%)	80,672 (20.0%)	17,566 (4.4%)	280,242 (69.5%)	24,901 (6.2%)
Norway	107,141 (76.1%)	33,656 (23.9%)	14,207 (10.1%)	13,551 (9.6%)	101,594 (72.2%)	11,445 (8.1%)
Portugal	147,713 (81.9%)	32,722 (18.1%)	26,725 (14.8%)	36,426 (20.2%)	108,825 (60.3%)	8,458 (4.7%)
Spain	931,866 (77.1%)	276,684 (22.9%)	223,099 (18.5%)	159,222 (13.2%)	789,087 (65.3%)	37,142 (3.1%)
Sweden	166,183 (84.0%)	31,638 (16.0%)	37,451 (18.9%)	13,433 (6.8%)	135,683 (68.6%)	11,253 (5.7%)
United Kingdom	1,478,703 (54.9%)	1,217,189 (45.1%)	427,175 (15.8%)	164,544 (6.1%)	1,844,942 (68.4%)	259,230 (9.6%)
United States	2,507,431 (60.8%)	1,617,529 (39.2%)	554,637 (13.4%)	301,641 (7.3%)	2,954,954 (71.6%)	313,726 (7.6%)

*excludes Respimat Reusable and short acting beta agonists; †FDC, LAMA/LABA/ICS. DPI, dry powder inhaler; FDC, fixed dose combination; ICS, inhaled corticosteroids; LABA; long-acting beta-agonists; LAMA, long-acting muscarinic antagonist; pMDI, pressurised metered dose inhaler.

Supplementary Table 2. Inhaler use per patient per year

	LAMA*	LAMA/LABA*	LABA/ICS	Triple FDC†	DPI	pMDI
Belgium	5.0	4.8	12.0	12.0	10.8	12.0
Denmark	3.9	7.3	12.0	12.0	9.4	12.0
France	3.8	5.0	12.0	12.0	9.7	12.0
Germany	3.8	6.6	11.9	12.0	9.0	12.0
Greece	6.4	6.7	9.4	12.0	8.3	12.0
Italy	7.6	7.5	12.0	12.0	10.3	12.0
Netherlands	2.7	7.1	12.0	12.0	8.8	12.0
Norway	4.7	8.8	12.0	12.0	10.6	12.0
Portugal	3.8	6.2	12.0	12.0	9.1	12.0
Spain	4.1	5.3	12.0	12.0	9.0	12.0
Sweden	3.9	6.3	12.0	12.0	9.7	12.0
United Kingdom	4.7	10.0	12.0	12.0	9.7	12.0
USA	5.8	12.0	11.4	12.0	9.9	12.0

*excludes Respimat Reusable; †FDC, LAMA/LABA/ICS. DPI, dry powder inhaler; FDC, fixed dose combination; ICS, inhaled corticosteroid; LABA; long-acting beta-agonists; LAMA, long-acting muscarinic antagonist; pMDI, pressurised metered dose inhalers.

Supplementary Table 3. Reduction in carbon footprint when replacing either LABA/ICS or triple FDC to Respimat Reusable over five years (2021–2025), as conducted in scenario analyses

	LABA/ICS				Triple FDC*			
	Before Respimat Reusable switch	After Spiolto Respimat Reusable switch			Before Respimat Reusable switch	After Spiolto Respimat Reusable switch		
	Cumulative CO_2e emissions (tonnes)	Cumulative CO_2e emissions (tonnes)	Difference in CO_2e emissions (tonnes)	Decrease in carbon footprint after switch (%)	Cumulative CO_2e emissions (tonnes)	Cumulative CO_2e emissions (tonnes)	Difference in CO_2e emissions (tonnes)	Decrease in carbon footprint after switch (%)
Belgium	20,880.0	3,035.9	-17,844.1	**85.5**	10,643.4	297.7	-10,345.7	**97.2**
Denmark	11,149.9	951.5	-10,198.5	**91.5**	7,550.6	177.2	-7,373.4	**97.7**
France	90,263.9	14,173.4	-76,090.5	**84.3**	24,089.3	913.3	-23,176.0	**96.2**
Germany	205,041.8	15,705.2	-189,336.7	**92.3**	52,958.0	1,468	-51,490.0	**97.2**
Greece	10,698.7	3,016.2	-7,682.5	**71.8**	4,405.9	68.7	-4,337.2	**98.4**
Italy	95,974.1	10,590.5	-85,383.6	**89.0**	20,043.2	616.0	-19,427.3	**96.9**
Netherlands	23,984.0	3,797.3	-20,186.7	**84.2**	18,218.7	337.4	-17,881.3	**98.1**
Norway	14,495.0	1,376.6	-13,118.4	**90.5**	6,021.1	155.1	-5,866.0	**97.4**
Portugal	30,397.2	1,474.6	-28,922.6	**95.1**	391.4	114.6	-276.8	**70.7**
Spain	121,882.2	10,692.1	-111,190.1	**91.2**	19,485.8	503.3	-18,982.6	**97.4**
Sweden	11,928.9	1,838.5	-10,090.4	**84.6**	5,742.3	152.5	-5,589.8	**97.3**

United Kingdom	527,201.7	24,999.0	-502,202.7	**95.3**	121,591.3	3,512.6	-118,078.7	**97.1**
United States	847,116.5	40,039.6	-807,076.8	**95.3**	17,395.3	4,251.0	-13,144.3	**75.6**
Total	**2,011,013.9**	**131,690.4**	**-1,879,323.6**	**93.5**	**308,536.4**	**12,567.2**	**-295,969.2**	**95.9**

*, †FDC, LAMA/LABA/ICS. CO_2e, carbon dioxide equivalent; FDC, fixed dose combination; ICS, inhaled corticosteroids; LABA; long-acting beta-agonists; LAMA, long-acting muscarinic antagonist.

Supplementary Table 4. Reduction in carbon footprint when replacing either pMDI/DPI or both with Respimat® Reusable from over five years (2021–2025), as conducted in scenario analyses

	DPI only				pMDI only				Both DPI and pMDI			
	Before Respimat Reusable switch	After Respimat Reusable switch			Before Respimat Reusable switch	After Respimat Reusable switch			Before Respimat Reusable switch	After Respimat Reusable switch		
	Cumulative CO_2e emissions (tonnes)	Cumulative CO_2e emissions (tonnes)	Difference in CO_2e emissions (tonnes)	Decrease in carbon footprint after switch (%)	Cumulative CO_2e emissions (tonnes)	Cumulative CO_2e emissions (tonnes)	Difference in CO_2e emissions (tonnes)	Decrease in carbon footprint after switch (%)	Cumulative CO_2e emissions (tonnes)	Cumulative CO_2e emissions (tonnes)	Difference in CO_2e emissions (tonnes)	Decrease in carbon footprint after switch (%)
Belgium	10,590.3	3,263.4	-7,327.0	**69.2**	21,238.7	642.6	-20,596.16	**97.0**	31,829.0	3,906.0	-27,923.0	**87.7**
Denmark	3,519.1	1,312.1	-2,206.9	**62.7**	16,374.5	365.9	-16,008.59	**97.8**	19,893.6	1,678.0	-18,215.6	**91.6**
France	47,659.9	16,401.9	-31,258.0	**65.6**	69,685.5	3,629.9	-66,055.59	**94.8**	117,345.4	20,031.8	-97,313.6	**82.9**
Germany	48,224.1	18,492.5	-29,731.6	**61.7**	223,675.7	6,710.6	-216,965.0	**97.0**	271,899.7	25,203.1	-246,696.6	**90.7**
Greece	9,091.2	3,694.1	-5,397.2	**59.4**	8,197.3	468.0	-7,729.3	**94.3**	17,288.5	4,162.1	-13,126.4	**75.9**
Italy	35,414.3	11,936.9	-23,477.4	**66.3**	89,063.2	3,941.2	-85,122.0	**95.6**	124,477.5	15,878.1	-108,599.4	**87.2**
Netherlands	9,561.4	3,518.1	-6,043.3	**63.2**	34,248.7	1,947.7	-32,300.9	**94.3**	43,810.1	5,465.8	-38,344.3	**87.5**

Norway	4,449.1	1,451.8	-2,997.4	**67.4**	17,511.9	456.0	-17,055.9	**97.4**	21,961.0	1,907.8	-20,053.2	**91.3**
Portugal	5,121.1	2,001.5	-3,119.6	**60.9**	26,513.7	443.4	-26,070.4	**98.3**	31,634.8	2,444.9	-29,189.9	**92.3**
Spain	32,995.1	12,626.8	-20,368.4	**61.7**	112,761.3	3,749.1	-109,012.3	**96.7**	145,756.5	16,375.9	-129,380.5	**88.8**
Sweden	6,456.6	2,251.8	-4,204.8	**65.1**	12,284.8	428.7	-11,856.1	**96.5**	18,741.4	2,680.5	-16,060.9	**85.7**
United Kingdom	57,758.8	20,036.4	-37,722.4	**65.3**	603,607.1	16,492.9	-587,114.2	**97.3**	661,365.9	36,529.3	-624,836.6	**94.5**
United States	100,309.6	33,975.7	-66,333.9	**66.1**	869,131.9	21,917.5	-847,214.4	**97.5**	969,441.5	55,893.2	-913,548.3	**94.2**
Total	371,150.6	130,963.0	-240,187.9	**64.7**	2,104,294.3	61,193.5	-2,043,100.8	**97.1**	2,475,444.9	192,156.5	-2,283,288.4	**92.2**

Supplementary Table 5. Sensitivity analysis: Belgium

Model parameter	Variable	Scenario	Before Respimat Reusable switch		After Respimat Reusable switch			
			Cumulative CO_2e emissions (tonnes)	Difference with base case	Cumulative CO_2e emissions (tonnes)	Change in CO_2e emissions after intervention (tonnes)	Difference vs. base case (%)	Decrease in carbon footprint after switch (%)
Sensitivity analysis for the main analyses								
LAMA								
		Base case	**394.2**		**281.1**	**-113.1**	**-**	**28.7%**
Extent of inhaler reuse in practice	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	394.2	-	554.5	160.3	241.8%	-40.7%
		12 devices/year	394.2	-	964.6	570.5	604.5%	-144.7%
	Number of LAMA devices used	*Base case: 5.02 devices/year*						
		6 devices/year	453.5	59.3	281.1	-172.4	-52.5%	38.0%
		12 devices/year	815.4	421.3	281.1	-534.3	-372.6%	65.5%
CO_2 data	**CO_2 data of Respimat Reusable**	*Base case: (data)*						
		+20% for Respimat Reusable	394.2	-	337.1	-57.1	49.5%	14.5%
		-20% for Respimat Reusable	394.2	-	225.1	-169.1	-49.5%	42.9%
	CO_2 data of	*Base case: (data)*						

	LAMA devices	+20% for LAMA devices	473.9	79.8	281.1	-192.9	-70.6%	40.7%
		-20% for LAMA devices	316.0	-78.2	281.1	-34.9	69.2%	11.0%
LAMA/LABA								
		Base case	**321.9**		**291.2**	**-30.7**		**9.5%**
Re-usability	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	321.9	-	574.5	252.6	922.8%	-78.5%
		12 devices/year	321.9	-	999.4	677.5	2306.9%	-210.4%
	Number of LAMA/LABA devices used	*Base case: 4.82 devices/year*						
		6 devices/year	383.2	61.3	291.2	-92.0	-199.7%	24.0%
		12 devices/year	694.4	372.5	291.2	-403.2	-1213.4%	58.1%
CO_2 data	**CO_2 data of Respimat Reusable**	*Base case: (data)*						
		+20% for Respimat Reusable	321.9	-	349.2	27.3	189.0%	-8.5%
		-20% for Respimat Reusable	321.9	-	233.2	-88.7	-189.0%	27.6%
	CO_2 data of LAMA/LABA devices	*Base case: (data)*						
		+20% for LAMA/LABA devices	386.7	64.8	291.2	-95.4	-210.9%	24.7%
		-20% for LAMA/LABA devices	257.9	-64.1	291.2	33.4	208.7%	-12.9%
Sensitivity analysis for the scenario analyses								
		Base case	**31,829.0**		**3,905.9**	**-27,923.1**		**87.7**
Extent of inhaler	**Number of Respimat**	*Base case: 2 devices/year*						
		6 devices/year	31,829.0	-	7,705.2	-24,123.9	13.6%	75.8

reuse in practice	**Reusable used**	12 devices/year	31,829.0	-	13,404.0	-18,425.0	34.0%	57.9
	Number of DPIs	*Base case: 10.76 devices/year*						
		6 devices/year	27,217.8	-5,815.5	3,905.9	-23,311.9	16.5%	85.6
		12 devices/year	33,033.2	1,204.2	3,905.9	-29,127.3	-4.3%	88.2
	Number of pMDI	*Base case: 12 devices/year*						
		6 devices/year (theoretical)	21,209.7	-10,619.4	3,905.9	-17,303.8	38.0%	81.6%
CO_2 data	**CO_2 data of Respimat Reusable**	*Base case: (data)*						
		+20% for Respimat Reusable	31,829.0	-	4,687.1	-27,141.9	2.8%	85.3
		-20% for Respimat Reusable	31,829.0	-	3,124.7	-28,704.3	-2.8%	90.2
	CO_2 data of DPI	*Base case: (data)*						
		+20% for DPI	33,947.1	2,118.1	3,905.9	-30,041.2	-7.6%	88.5
		-20% for DPI	29,711.0	-2,118.1	3,905.9	-25,805.1	7.6%	86.9
	CO_2 data of pMDI	*Base case: (data)*						
		+20% for pMDI	36,076.8	4,247.7	3,905.9	-32,170.9	-15.2%	89.2
		-20% for pMDI	27,581.3	-4,247.7	3,905.9	-23,675.4	15.2%	85.8
Market share	**Current prescription of devices**	Base case:						
		Total patients on DPI and pMDI in 2020: - 10%	28,646.1	-3,182.9	3,515.3	-25,130.8	10.0%	87.7
		Total patients on DPI and pMDI in 2020: + 10%	35,011.9	3,182.9	4,296.5	-30,715.4	-10.0%	87.7
		Total patients on DPI in 2020: - 10%; Total patient on pMDI in 2020: +20%	31,823.2	-5.8	4,494.3	-27,328.9	2.1%	85.9
		Total patients on DPI in 2020: - 20%; Total patient on pMDI in 2020: +10%	31,834.8	5.8	3,317.5	-28,517.3	-2.1%	89.6
		Total patients on DPI in 2020: -10%;	35,017.7	3,188.7	3,708.1	-31,309.7	-12.1%	89.4

		Total patient on pMDI in 2020: +20%						
		Total patients on DPI in 2020: +10%; Total patient on pMDI in 2020: -20%	28,640.3	-3,188.7	4,103.7	-24,536.6	12.1%	85.7
	Currently prescribed class	Base case						
		LAMA: +20%; other classes: -5%	30,726.1	-1,103.0	3,780.9	-26,945.2	3.5%	87.7
		LAMA: -20%; other classes: +5%	33,752.9	1,923.9	4,030.9	-29,722.0	-6.4%	88.1
		LABA/ICS: +20%; other classes: -5%	35,847.5	4,018.5	4,469.6	-31,377.9	-12.4%	87.5
		LABA/ICS: -20%; other classes: +5%	28,631.5	-3,197.5	3,342.2	-25,289.3	9.4%	88.3
		LAMA/LABA: +20%; other classes: -5%	30,708.0	-1,121.0	3,783.4	-26,924.6	3.6%	87.7
		LAMA/LABA: -20%; other classes: +5%	33,771.0	1,942.0	4,028.4	-29,742.6	-6.5%	88.1
		LAMA/LABA/ICS: +20%; other classes: -5%	33,288.4	1,459.4	3,785.0	-29,503.4	-5.7%	88.6
		LAMA/LABA/ICS: -20%; other classes: +5%	31,190.6	-638.4	4,026.8	-27,163.8	2.7%	87.1
Extent of the switch	**Switch of devices**	*Base case: 100% switch DPI and pMDI to Respimat Reusable*						
		50% switch of DPI to Respimat Reusable (100% for pMDI)	31,829.0	-	7,569.4	-24,259.6	13.1%	76.2
		50% switch of pMDI to Respimat Reusable (100% for DPI)	31,829.0	-	14,204.0	-17,625.0	36.9%	55.4
		50% switch of DPI and pMDI to Respimat Reusable	31,829.0	-	17,867.5	-13,961.6	50.0%	43.9
	Switch of therapeutic classes	*Base case: 100% switch all therapeutic classes to Spiriva/Spiolto Respimat Reusable*						
		50% switch of LAMA (excluding	32,239.5	410.5	3,962.4	-28,277.1	-1.3%	87.7

		Spiriva Respimat Reusable) to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)						
		50% switch of LAMA/LABA (excluding Spiolto Respimat Reusable) to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	32,239.5	410.5	3,921.3	-28,318.3	-1.4%	87.8
		50% switch of LABA/ICS to Spiriva/ Spiolto Respimat Reusable (other classes: 100% switch)	32,239.5	410.5	12,828.0	-19,411.6	30.5%	60.2
		50% switch of LAMA/LABA/ICS to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	32,239.5	410.5	9,078.8	-23,160.7	17.1%	71.8

CO2e, carbon dioxide equivalent; DPI, dry powder inhaler; ICS, inhaled corticosteroid; LABA; long-acting beta-agonists; LAMA, long-acting muscarinic antagonist; pMDI, pressurised metered dose inhalers.

Supplementary Table 6. Sensitivity analysis: Denmark

Model parameter	Variable	Scenario	Before Respimat Reusable switch		After Respimat Reusable switch			
			Cumulative CO_2e emissions (tonnes)	Difference with base case	Cumulative CO_2e emissions (tonnes)	Change in CO_2e emissions after intervention (tonnes)	Difference vs. base case (%)	Decrease in carbon footprint after switch (%)
Sensitivity analysis for the main analyses								
LAMA								
		Base case	**345.9**		**252.8**	**-93.1**	**-**	**26.9%**
Re-usability	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	345.9	-	498.7	152.9	264.3%	-44.2%
		12 devices/year	345.9	-	867.6	521.7	660.7%	-150.8%
	Number of LAMA devices used	*Base case: 3.93 devices/year*						
		6 devices/year	468.3	122.4	252.8	-215.4	-131.5%	46.0%
		12 devices/year	822.4	476.5	252.8	-569.6	-512.1%	69.3%
CO_2 data	**CO_2 data of Respimat Reusable**	*Base case: (data)*						
		+20% for Respimat Reusable	345.9	-	303.2	-42.7	54.1%	12.3%
		-20% for Respimat Reusable	345.9	-	202.4	-143.4	-54.1%	41.5%
	CO_2 data of LAMA devices	*Base case: (data)*						
		+20% for LAMA devices	415.0	69.1	252.8	-162.2	-74.2%	39.1%
		-20% for LAMA devices	289.5	-56.4	252.8	-36.6	60.6%	12.7%
LAMA/LABA								

		Base case	**803.6**		**296.6**	**-507.1**	**-**	**63.1%**
Re-usability	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	803.6	-	585.0	-218.6	-134.9%	27.2%
		12 devices/year	803.6	-	1,017.7	214.1	330.1%	-26.6%
	Number of LAMA/LABA devices used	*Base case: 7.28 devices/year*						
		6 devices/year	671.0	-132.6	296.6	-374.5	-302.4%	55.8%
		12 devices/year	1,293.8	490.2	296.6	-997.3	-971.7%	77.1%
CO_2 data	**CO_2 data of Respimat Reusable**	*Base case: (data)*						
		+20% for Respimat Reusable	803.6	-	355.7	-448.0	-381.4%	55.7%
		-20% for Respimat Reusable	803.6	-	237.5	-566.2	-508.4%	70.5%
	CO_2 data of LAMA/LABA devices	*Base case: (data)*						
		+20% for LAMA/LABA devices	964.1	160.4	296.6	-667.5	-617.3%	69.2%
		-20% for LAMA/LABA devices	643.1	-160.6	296.6	-346.5	-272.3%	53.9%
Sensitivity analysis for the scenario analyses								
		Base case	**19,893.5**		**1,678.0**	**-18,215.5**	**-**	**91.6**
Extent of inhaler reuse in practice	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	19,893.5	-	3,310.3	-16,583.3	9.0%	83.4
		12 devices/year	19,893.5	-	5,758.6	-14,135.0	22.4%	71.1
	Number of DPIs	*Base case: 8.77 devices/year*						
		6 devices/year	18,685.6	-2,148.5	1,678.0	-17,007.6	6.6%	91.0
		12 devices/year	20,834.2	940.6	1,678.0	-19,156.1	-5.2%	91.9
	Number of pMDI	*Base case: 12 devices/year*						
		6 devices/year (theoretical)	11,706.3	-8,187.2	1,678.0	-10,028.3	44.9%	85.7
CO_2 data	**CO_2 data of**	*Base case: (data)*						

	Respimat Reusable	+20% for Respimat Reusable	19,893.5	-	2,013.6	-17,879.9	1.8%	89.9
		-20% for Respimat Reusable	19,893.5	-	1,342.4	-18,551.1	-1.8%	93.3
	CO_2 data of DPI	*Base case: (data)*						
		+20% for DPI	20,597.4	703.8	1,678.0	-18,919.3	-3.9%	91.9
		-20% for DPI	19,189.7	-703.8	1,678.0	-17,511.7	3.9%	91.3
	CO_2 data of pMDI	*Base case: (data)*						
		+20% for pMDI	23,168.4	3,274.9	1,678.0	-21,490.4	-18.0%	92.8
		-20% for pMDI	16,618.6	-3,274.9	1,678.0	-14,940.6	18.0%	89.9
Market share	**Current prescription of devices**	Base case:						
		Total patients on DPI and pMDI in 2020: - 10%	17,904.2	-1,989.4	1,510.2	-16,394.0	10.0%	91.6
		Total patients on DPI and pMDI in 2020: + 10%	21,882.9	1,989.4	1,845.8	-20,037.1	-10.0%	91.6
		Total patients on DPI in 2020: - 10%; Total patient on pMDI in 2020: +20%	18,959.9	-933.6	1,903.9	-17,056.0	6.4%	90.0
		Total patients on DPI in 2020: - 20%; Total patient on pMDI in 2020: +10%	20,827.2	933.6	1,452.2	-19,375.0	-6.4%	93.0
		Total patients on DPI in 2020: -10%; Total patient on pMDI in 2020: +20%	22,816.5	2,923.0	1,620.0	-21,196.5	-16.4%	92.9
		Total patients on DPI in 2020: +10%; Total patient on pMDI in 2020: -20%	16,970.6	-2,923.0	1,736.1	-15,234.5	16.4%	89.8
	Currently prescribed class	Base case						
		LAMA: +20%; other classes: -5%	18,944.0	-949.5	1,657.3	-17,286.7	5.1%	91.3
		LAMA: -20%; other classes: +5%	20,756.1	862.5	1,698.7	-19,057.3	-4.6%	91.8
		LABA/ICS: +20%; other classes: -5%	21,645.0	1,751.5	1,832.0	-19,813.0	-8.8%	91.5
		LABA/ICS: -20%; other classes: +5%	18,055.0	-1,838.5	1,524.1	-16,531.0	9.2%	91.6

		LAMA/LABA: +20%; other classes: -5%	19,058.4	-835.1	1,668.3	-17,390.2	4.5%	91.2
		LAMA/LABA: -20%; other classes: +5%	20,641.6	748.1	1,687.8	-18,953.8	-4.1%	91.8
		LAMA/LABA/ICS: +20%; other classes: -5%	20,745.2	851.6	1,638.4	-19,106.7	-4.9%	92.1
		LAMA/LABA/ICS: -20%; other classes: +5%	18,954.9	-938.7	1,717.6	-17,237.2	5.4%	90.9
Extent of the switch	**Switch of devices**	*Base case: 100% switch DPI and pMDI to Respimat Reusable*						
		50% switch of DPI to Respimat Reusable (100% for pMDI)	19,893.5	-	2,781.5	-17,112.0	6.1%	86.0
		50% switch of pMDI to Respimat Reusable (100% for DPI)	19,893.5	-	9,682.3	-10,211.2	43.9%	51.3
		50% switch of DPI and pMDI to Respimat Reusable	19,893.5	-	10,785.8	-9,107.8	50.0%	45.8
	Switch of therapeutic classes	*Base case: 100% switch all therapeutic classes to Spiriva/Spiolto Respimat Reusable*						
		50% switch of LAMA (excluding Spiriva Respimat Reusable) to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	19,850.0	-43.5	1,724.6	-18,125.5	0.5%	91.3
		50% switch of LAMA/LABA (excluding Spiolto Respimat Reusable) to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	19,850.0	-43.5	1,931.6	-17,918.5	1.6%	90.3
		50% switch of LABA/ICS to Spiriva/ Spiolto Respimat Reusable (other	19,850.0	-43.5	6,777.3	-13,072.8	28.2%	65.9

		classes: 100% switch)						
		50% switch of LAMA/LABA/ICS to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	19,850.0	-43.5	5,364.7	-14,485.3	20.5%	73.0

CO2e, carbon dioxide equivalent; DPI, dry powder inhaler; ICS, inhaled corticosteroid; LABA; long-acting beta-agonists; LAMA, long-acting muscarinic antagonist; pMDI, pressurised metered dose inhalers.

Supplementary Table 7. Sensitivity analysis: France

Model parameter	Variable	Scenario	Before Respimat Reusable switch		After Respimat Reusable switch			
			Cumulative CO_2e emissions (tonnes)	Difference with base case	Cumulative CO_2e emissions (tonnes)	Change in CO_2e emissions after intervention (tonnes)	Difference vs. base case (%)	Decrease in carbon footprint after switch (%)
Sensitivity analysis for the main analyses								
LAMA								
		Base case	**3,582.6**		**2,742.8**	**-839.8**	**-**	**23.4%**
Re-usability	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	3,582.6	-	5,410.7	1,828.1	317.7%	-51.0%
		12 devices/year	3,582.6	-	9,412.6	5,830.0	794.2%	-162.7%
	Number of LAMA devices used	*Base case: 3.78 devices/year*						
		6 devices/year	4,966.3	1,383.7	2,742.8	-2,223.5	-164.8%	44.8%
		12 devices/year	8,708.3	5,125.7	2,742.8	-5,965.5	-610.3%	68.5%
CO_2 data	**CO_2 data of Respimat Reusable**	*Base case: (data)*						
		+20% for Respimat Reusable	3,582.6	-	3,291.4	-291.2	65.3%	8.1%
		-20% for Respimat Reusable	3,582.6		2,194.3	-1,388.3	-65.3%	38.8%
	CO_2 data of LAMA devices	*Base case: (data)*						
		+20% for LAMA devices	4,301.1	718.5	2,742.8	-1,558.3	-85.6%	36.2%
		-20% for LAMA devices	2,867.4	-715.2	2,742.8	-124.6	85.2%	4.3%
LAMA/LABA								

		Base case	**2,496.5**		**2,202.3**	**-294.2**		**11.8%**
Re-usability	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	2,496.5	-	4,344.5	1,848.0	728.1%	-74.0%
		12 devices/year	2,496.5	-	7,557.8	5,061.3	1820.4%	-202.7%
	Number of LAMA/LABA devices used	*Base case: 4.95 devices/year*						
		6 devices/year	2,914.7	418.2	2,202.3	-712.4	-142.1%	24.4%
		12 devices/year	5,294.0	2,797.5	2,202.3	-3,091.7	-950.9%	58.4%
CO_2 data	**CO_2 data of Respimat Reusable**	*Base case: (data)*						
		+20% for Respimat Reusable	2,496.5		4,904.7	2,408.2	918.6%	-96.5%
		-20% for Respimat Reusable	2,496.5		3,269.8	773.3	362.8%	-31.0%
	CO_2 data of LAMA/LABA devices	*Base case: (data)*						
		+20% for LAMA/LABA devices	2,997.2	500.7	2,202.3	-794.9	-170.2%	26.5%
		-20% for LAMA/LABA devices	1,998.1	-498.4	2,202.3	204.2	169.4%	-10.2%
Sensitivity analysis for the scenario analyses								
		Base case	**117,345.4**		**20,031.9**	**-97,313.6**	**-**	**82.9**
Extent of inhaler reuse in practice	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	117,345.4	-	39,516.7	-77,828.7	20.0%	66.3
		12 devices/year	117,345.4	-	68,744.1	-48,601.4	50.1%	41.4
	Number of DPIs	*Base case: 9.68 devices/year*						
		6 devices/year	99,900.3	-28,455.2	20,031.9	-79,868.4	17.9%	79.9
		12 devices/year	128,355.5	11,010.1	20,031.9	-108,323.7	-11.3%	84.4
	Number of pMDI	*Base case: 12 devices/year*						
		6 devices/year (theoretical)	82,502.7	-34,842.8	20,031.9	-62,470.8	35.8%	75.7
CO_2 data	**CO_2 data of**	*Base case: (data)*						

	Respimat Reusable	+20% for Respimat Reusable	117,345.4	-	24,038.2	-93,307.2	4.1%	79.5
		-20% for Respimat Reusable	117,345.4	-	16,025.5	-101,319.9	-4.1%	86.3
	CO_2 data of DPI	*Base case: (data)*						
		+20% for DPI	126,877.4	9,532.0	20,031.9	-106,845.6	-9.8%	84.2
		-20% for DPI	107,813.5	-9,532.0	20,031.9	-87,781.6	9.8%	81.4
	CO_2 data of pMDI	*Base case: (data)*						
		+20% for pMDI	131,282.5	13,937.1	20,031.9	-111,250.7	-14.3%	84.7
		-20% for pMDI	103,408.3	-13,937.1	20,031.9	-83,376.5	14.3%	80.6
Market share	**Current prescription of devices**	Base case:						
		Total patients on DPI and pMDI in 2020: - 10%	105,610.9	-11,734.5	18,028.7	-87,582.2	10.0%	82.9
		Total patients on DPI and pMDI in 2020: + 10%	129,080.0	11,734.5	22,035.1	-107,044.9	-10.0%	82.9
		Total patients on DPI in 2020: - 10%; Total patient on pMDI in 2020: +20%	119,908.9	2,563.4	22,949.3	-96,959.6	0.4%	80.9
		Total patients on DPI in 2020: - 20%; Total patient on pMDI in 2020: +10%	114,782.0	-2,563.4	17,114.5	-97,667.5	-0.4%	85.1
		Total patients on DPI in 2020: -10%; Total patient on pMDI in 2020: +20%	126,516.5	9,171.1	19,117.7	-107,398.9	-10.4%	84.9
		Total patients on DPI in 2020: +10%; Total patient on pMDI in 2020: -20%	108,174.3	-9,171.1	20,946.1	-87,228.2	10.4%	80.6
	Currently prescribed class	Base case						
		LAMA: +20%; other classes: -5%	115,306.4	-2,039.0	19,716.0	-95,590.4	1.8%	82.9
		LAMA: -20%; other classes: +5%	125,558.3	8,212.9	20,347.8	-105,210.6	-8.1%	83.8
		LABA/ICS: +20%; other classes: -5%	136,976.7	19,631.3	22,573.6	-114,403.1	-17.6%	83.5
		LABA/ICS: -20%; other classes: +5%	103,888.0	-13,457.4	17,490.1	-86,397.9	11.2%	83.2

		LAMA/LABA: +20%; other classes: -5%	115,034.9	-2,310.5	19,580.9	-95,454.0	1.9%	83.0
		LAMA/LABA: -20%; other classes: +5%	125,829.9	8,484.4	20,482.9	-105,347.0	-8.3%	83.7
		LAMA/LABA/ICS: +20%; other classes: -5%	120,433.1	3,087.6	19,258.6	-101,174.5	-4.0%	84.0
		LAMA/LABA/ICS: -20%; other classes: +5%	120,431.7	3,086.2	20,805.1	-99,626.5	-2.4%	82.7
Extent of the switch	**Switch of devices**	*Base case: 100% switch DPI and pMDI to Respimat Reusable*						
		50% switch of DPI to Respimat Reusable (100% for pMDI)	117,345.4	-	35,660.9	-81,684.6	16.1%	69.6
		50% switch of pMDI to Respimat Reusable (100% for DPI)	117,345.4	-	53,059.7	-64,285.8	33.9%	54.8
		50% switch of DPI and pMDI to Respimat Reusable	117,345.4	-	68,688.7	-48,656.8	50.0%	41.5
	Switch of therapeutic classes	*Base case: 100% switch all therapeutic classes to Spiriva/Spiolto Respimat Reusable*						
		50% switch of LAMA (excluding Spiriva Respimat Reusable) to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	120,432.4	3,086.9	20,451.8	-99,980.6	-2.7%	83.0
		50% switch of LAMA/LABA (excluding Spiolto Respimat Reusable) to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	120,432.4	3,086.9	20,179.0	-100,253.4	-3.0%	83.2
		50% switch of LABA/ICS to Spiriva/ Spiolto Respimat Reusable (other	120,432.4	3,086.9	58,077.1	-62,355.3	35.9%	51.8

		classes: 100% switch)						
		50% switch of LAMA/LABA/ICS to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	120,432.4	3,086.9	31,619.9	-88,812.5	8.7%	73.7

CO_2e, carbon dioxide equivalent; DPI, dry powder inhaler; ICS, inhaled corticosteroid; LABA; long-acting beta-agonists; LAMA, long-acting muscarinic antagonist; pMDI, pressurised metered dose inhalers.

Supplementary Table 8. Sensitivity analysis: Germany

Model parameter	Variable	Scenario	Before Respimat Reusable switch		After Respimat Reusable switch			
			Cumulative CO_2e emissions (tonnes)	Difference with base case	Cumulative CO_2e emissions (tonnes)	Change in CO_2e emissions after intervention (tonnes)	Difference vs. base case (%)	Decrease in carbon footprint after switch (%)
Sensitivity analysis for the main analyses								
LAMA								
		Base case	**5,042.2**		**3,788.6**	**-1,253.6**	**-**	**24.9%**
Re-usability	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	5,042.2	-	7,473.7	2,431.5	294.0%	-48.2%
		12 devices/year	5,042.2	-	13,001.4	7,959.2	734.9%	-157.9%
	Number of LAMA devices used	*Base case: 3.78 devices/year*						
		6 devices/year	6,988.2	1,946.0	3,788.6	-3,199.6	-155.2%	45.8%
		12 devices/year	12,245.3	7,203.1	3,788.6	-8,456.7	-574.6%	69.1%
CO_2 data	**CO_2 data of Respimat Reusable**	*Base case: (data)*						
		+20% for Respimat Reusable	5,042.2	-	4,543.5	-498.7	60.2%	9.9%
		-20% for Respimat Reusable	5,042.2		3,033.7	-2,008.6	-60.2%	39.8%
	CO_2 data of LAMA devices	*Base case: (data)*						
		+20% for LAMA devices	5,934.1	891.9	3,788.6	-2,145.5	-71.1%	36.2%
		-20% for LAMA devices	3,963.4	-1,078.8	3,788.6	-174.8	86.1%	4.4%
LAMA/LABA								

		Base case	**8,560.3**		**4,241.4**	**-4,318.8**		**50.5%**
Re-usability	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	8,560.3	-	8,367.0	-193.2	95.5%	2.3%
		12 devices/year	8,560.3	-	14,555.5	5,995.2	238.8%	-70.0%
	Number of LAMA/LABA devices used	*Base case: 6.61 devices/year*						
		6 devices/year	7,844.3	-716.0	4,241.4	-3,602.8	16.6%	45.9%
		12 devices/year	14,900.6	6,340.3	4,241.4	-10,659.2	-146.8%	71.5%
CO_2 data	**CO_2 data of Respimat Reusable**	*Base case: (data)*						
		+20% for Respimat Reusable	8,560.3		5,086.6	-3,473.7	19.6%	40.6%
		-20% for Respimat Reusable	8,560.3		3,396.3	-5,164.0	-19.6%	60.3%
	CO_2 data of LAMA/LABA devices	*Base case: (data)*						
		+20% for LAMA/LABA devices	10,258.5	1,698.3	4,241.4	-6,017.1	-39.3%	58.7%
		-20% for LAMA/LABA devices	6,855.0	-1,705.3	4,241.4	-2,613.6	39.5%	38.1%
Sensitivity analysis for the scenario analyses								
		Base case	**271,899.7**		**25,203.2**	**-246,696.6**	**-**	**90.7**
Extent of inhaler reuse in practice	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	271,899.7	-	49,718.1	-222,181.7	9.9%	81.7
		12 devices/year	271,899.7	-	86,490.5	-185,409.2	24.8%	68.2
	Number of DPIs	*Base case: 9.00 devices/year*						
		6 devices/year	256,675.8	-30,404.6	25,203.2	-231,472.7	6.2%	90.2
		12 devices/year	287,080.4	15,180.6	25,203.2	-261,877.2	-6.2%	91.2
	Number of pMDI	*Base case: 12 devices/year*						
		6 devices/year (theoretical)	160,061.9	-111,837.8	25,203.2	-134,858.8	45.3%	84.3
CO_2 data	**CO_2 data of**	*Base case: (data)*						

	Respimat Reusable	+20% for Respimat Reusable	271,899.7	-	30,243.8	-241,656.0	2.0%	88.9
		-20% for Respimat Reusable	271,899.7	-	20,162.5	-251,737.2	-2.0%	92.6
	CO_2 data of DPI	*Base case: (data)*						
		+20% for DPI	281,544.6	9,644.8	25,203.2	-256,341.4	-3.9%	91.0
		-20% for DPI	262,254.9	-9,644.8	25,203.2	-237,051.8	3.9%	90.4
	CO_2 data of pMDI	*Base case: (data)*						
		+20% for pMDI	316,634.9	44,735.1	25,203.2	-291,431.7	-18.1%	92.0
		-20% for pMDI	227,164.6	-44,735.1	25,203.2	-201,961.5	18.1%	88.9
Market share	**Current prescription of devices**	Base case:						
		Total patients on DPI and pMDI in 2020: - 10%	244,709.8	-27,190.0	22,682.8	-222,026.9	10.0%	90.7
		Total patients on DPI and pMDI in 2020: + 10%	299,089.7	27,190.0	27,723.5	-271,366.3	-10.0%	90.7
		Total patients on DPI in 2020: - 10%; Total patient on pMDI in 2020: +20%	259,177.0	-12,722.8	28,230.6	-230,946.4	6.4%	89.1
		Total patients on DPI in 2020: - 20%; Total patient on pMDI in 2020: +10%	284,622.5	12,722.8	22,175.7	-262,446.8	-6.4%	92.2
		Total patients on DPI in 2020: -10%; Total patient on pMDI in 2020: +20%	311,812.5	39,912.7	24,696.0	-287,116.4	-16.4%	92.1
		Total patients on DPI in 2020: +10%; Total patient on pMDI in 2020: -20%	231,987.0	-39,912.7	25,710.3	-206,276.7	16.4%	88.9
	Currently prescribed class	Base case						
		LAMA: +20%; other classes: -5%	259,282.8	-12,617.0	24,890.1	-234,392.6	5.0%	90.4
		LAMA: -20%; other classes: +5%	283,921.9	12,022.2	25,516.2	-258,405.7	-4.7%	91.0
		LABA/ICS: +20%; other classes: -5%	309,282.7	37,382.9	27,869.3	-281,413.4	-14.1%	91.0
		LABA/ICS: -20%; other classes: +5%	233,922.09	-37,977.8	22,537.0	-211,385.0	14.3%	90.4

		LAMA/LABA: +20%; other classes: -5%	260,162.3	-11,737.5	25,003.4	-235,158.9	4.7%	90.4
		LAMA/LABA: -20%; other classes: +5%	283,042.4	11,142.6	25,403.0	-257,639.4	-4.4%	91.0
		LAMA/LABA/ICS: +20%; other classes: -5%	271,261.7	-638.0	24,310.0	-246,951.7	-0.1%	91.0
		LAMA/LABA/ICS: -20%; other classes: +5%	271,942.9	43.2	26,096.3	-245,846.6	0.3%	90.4
Extent of the switch	**Switch of devices**	*Base case: 100% switch DPI and pMDI to Respimat Reusable*						
		50% switch of DPI to Respimat Reusable (100% for pMDI)	271,899.7	-	40,068.9	-231,830.8	6.0%	85.3
		50% switch of pMDI to Respimat Reusable (100% for DPI)	271,899.7	-	133,685.7	-138,214.1	44.0%	50.8
		50% switch of DPI and pMDI to Respimat Reusable	271,899.7	-	148,551.5	-123,348.3	50.0%	45.4
	Switch of therapeutic classes	*Base case: 100% switch all therapeutic classes to Spiriva/Spiolto Respimat Reusable*						
		50% switch of LAMA (excluding Spiriva Respimat Reusable) to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	271,602.3	-297.4	25,830.0	-245,772.4	0.4%	90.5
		50% switch of LAMA/LABA (excluding Spiolto Respimat Reusable) to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	271,602.3	-297.4	27,362.6	-244,239.8	1.0%	89.9
		50% switch of LABA/ICS to Spiriva/ Spiolto Respimat Reusable (other	271,602.3	-297.4	119,871.5	-151,730.8	38.5%	55.9

		classes: 100% switch)						
		50% switch of LAMA/LABA/ICS to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	271,602.3	-297.4	50,948.2	-220,654.2	10.6%	81.2

CO_2e, carbon dioxide equivalent; DPI, dry powder inhaler; ICS, inhaled corticosteroid; LABA; long-acting beta-agonists; LAMA, long-acting muscarinic antagonist; pMDI, pressurised metered dose inhalers.

Supplementary Table 9. Sensitivity analysis: Greece

Model parameter	Variable	Scenario	Before Respimat Reusable switch		After Respimat Reusable switch			
			Cumulative CO_2e emissions (tonnes)	Difference with base case	Cumulative CO_2e emissions (tonnes)	Change in CO_2e emissions after intervention (tonnes)	Difference vs. base case (%)	Decrease in carbon footprint after switch (%)
Sensitivity analysis for the main analyses								
LAMA								
		Base case	**1,022.6**		**574.5**	**-448.1**	**-**	**43.8%**
Re-usability	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	1,022.6	-	1,133.3	110.7	124.7%	-10.8%
		12 devices/year	1,022.6	-	1,971.5	948.9	311.7%	-92.8%
	Number of LAMA devices used	*Base case: 6.44 devices/year*						
		6 devices/year	964.0	-58.7	574.5	-389.5	13.1%	40.4%
		12 devices/year	1,770.8	748.2	574.5	-1,196.3	-166.9%	67.6%
CO_2 data	**CO_2 data of Respimat Reusable**	*Base case: (data)*						
		+20% for Respimat Reusable	1,022.6	-		-1,022.6	-128.2%	100.0%
		-20% for Respimat Reusable	1,022.6	-		-1,022.6	-128.2%	100.0%
	CO_2 data of LAMA devices	*Base case: (data)*						
		+20% for LAMA devices	1,226.6	204.0	574.5	-652.1	-45.5%	53.2%
		-20% for LAMA devices	819.0	-203.7	574.5	-244.5	45.4%	29.9%
LAMA/LABA								

		Base case	**782.2**		**502.7**	**-279.6**		**35.7%**
Re-usability	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	782.2	-	991.6	209.4	174.9%	-26.8%
		12 devices/year	782.2	-	1,725.1	942.8	437.3%	-120.5%
	Number of LAMA/LABA devices used	*Base case: 6.69 devices/year*						
		6 devices/year	711.1	-71.2	502.7	-208.4	25.5%	29.3%
		12 devices/year	1,330.1	547.9	502.7	-827.5	-196.0%	62.2%
CO_2 data	**CO_2 data of Respimat Reusable**	*Base case: (data)*						
		+20% for Respimat Reusable	782.2	-	602.9	-179.4	35.8%	22.9%
		-20% for Respimat Reusable	782.2	-	402.5	-379.7	-35.8%	48.5%
	CO_2 data of LAMA/LABA devices	*Base case: (data)*						
		+20% for LAMA/LABA devices	936.8	154.5	502.7	-434.1	-55.3%	46.3%
		-20% for LAMA/LABA devices	625.7	-156.6	502.7	-123.0	56.0%	19.7%
Sensitivity analysis for the scenario analyses								
		Base case	**17,288.5**		**4,162.0**	**-13,126.4**	**-**	**75.9**
Extent of inhaler reuse in practice	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	17,288.5	-	10,782.4	-6,506.1	50.4%	37.6
		12 devices/year	17,288.5	-	18,757.2	1,468.8	111.2%	-8.5
	Number of DPIs	*Base case: 8.28 devices/year*						
		6 devices/year	14,982.4	-6,071.1	4,162.0	-10,820.3	17.6%	72.2
		12 devices/year	21,053.5	3,765.0	4,162.0	-16,891.5	-28.7%	80.2
	Number of pMDI	*Base case: 12 devices/year*						
		6 devices/year (theoretical)	13,189.8	-4,098.6	4,162.0	-9,027.8	31.2%	68.4
CO_2 data	**CO_2 data of**	*Base case: (data)*						

	Respimat Reusable	+20% for Respimat Reusable	17,288.5	-	4,994.5	-12,294.0	6.3%	71.1
		-20% for Respimat Reusable	17,288.5	-	3,329.6	-13,958.8	-6.3%	80.7
	CO_2 data of DPI	*Base case: (data)*						
		+20% for DPI	19,106.7	1,818.2	4,162.0	-14,944.7	-13.9%	78.2
		-20% for DPI	15,470.2	-1,818.2	4,162.0	-11,308.2	13.9%	73.1
	CO_2 data of pMDI	*Base case: (data)*						
		+20% for pMDI	18,927.9	1,639.5	4,162.0	-14,765.9	-12.5%	78.0
		-20% for pMDI	15,649.0	-1,639.5	4,162.0	-11,487.0	12.5%	73.4
Market share	**Current prescription of devices**	Base case:						
		Total patients on DPI and pMDI in 2020: - 10%	15,559.6	-1,728.8	3,745.8	-11,813.8	10.0%	75.9
		Total patients on DPI and pMDI in 2020: + 10%	19,017.3	1,728.8	4,578.3	-14,439.1	-10.0%	75.9
		Total patients on DPI in 2020: - 10%; Total patient on pMDI in 2020: +20%	18,287.0	998.5	4,854.0	-13,432.9	-2.3%	73.5
		Total patients on DPI in 2020: - 20%; Total patient on pMDI in 2020: +10%	16,290.0	-998.5	3,470.0	-12,819.9	2.3%	78.7
		Total patients on DPI in 2020: -10%; Total patient on pMDI in 2020: +20%	18,018.8	730.3	3,886.2	-14,132.6	-7.7%	78.4
		Total patients on DPI in 2020: +10%; Total patient on pMDI in 2020: -20%	16,558.1	-730.3	4,437.8	-12,120.3	7.7%	73.2
	Currently prescribed class	Base case						
		LAMA: +20%; other classes: -5%	16,319.7	-968.8	4,097.6	-12,222.1	6.9%	74.9
		LAMA: -20%; other classes: +5%	17,499.3	210.8	4,226.5	-13,272.8	-1.1%	75.8
		LABA/ICS: +20%; other classes: -5%	18,738.7	1,450.2	4,708.0	-14,030.7	-6.9%	74.9
		LABA/ICS: -20%; other classes: +5%	15,080.3	-2,208.2	3,616.1	-11,464.2	12.7%	76.0

		LAMA/LABA: +20%; other classes: -5%	16,259.6	-1,028.9	4,079.6	-12,180.0	7.2%	74.9
		LAMA/LABA: -20%; other classes: +5%	17,559.4	270.9	4,244.5	-13,314.9	-1.4%	75.8
		LAMA/LABA/ICS: +20%; other classes: -5%	17,165.5	-123.0	3,971.1	-13,194.4	-0.5%	76.9
		LAMA/LABA/ICS: -20%; other classes: +5%	16,653.5	-635.0	4,353.0	-12,300.5	6.3%	73.9
Extent of the switch	**Switch of devices**	*Base case: 100% switch DPI and pMDI to Respimat Reusable*						
		50% switch of DPI to Respimat Reusable (100% for pMDI)	17,288.5	-	6,860.6	-10,427.8	20.6%	60.3
		50% switch of pMDI to Respimat Reusable (100% for DPI)	17,288.5	-	8,026.7	-9,261.8	29.4%	53.6
		50% switch of DPI and pMDI to Respimat Reusable	17,288.5	-	10,725.3	-6,563.2	50.0%	38.0
	Switch of therapeutic classes	*Base case: 100% switch all therapeutic classes to Spiriva/Spiolto Respimat Reusable*						
		50% switch of LAMA (excluding Spiriva Respimat Reusable) to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	16,909.5	-379.0	4,386.1	-12,523.4	4.6%	74.1
		50% switch of LAMA/LABA (excluding Spiolto Respimat Reusable) to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	16,909.5	-379.0	4,301.8	-12,607.7	4.0%	74.6
		50% switch of LABA/ICS to Spiriva/ Spiolto Respimat Reusable (other	16,909.5	-379.0	8,003.3	-8,906.2	32.2%	52.7

		classes: 100% switch)						
		50% switch of LAMA/LABA/ICS to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	16,909.5	-379.0	6,330.7	-10,578.8	19.4%	62.6

CO_2e, carbon dioxide equivalent; DPI, dry powder inhaler; ICS, inhaled corticosteroid; LABA; long-acting beta-agonists; LAMA, long-acting muscarinic antagonist; pMDI, pressurised metered dose inhalers.

Supplementary Table 10. Sensitivity analysis: Italy

Model parameter	Variable	Scenario	Before Respimat Reusable switch		After Respimat Reusable switch			
			Cumulative CO_2e emissions (tonnes)	Difference with base case	Cumulative CO_2e emissions (tonnes)	Change in CO_2e emissions after intervention (tonnes)	Difference vs. base case (%)	Decrease in carbon footprint after switch (%)
Sensitivity analysis for the main analyses								
LAMA								
		Base case	**7,850.9**		**3,852.0**	**-3,999.0**	**-**	**50.9%**
Re-usability	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	7,850.9	-	7,598.7	-252.2	93.7%	3.2%
		12 devices/year	7,850.9	-	13,218.9	5,368.0	234.2%	-68.4%
	Number of LAMA devices used	*Base case: 7.56 devices/year*	**7,850.9**		**3,852.0**	**-3,999.0**	**0.0%**	**50.9%**
		6 devices/year	6,395.8	-1,455.1	3,852.0	-2,543.8	36.4%	39.8%
		12 devices/year	11,977.8	4,126.9	3,852.0	-8,125.8	-103.2%	67.8%
CO_2 data	**CO_2 data of Respimat Reusable**	*Base case: (data)*						
		+20% for Respimat Reusable	7,850.9	-	4,619.5	-3,231.4	19.2%	41.2%
		-20% for Respimat Reusable	7,850.9	-	3,084.4	-4,766.5	-19.2%	60.7%
	CO_2 data of LAMA devices	*Base case: (data)*						
		+20% for LAMA devices	9,440.0	1,589.1	3,852.0	-5,588.0	-39.7%	59.2%
		-20% for LAMA devices	6,282.0	-1,569.0	3,852.0	-2,430.0	39.2%	38.7%
LAMA/LABA								

		Base case	**1,474.2**		**819.6**	**-654.6**		**44.4%**
Re-usability	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	1,474.2	-	1,616.9	142.7	121.8%	-9.7%
		12 devices/year	1,474.2	-	2,812.8	1,338.6	304.5%	-90.8%
	Number of LAMA/LABA devices used	*Base case: 7.54 devices/year*						
		6 devices/year	1,198.7	-275.5	819.6	-379.1	42.1%	31.6%
		12 devices/year	2,271.5	797.2	819.6	-1,451.8	-121.8%	63.9%
CO_2 data	**CO_2 data of Respimat Reusable**	*Base case: (data)*						
		+20% for Respimat Reusable	1,474.2	-	983.0	-491.3	25.0%	33.3%
		-20% for Respimat Reusable	1,474.2	-	656.3	-817.9	-25.0%	55.5%
	CO_2 data of LAMA/LABA devices	*Base case: (data)*						
		+20% for LAMA/LABA devices	1,769.5	295.3	819.6	-949.9	-45.1%	53.7%
		-20% for LAMA/LABA devices	1,180.4	-293.8	819.6	-360.8	44.9%	30.6%
Sensitivity analysis for the scenario analyses								
		Base case	**124,477.5**		**15,878.1**	**-108,599.5**	**-**	**87.2**
Extent of inhaler reuse in practice	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	124,477.5	-	31,322.6	-93,155.0	14.2%	74.8
		12 devices/year	124,477.5	-	54,489.3	-69,988.2	35.6%	56.2
	Number of DPIs	*Base case: 10.25 devices/year*						
		6 devices/year	110,179.7	-20,170.2	15,878.1	-94,301.6	13.2%	85.6
		12 devices/year	130,349.9	5,872.4	15,878.1	-114,471.8	-5.4%	87.8
	Number of pMDI	*Base case: 12 devices/year*						
		6 devices/year (theoretical)	79,945.9	-44,531.6	15,878.1	-64,067.9	41.0%	80.1
CO_2 data	**CO_2 data of**	*Base case: (data)*						

	Respimat Reusable	+20% for Respimat Reusable	124,477.5	-	19,053.7	-105,423.8	2.9%	84.7
		-20% for Respimat Reusable	124,477.5	-	12,702.5	-111,775.1	-2.9%	89.8
	CO_2 data of DPI	*Base case: (data)*						
		+20% for DPI	131,560.4	7,082.9	15,878.1	-115,682.3	-6.5%	87.9
		-20% for DPI	117,394.7	-7,082.9	15,878.1	-101,516.6	6.5%	86.5
	CO_2 data of pMDI	*Base case: (data)*						
		+20% for pMDI	142,290.2	17,812.6	15,878.1	-126,412.1	-16.4%	88.8
		-20% for pMDI	106,664.9	-17,812.6	15,878.1	-90,786.8	16.4%	85.1
Market share	**Current prescription of devices**	Base case:						
		Total patients on DPI and pMDI in 2020: - 10%	112,029.8	-12,447.8	14,290.3	-97,739.5	10.0%	87.2
		Total patients on DPI and pMDI in 2020: + 10%	136,925.3	12,447.8	17,465.9	-119,459.4	-10.0%	87.2
		Total patients on DPI in 2020: - 10%; Total patient on pMDI in 2020: +20%	122,654.1	-1,823.5	17,871.3	-104,782.7	3.5%	85.4
		Total patients on DPI in 2020: - 20%; Total patient on pMDI in 2020: +10%	126,301.0	1,823.5	13,884.8	-112,416.2	-3.5%	89.0
		Total patients on DPI in 2020: -10%; Total patient on pMDI in 2020: +20%	138,748.7	14,271.2	15,472.6	-123,276.1	-13.5%	88.8
		Total patients on DPI in 2020: +10%; Total patient on pMDI in 2020: -20%	110,206.3	-14,271.2	16,283.5	-93,922.8	13.5%	85.2
	Currently prescribed class	Base case						
		LAMA: +20%; other classes: -5%	121,038.1	-3,439.5	16,047.2	-104,990.9	3.3%	86.7
		LAMA: -20%; other classes: +5%	129,646.9	5,169.3	15,709.0	-113,937.9	-4.9%	87.9
		LABA/ICS: +20%; other classes: -5%	143,068.9	18,591.3	17,731.8	-125,337.1	-15.4%	87.6
		LABA/ICS: -20%; other classes: +5%	107,616.1	-16,861.5	14,024.3	-93,591.7	13.8%	87.0

		LAMA/LABA: +20%; other classes: -5%	119,443.9	-5,033.6	15,289.1	-104,154.8	4.1%	87.2
		LAMA/LABA: -20%; other classes: +5%	131,241.0	6,763.5	16,467.1	-114,774.0	-5.7%	87.5
		LAMA/LABA/ICS: +20%; other classes: -5%	124,086.2	-391.4	15,238.2	-108,848.0	-0.2%	87.7
		LAMA/LABA/ICS: -20%; other classes: +5%	126,598.8	2,121.3	16,518.0	-110,080.8	-1.4%	87.0
Extent of the switch	**Switch of devices**	*Base case: 100% switch DPI and pMDI to Respimat Reusable*						
		50% switch of DPI to Respimat Reusable (100% for pMDI)	124,477.5	-	27,616.8	-96,860.8	10.8%	77.8
		50% switch of pMDI to Respimat Reusable (100% for DPI)	124,477.5	-	58,439.1	-66,038.4	39.2%	53.1
		50% switch of DPI and pMDI to Respimat Reusable	124,477.5	-	70,177.8	-54,299.7	50.0%	43.6
	Switch of therapeutic classes	*Base case: 100% switch all therapeutic classes to Spiriva/Spiolto Respimat Reusable*						
		50% switch of LAMA (excluding Spiriva Respimat Reusable) to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	125,342.5	864.9	17,877.6	-107,464.9	1.0%	85.7
		50% switch of LAMA/LABA (excluding Spiolto Respimat Reusable) to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	125,342.5	864.9	16,205.4	-109,137.1	-0.5%	87.1
		50% switch of LABA/ICS to Spiriva/ Spiolto Respimat Reusable (other	125,342.5	864.9	58,569.8	-66,772.6	38.5%	53.3

		classes: 100% switch)						
		50% switch of LAMA/LABA/ICS to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	125,342.5	864.9	25,591.7	-99,750.8	8.1%	79.6

CO2e, carbon dioxide equivalent; DPI, dry powder inhaler; ICS, inhaled corticosteroid; LABA; long-acting beta-agonists; LAMA, long-acting muscarinic antagonist; pMDI, pressurised metered dose inhalers.

Supplementary Table 11. Sensitivity analysis: Netherlands

Model parameter	Variable	Scenario	Before Respimat Reusable switch		After Respimat Reusable switch			
			Cumulative CO_2e emissions (tonnes)	Difference with base case	Cumulative CO_2e emissions (tonnes)	Change in CO_2e emissions after intervention (tonnes)	Difference vs. base case (%)	Decrease in carbon footprint after switch (%)
Sensitivity analysis for the main analyses								
LAMA								
		Base case	**1,260.2**		**1,093.1**	**-167.1**	**-**	**13.3%**
Re-usability	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	1,260.2	-	2,156.4	896.2	636.5%	-71.1%
		12 devices/year	1,260.2	-	3,751.3	2,491.1	1591.1%	-197.7%
	Number of LAMA devices used	*Base case: 2.66 devices/year*						
		6 devices/year	2,106.1	846.0	1,093.1	-1,013.0	-506.4%	48.1%
		12 devices/year	3,624.5	2,364.3	1,093.1	-2,531.4	-1415.2%	69.8%
CO_2 data	**CO_2 data of Respimat Reusable**	*Base case: (data)*						
		+20% for Respimat Reusable	1,260.2	-	1,310.9	50.8	130.4%	-4.0%
		-20% for Respimat Reusable	1,260.2	-	875.3	-384.9	-130.4%	30.5%
	CO_2 data of LAMA devices	*Base case: (data)*						
		+20% for LAMA devices	1,507.8	247.6	1,093.1	-414.7	-148.2%	27.5%
		-20% for LAMA devices	1,007.5	-252.7	1,093.1	85.6	151.2%	-8.5%
LAMA/LABA								

		Base case	**773.6**		**238.0**	**-535.6**		**69.2%**
Re-usability	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	773.6	-	469.5	-304.1	43.2%	39.3%
		12 devices/year	773.6	-	816.8	43.2	108.1%	-5.6%
	Number of LAMA/LABA devices used	*Base case: 7.13 devices/year*						
		6 devices/year	657.6	-116.1	238.0	-419.5	21.7%	63.8%
		12 devices/year	1,275.1	501.5	238.0	-1,037.1	-93.6%	81.3%
CO_2 data	**CO_2 data of Respimat Reusable**	*Base case: (data)*						
		+20% for Respimat Reusable	773.6	-	285.4	-488.2	8.9%	63.1%
		-20% for Respimat Reusable	773.6	-	190.6	-583.1	-8.9%	75.4%
	CO_2 data of LAMA/LABA devices	*Base case: (data)*						
		+20% for LAMA/LABA devices	927.6	154.0	238.0	-689.6	-28.8%	74.3%
		-20% for LAMA/LABA devices	618.8	-154.8	238.0	-380.8	28.9%	61.5%
Sensitivity analysis for the scenario analyses								
		Base case	**43,810.0**		**5,465.8**	**-38,344.2**	**-**	**87.5**
Extent of inhaler reuse in practice	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	43,810.0	-	10,782.4	-33,027.7	13.9%	75.4
		12 devices/year	43,810.0	-	18,757.2	-25,052.8	34.7%	57.2
	Number of DPIs	*Base case: 8.77 devices/year*						
		6 devices/year	40,990.2	-6,113.8	5,465.8	-35,524.4	7.4%	86.7
		12 devices/year	47,104.1	3,294.0	5,465.8	-41,638.3	-8.6%	88.4
	Number of pMDI	*Base case: 12 devices/year*						
		6 devices/year (theoretical)	26,685.7	-17,124.3	5,465.8	-21,219.9	44.7%	79.5
CO_2 data	**CO_2 data of**	*Base case: (data)*						

	Respimat Reusable	+20% for Respimat Reusable	43,810.0	-	6,559.0	-37,251.1	2.9%	85.0
		-20% for Respimat Reusable	43,810.0	-	4,372.7	-39,437.4	-2.9%	90.0
	CO_2 data of DPI	*Base case: (data)*						
		+20% for DPI	45,722.3	1,912.3	5,465.8	-40,256.5	-5.0%	88.0
		-20% for DPI	41,897.8	-1,912.3	5,465.8	-36,431.9	5.0%	87.0
	CO_2 data of pMDI	*Base case: (data)*						
		+20% for pMDI	50,659.8	6,849.7	5,465.8	-45,194.0	-17.9%	89.2
		-20% for pMDI	36,960.3	-6,849.7	5,465.8	-31,494.5	17.9%	85.2
Market share	**Current prescription of devices**	Base case:						
		Total patients on DPI and pMDI in 2020: - 10%	39,429.0	-4,381.0	4,919.2	-34,509.8	10.0%	87.5
		Total patients on DPI and pMDI in 2020: + 10%	48,191.0	4,381.0	6,012.4	-42,178.6	-10.0%	87.5
		Total patients on DPI in 2020: - 10%; Total patient on pMDI in 2020: +20%	42,297.5	-1,512.6	5,974.7	-36,322.8	5.3%	85.9
		Total patients on DPI in 2020: - 20%; Total patient on pMDI in 2020: +10%	45,322.6	1,512.6	4,957.0	-40,365.7	-5.3%	89.1
		Total patients on DPI in 2020: -10%; Total patient on pMDI in 2020: +20%	49,703.6	5,893.6	5,503.5	-44,200.1	-15.3%	88.9
		Total patients on DPI in 2020: +10%; Total patient on pMDI in 2020: -20%	37,916.4	-5,893.6	5,428.1	-32,488.4	15.3%	85.7
	Currently prescribed class	Base case						
		LAMA: +20%; other classes: -5%	42,339.8	-1,470.3	5,465.8	-36,874.0	3.8%	87.1
		LAMA: -20%; other classes: +5%	46,133.3	2,323.3	5,465.8	-40,667.5	-6.1%	88.2
		LABA/ICS: +20%; other classes: -5%	48,020.7	4,210.7	6,141.8	-41,878.9	-9.2%	87.2
		LABA/ICS: -20%; other classes: +5%	40,452.4	-3,357.7	4,789.8	-35,662.6	7.0%	88.2

		LAMA/LABA: +20%; other classes: -5%	42,218.1	-1,591.9	5,252.0	-36,966.1	3.6%	87.6
		LAMA/LABA: -20%; other classes: +5%	46,255.0	2,444.9	5,679.6	-40,575.4	-5.8%	87.7
		LAMA/LABA/ICS: +20%; other classes: -5%	46,579.4	2,769.4	5,276.9	-41,302.5	-7.7%	88.7
		LAMA/LABA/ICS: -20%; other classes: +5%	41,893.7	-1,916.3	5,654.8	-36,239.0	5.5%	86.5
Extent of the switch	**Switch of devices**	*Base case: 100% switch DPI and pMDI to Respimat Reusable*						
		50% switch of DPI to Respimat Reusable (100% for pMDI)	43,810.0	-	8,487.5	-35,322.6	7.9%	80.6
		50% switch of pMDI to Respimat Reusable (100% for DPI)	43,810.0	-	21,616.3	-22,193.8	42.1%	50.7
		50% switch of DPI and pMDI to Respimat Reusable	43,810.0	-	24,637.9	-19,172.1	50.0%	43.8
	Switch of therapeutic classes	*Base case: 100% switch all therapeutic classes to Spiriva/Spiolto Respimat Reusable*						
		50% switch of LAMA (excluding Spiriva Respimat Reusable) to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	44,236.6	426.5	5,549.3	-38,687.2	-0.9%	87.5
		50% switch of LAMA/LABA (excluding Spiolto Respimat Reusable) to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	44,236.6	426.5	5,733.6	-38,502.9	-0.4%	87.0
		50% switch of LABA/ICS to Spiriva/ Spiolto Respimat Reusable (other	44,236.6	426.5	15,559.2	-28,677.4	25.2%	64.8

		classes: 100% switch)						
		50% switch of LAMA/LABA/ICS to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	44,236.56	426.52	14,406.47	-29,830.10	22.2%	67.4

CO_2e, carbon dioxide equivalent; DPI, dry powder inhaler; ICS, inhaled corticosteroid; LABA; long-acting beta-agonists; LAMA, long-acting muscarinic antagonist; pMDI, pressurised metered dose inhalers.

Supplementary Table 12. Sensitivity analysis: Norway

Model parameter	Variable	Scenario	Before Respimat Reusable switch		After Respimat Reusable switch			
			Cumulative CO_2e emissions (tonnes)	Difference with base case	Cumulative CO_2e emissions (tonnes)	Change in CO_2e emissions after intervention (tonnes)	Difference vs. base case (%)	Decrease in carbon footprint after switch (%)
Sensitivity analysis for the main analyses								
LAMA								
		Base case	**296.4**		**192.5**	**-103.9**	**-**	**35.1%**
Re-usability	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	296.4	-	379.8	83.3	180.2%	-28.1%
		12 devices/year	296.4	-	660.6	364.2	450.4%	-122.9%
	Number of LAMA devices used	*Base case: 4.69 devices/year*						
		6 devices/year	357.1	60.7	192.5	-164.6	-58.4%	46.1%
		12 devices/year	634.5	338.1	192.5	-442.0	-325.3%	69.7%
CO_2 data	**CO_2 data of Respimat Reusable**	*Base case: (data)*						
		+20% for Respimat Reusable	296.4	-	230.9	-65.6	36.9%	22.1%
		-20% for Respimat Reusable	296.4	-	154.1	-142.3	-36.9%	48.0%
	CO_2 data of LAMA devices	*Base case: (data)*						
		+20% for LAMA devices	356.4	59.9	192.5	-163.9	-57.7%	46.0%
		-20% for LAMA devices	237.4	-59.0	192.5	-44.9	56.8%	18.9%
LAMA/LABA								

		Base case	**1,009.4**		**183.6**	**-825.8**		**81.8%**
Re-usability	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	1,009.4	-	362.2	-647.2	21.6%	64.1%
		12 devices/year	1,009.4	-	630.1	-379.3	54.1%	37.6%
	Number of LAMA/LABA devices used	*Base case: 8.76 devices/year*						
		6 devices/year	697.9	-311.5	183.6	-514.3	37.7%	73.7%
		12 devices/year	1,375.4	365.9	183.6	-1,191.7	-44.3%	86.6%
CO_2 data	**CO_2 data of Respimat Reusable**	*Base case: (data)*						
		+20% for Respimat Reusable	1,009.4	-	220.2	-789.2	4.4%	78.2%
		-20% for Respimat Reusable	1,009.4	-	147.0	-862.4	-4.4%	85.4%
	CO_2 data of LAMA/LABA devices	*Base case: (data)*						
		+20% for LAMA/LABA devices	1,211.3	201.9	183.6	-1,027.7	-24.4%	84.8%
		-20% for LAMA/LABA devices	807.6	-201.9	183.6	-623.9	24.4%	77.3%
Sensitivity analysis for the scenario analyses								
		Base case	**21,961.0**		**1,907.8**	**-20,053.2**	**-**	**91.3**
Extent of inhaler reuse in practice	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	21,961.0	-	3,763.5	-18,197.5	9.3%	82.9
		12 devices/year	21,961.0	-	6,547.1	-15,414.0	23.1%	70.2
	Number of DPIs	*Base case: 10.62 devices/year*						
		6 devices/year	20,069.0	-2,456.9	1,907.8	-18,161.2	9.4%	90.5
		12 devices/year	22,525.9	564.9	1,907.8	-20,618.1	-2.8%	91.5
	Number of pMDI	*Base case: 12 devices/year*						
		6 devices/year (theoretical)	13,205.1	-8,756.0	1,907.8	-11,297.3	43.7%	85.6
CO_2 data	**CO_2 data of**	*Base case: (data)*						

	Respimat Reusable	+20% for Respimat Reusable	21,961.0	-	2,289.4	-19,671.7	1.9%	89.6
		-20% for Respimat Reusable	21,961.0	-	1,526.2	-20,434.8	-1.9%	93.1
	CO_2 data of DPI	*Base case: (data)*						
		+20% for DPI	22,850.9	889.8	1,907.8	-20,943.1	-4.4%	91.7
		-20% for DPI	21,071.2	-889.8	1,907.8	-19,163.4	4.4%	90.9
	CO_2 data of pMDI	*Base case: (data)*						
		+20% for pMDI	25,463.4	3,502.4	1,907.8	-23,555.6	-17.5%	92.5
		-20% for pMDI	18,458.7	-3,502.4	1,907.8	-16,550.9	17.5%	89.7
Market share	**Current prescription of devices**	Base case:						
		Total patients on DPI and pMDI in 2020: - 10%	19,764.9	-2,196.1	1,717.0	-18,047.9	10.0%	91.3
		Total patients on DPI and pMDI in 2020: + 10%	24,157.1	2,196.1	2,098.6	-22,058.6	-10.0%	91.3
		Total patients on DPI in 2020: - 10%; Total patient on pMDI in 2020: +20%	21,099.7	-861.4	2,152.6	-18,947.1	5.5%	89.8
		Total patients on DPI in 2020: - 20%; Total patient on pMDI in 2020: +10%	22,822.4	861.4	1,663.1	-21,159.3	-5.5%	92.7
		Total patients on DPI in 2020: -10%; Total patient on pMDI in 2020: +20%	25,018.5	3,057.5	1,853.8	-23,164.7	-15.5%	92.6
		Total patients on DPI in 2020: +10%; Total patient on pMDI in 2020: -20%	18,903.6	-3,057.5	1,961.8	-16,941.8	15.5%	89.6
	Currently prescribed class	Base case						
		LAMA: +20%; other classes: -5%	20,804.9	-1,156.1	1,860.5	-18,944.4	5.5%	91.1
		LAMA: -20%; other classes: +5%	22,838.9	877.9	1,955.1	-20,883.8	-4.1%	91.4
		LABA/ICS: +20%; other classes: -5%	24,354.6	2,393.5	2,156.6	-22,198.0	-10.7%	91.1
		LABA/ICS: -20%; other classes: +5%	19,289.3	-2,671.8	1,659.0	-17,630.2	12.1%	91.4

		LAMA/LABA: +20%; other classes: -5%	20,983.2	-977.9	1,858.3	-19,124.9	4.6%	91.1
		LAMA/LABA: -20%; other classes: +5%	22,660.7	699.6	1,957.3	-20,703.4	-3.2%	91.4
		LAMA/LABA/ICS: +20%; other classes: -5%	22,236.1	275.1	1,851.2	-20,384.9	-1.7%	91.7
		LAMA/LABA/ICS: -20%; other classes: +5%	21,407.7	-553.3	1,964.4	-19,443.3	3.0%	90.8
Extent of the switch	**Switch of devices**	*Base case: 100% switch DPI and pMDI to Respimat Reusable*						
		50% switch of DPI to Respimat Reusable (100% for pMDI)	21,961.0	-	3,406.5	-18,554.6	7.5%	84.5
		50% switch of pMDI to Respimat Reusable (100% for DPI)	21,961.0	-	10,435.7	-11,525.3	42.5%	52.5
		50% switch of DPI and pMDI to Respimat Reusable	21,961.0	-	11,934.4	-10,026.6	50.0%	45.7
	Switch of therapeutic classes	*Base case: 100% switch all therapeutic classes to Spiriva/Spiolto Respimat Reusable*						
		50% switch of LAMA (excluding Spiriva Respimat Reusable) to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	21,821.9	-139.1	1,959.8	-19,862.2	1.0%	91.0
		50% switch of LAMA/LABA (excluding Spiolto Respimat Reusable) to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	21,821.9	-139.1	2,320.7	-19,501.2	2.8%	89.4
		50% switch of LABA/ICS to Spiriva/ Spiolto Respimat Reusable (other	21,821.9	-139.1	8,467.0	-13,354.9	33.4%	61.2

		classes: 100% switch)						
		50% switch of LAMA/LABA/ICS to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	21,821.9	-139.1	4,840.8	-16,981.1	15.3%	77.8

CO_2e, carbon dioxide equivalent; DPI, dry powder inhaler; ICS, inhaled corticosteroid; LABA; long-acting beta-agonists; LAMA, long-acting muscarinic antagonist; pMDI, pressurised metered dose inhalers.

Supplementary Table 13. Sensitivity analysis: Portugal

Model parameter	Variable	Scenario	Before Respimat Reusable switch		After Respimat Reusable switch			
			Cumulative CO_2e emissions (tonnes)	Difference with base case	Cumulative CO_2e emissions (tonnes)	Change in CO_2e emissions after intervention (tonnes)	Difference vs. base case (%)	Decrease in carbon footprint after switch (%)
Sensitivity analysis for the main analyses								
LAMA								
		Base case	**466.7**		**362.1**	**-104.5**	**-**	**22.4%**
Re-usability	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	466.7	-	714.4	247.7	336.9%	-53.1%
		12 devices/year	466.7	-	1,242.7	776.0	842.3%	-166.3%
	Number of LAMA devices used	*Base case: 3.84 devices/year*						
		6 devices/year	640.8	174.1	362.1	-278.7	-166.6%	43.5%
		12 devices/year	1,125.4	658.7	362.1	-763.3	-630.1%	67.8%
CO_2 data	**CO_2 data of Respimat Reusable**	*Base case: (data)*						
		+20% for Respimat Reusable	466.7	-	434.3	-32.4	69.0%	6.9%
		-20% for Respimat Reusable	466.7	-	290.0	-176.7	-69.0%	37.9%
	CO_2 data of LAMA devices	*Base case: (data)*						
		+20% for LAMA devices	558.9	92.3	362.1	-196.8	-88.2%	35.2%
		-20% for LAMA devices	363.2	-103.5	362.1	-1.1	99.0%	0.3%
LAMA/LABA								

		Base case	**706.9**		**493.6**	**-213.3**		**30.2%**
Re-usability	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	706.9	-	973.7	266.8	225.1%	-37.7%
		12 devices/year	706.9	-	1,693.8	987.0	562.7%	-139.6%
	Number of LAMA/LABA devices used	*Base case: 6.21 devices/year*						
		6 devices/year	912.5	205.6	493.6	-418.9	-96.4%	45.9%
		12 devices/year	1,273.8	566.9	493.6	-780.2	-265.8%	61.3%
CO_2 data	**CO_2 data of Respimat Reusable**	*Base case: (data)*						
		+20% for Respimat Reusable	706.9	-	591.9	-114.9	46.1%	16.3%
		-20% for Respimat Reusable	706.9	-	395.2	-311.6	-46.1%	44.1%
	CO_2 data of LAMA/LABA devices	*Base case: (data)*						
		+20% for LAMA/LABA devices	848.9	142.0	493.6	-355.3	-66.6%	41.9%
		-20% for LAMA/LABA devices	565.2	-141.7	493.6	-71.6	66.4%	12.7%
Sensitivity analysis for the scenario analyses								
		Base case	**31,634.8**		**2,444.9**	**-29,189.9**	**-**	**92.3**
Extent of inhaler reuse in practice	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	31,634.8	-	4,823.0	-26,811.8	8.1%	84.8
		12 devices/year	31,634.8	-	8,390.2	-23,244.6	20.4%	73.5
	Number of DPIs	*Base case: 9.10 devices/year*						
		6 devices/year	29,978.1	-3,209.7	2,444.9	-27,533.2	5.7%	91.8
		12 devices/year	33,187.7	1,552.9	2,444.9	-30,742.8	-5.3%	92.6
	Number of pMDI	*Base case: 12 devices/year*						
		6 devices/year (theoretical)	18,377.9	-13,256.9	2,444.9	-15,933.0	45.4%	86.7

CO_2 data	**CO_2 data of Respimat Reusable**	*Base case: (data)*						
		+20% for Respimat Reusable	31,634.8	-	2,933.9	-28,700.9	1.7%	90.7
		-20% for Respimat Reusable	31,634.8	-	1,955.9	-29,678.9	-1.7%	93.8
	CO_2 data of DPI	*Base case: (data)*						
		+20% for DPI	32,659.0	1,024.2	2,444.9	-30,214.1	-3.5%	92.5
		-20% for DPI	30,610.6	-1,024.2	2,444.9	-28,165.7	3.5%	92.0
	CO_2 data of pMDI	*Base case: (data)*						
		+20% for pMDI	36,937.6	5,302.7	2,444.9	-34,492.7	-18.2%	93.4
		-20% for pMDI	26,332.1	-5,302.7	2,444.9	-23,887.2	18.2%	90.7
Market share	**Current prescription of devices**	Base case:						
		Total patients on DPI and pMDI in 2020: - 10%	28,471.3	-3,163.5	2,200.4	-26,270.9	10.0%	92.3
		Total patients on DPI and pMDI in 2020: + 10%	34,798.3	3,163.5	2,689.4	-32,108.9	-10.0%	92.3
		Total patients on DPI in 2020: - 10%; Total patient on pMDI in 2020: +20%	30,007.6	-1,627.2	2,800.9	-27,206.8	6.8%	90.7
		Total patients on DPI in 2020: - 20%; Total patient on pMDI in 2020: +10%	33,262.0	1,627.2	2,088.9	-31,173.0	-6.8%	93.7
		Total patients on DPI in 2020: -10%; Total patient on pMDI in 2020: +20%	36,425.4	4,790.6	2,333.4	-34,092.0	-16.8%	93.6
		Total patients on DPI in 2020: +10%; Total patient on pMDI in 2020: -20%	26,844.2	-4,790.6	2,556.4	-24,287.8	16.8%	90.5
	Currently prescribed class	Base case						
		LAMA: +20%; other classes: -5%	30,480.7	-1,154.1	2,413.2	-28,067.5	3.8%	92.1
		LAMA: -20%; other classes: +5%	33,443.6	1,808.7	2,476.6	-30,966.9	-6.1%	92.6
		LABA/ICS: +20%; other classes: -5%	37,963.3	6,328.5	2,691.3	-35,272.0	-20.8%	92.9

		LABA/ICS: -20%; other classes: +5%	25,960.9	-5,673.9	2,198.5	-23,762.4	18.6%	91.5
		LAMA/LABA: +20%; other classes: -5%	30,540.7	-1,094.1	2,446.0	-28,094.7	3.8%	92.0
		LAMA/LABA: -20%; other classes: +5%	33,383.5	1,748.7	2,443.7	-30,939.8	-6.0%	92.7
		LAMA/LABA/ICS: +20%; other classes: -5%	30,461.9	-1,172.9	2,351.3	-28,110.6	3.7%	92.3
		LAMA/LABA/ICS: -20%; other classes: +5%	33,462.4	1,827.6	2,538.5	-30,923.9	-5.9%	92.4
Extent of the switch	**Switch of devices**	*Base case: 100% switch DPI and pMDI to Respimat Reusable*						
		50% switch of DPI to Respimat Reusable (100% for pMDI)	31,634.8	-	4,004.7	-27,630.1	5.3%	87.3
		50% switch of pMDI to Respimat Reusable (100% for DPI)	31,634.8	-	15,480.1	-16,154.7	44.7%	51.1
		50% switch of DPI and pMDI to Respimat Reusable	31,634.8	-	17,039.8	-14,595.0	50.0%	46.1
	Switch of therapeutic classes	*Base case: 100% switch all therapeutic classes to Spiriva/Spiolto Respimat Reusable*						
		50% switch of LAMA (excluding Spiriva Respimat Reusable) to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	31,962.1	327.3	2,497.2	-29,464.9	-0.9%	92.2
		50% switch of LAMA/LABA (excluding Spiolto Respimat Reusable) to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	31,962.1	327.3	2,551.5	-29,410.6	-0.8%	92.0
		50% switch of LABA/ICS to Spiriva/	31,962.1	327.3	16,906.2	-15,055.9	48.4%	47.1

		Spiolto Respimat Reusable (other classes: 100% switch)						
		50% switch of LAMA/LABA/ICS to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	31,962.1	327.3	2,583.3	-29,378.8	-0.6%	91.9

CO_2e, carbon dioxide equivalent; DPI, dry powder inhaler; ICS, inhaled corticosteroid; LABA; long-acting beta-agonists; LAMA, long-acting muscarinic antagonist; pMDI, pressurised metered dose inhalers.

Supplementary Table 14. Sensitivity analysis: Spain

Model parameter	Variable	Scenario	Before Respimat Reusable switch		After Respimat Reusable switch			
			Cumulative CO_2e emissions (tonnes)	Difference with base case	Cumulative CO_2e emissions (tonnes)	Change in CO_2e emissions after intervention (tonnes)	Difference vs. base case (%)	Decrease in carbon footprint after switch (%)
Sensitivity analysis for the main analyses								
LAMA								
		Base case	**4,163.0**		**3,023.0**	**-1,140.0**	**-**	**27.4%**
Re-usability	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	4,163.0	-	5,963.4	1,800.4	257.9%	-43.2%
		12 devices/year	4,163.0	-	10,374.1	6,211.1	644.8%	-149.2%
	Number of LAMA devices used	*Base case: 4.07 devices/year*						
		6 devices/year	5,513.6	1,350.6	3,023.0	-2,490.6	-118.5%	45.2%
		12 devices/year	9,708.7	5,545.7	3,023.0	-6,685.7	-486.5%	68.9%
CO_2 data	**CO_2 data of Respimat Reusable**	*Base case: (data)*						
		+20% for Respimat Reusable	4,163.0	-	3,625.4	-537.6	52.8%	12.9%
		-20% for Respimat Reusable	4,163.0	-	2,420.6	-1,742.4	-52.8%	41.9%
	CO_2 data of LAMA devices	*Base case: (data)*						
		+20% for LAMA devices	4,995.6	832.6	3,023.0	-1,972.6	-73.0%	39.5%
		-20% for LAMA devices	3,330.4	-832.6	3,023.0	-307.4	73.0%	9.2%
LAMA/LABA								

		Base case	**2,607.9**		**2,157.5**	**-450.4**		**17.3%**
Re-usability	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	2,607.9	-	4,256.0	1,648.1	465.9%	-63.2%
		12 devices/year	2,607.9	-	7,403.8	4,795.9	1164.7%	-183.9%
	Number of LAMA/LABA devices used	*Base case: 5.29 devices/year*						
		6 devices/year	2,892.3	284.4	2,157.5	-734.8	-63.1%	25.4%
		12 devices/year	5,285.5	2,677.6	2,157.5	-3,128.1	-594.4%	59.2%
CO_2 data	**CO_2 data of Respimat Reusable**	*Base case: (data)*						
		+20% for Respimat Reusable	2,607.9	-	2,587.4	-20.5	95.4%	0.8%
		-20% for Respimat Reusable	2,607.9	-	1,727.6	-880.3	-95.4%	33.8%
	CO_2 data of LAMA/LABA devices	*Base case: (data)*						
		+20% for LAMA/LABA devices	3,129.5	521.6	2,157.5	-972.0	-115.8%	31.1%
		-20% for LAMA/LABA devices	2,086.3	-521.6	2,157.5	71.1	115.8%	-3.4%
Sensitivity analysis for the scenario analyses								
		Base case	**145,756.5**		**16,375.9**	**-129,380.6**	**-**	**88.8%**
Extent of inhaler reuse in practice	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	145,756.5	-	32,304.5	-113,451.9	12.3%	77.8%
		12 devices/year	145,756.5	-	56,197.6	-89,558.9	30.8%	61.4%
	Number of DPIs	*Base case: 8.95 devices/year*						
		6 devices/year	135,470.6	-20,891.7	16,375.9	-119,094.8	8.0%	87.9%
		12 devices/year	156,362.3	10,605.8	16,375.9	-139,986.4	-8.2%	89.5%
	Number of pMDI	*Base case: 12 devices/year*						
		6 devices/year (theoretical)	89,375.8	-56,380.7	16,375.9	-72,999.9	43.6%	81.7%
CO_2 data	**CO_2 data of**	*Base case: (data)*						

	Respimat Reusable	+20% for Respimat Reusable	145,756.5	-	19,651.0	-126,105.4	2.5%	86.5%
		-20% for Respimat Reusable	145,756.5	-	13,100.7	-132,655.8	-2.5%	91.0%
	CO_2 data of DPI	*Base case: (data)*						
		+20% for DPI	152,355.5	6,599.0	16,375.9	-135,979.6	-5.1%	89.3%
		-20% for DPI	139,157.4	-6,599.0	16,375.9	-122,781.6	5.1%	88.2%
	CO_2 data of pMDI	*Base case: (data)*						
		+20% for pMDI	168,308.7	22,552.3	16,375.9	-151,932.9	-17.4%	90.3%
		-20% for pMDI	123,204.2	-22,552.3	16,375.9	-106,828.3	17.4%	86.7%
Market share	**Current prescription of devices**	Base case:						
		Total patients on DPI and pMDI in 2020: - 10%	131,180.8	-14,575.6	14,738.3	-116,442.5	10.0%	88.8%
		Total patients on DPI and pMDI in 2020: + 10%	160,332.1	14,575.6	18,013.4	-142,318.7	-10.0%	88.8%
		Total patients on DPI in 2020: - 10%; Total patient on pMDI in 2020: +20%	141,079.4	-4,677.1	18,526.3	-122,553.1	5.3%	86.9%
		Total patients on DPI in 2020: - 20%; Total patient on pMDI in 2020: +10%	150,433.6	4,677.1	14,225.4	-136,208.2	-5.3%	90.5%
		Total patients on DPI in 2020: -10%; Total patient on pMDI in 2020: +20%	165,009.2	19,252.8	15,863.0	-149,146.2	-15.3%	90.4%
		Total patients on DPI in 2020: +10%; Total patient on pMDI in 2020: -20%	126,503.7	-19,252.8	16,888.7	-109,615.0	15.3%	86.6%
	Currently prescribed class	Base case						
		LAMA: +20%; other classes: -5%	141,772.7	-3,983.7	16,312.8	-125,459.9	3.0%	88.5%
		LAMA: -20%; other classes: +5%	154,505.1	8,748.7	16,438.9	-138,066.2	-6.7%	89.4%
		LABA/ICS: +20%; other classes: -5%	171,202.5	25,446.1	18,230.1	-152,972.5	-18.2%	89.4%
		LABA/ICS: -20%; other classes: +5%	125,075.3	-20,681.1	14,521.6	-110,553.7	14.6%	88.4%

		LAMA/LABA: +20%; other classes: -5%	141,384.0	-4,372.5	16,096.4	-125,287.5	3.2%	88.6%
		LAMA/LABA: -20%; other classes: +5%	154,893.9	9,137.5	16,655.3	-138,238.6	-6.8%	89.2%
		LAMA/LABA/ICS: +20%; other classes: -5%	145,603.5	-153.0	15,682.9	-129,920.6	-0.4%	89.2%
		LAMA/LABA/ICS: -20%; other classes: +5%	150,674.4	4,918.0	17,068.8	-133,605.6	-3.3%	88.7%
Extent of the switch	**Switch of devices**	*Base case: 100% switch DPI and pMDI to Respimat Reusable*						
		50% switch of DPI to Respimat Reusable (100% for pMDI)	145,756.5	-	26,560.0	-119,196.4	7.9%	81.8%
		50% switch of pMDI to Respimat Reusable (100% for DPI)	145,756.5	-	70,882.0	-74,874.5	42.1%	51.4%
		50% switch of DPI and pMDI to Respimat Reusable	145,756.5	-	81,066.2	-64,690.3	50.0%	44.4%
	Switch of therapeutic classes	*Base case: 100% switch all therapeutic classes to Spiriva/Spiolto Respimat Reusable*						
		50% switch of LAMA (excluding Spiriva Respimat Reusable) to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	148,138.9	2,382.5	16,945.9	-131,193.1	-1.4%	88.6%
		50% switch of LAMA/LABA (excluding Spiolto Respimat Reusable) to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	148,138.9	2,382.5	16,601.1	-131,537.9	-1.7%	88.8%
		50% switch of LABA/ICS to Spiriva/ Spiolto Respimat Reusable (other	148,138.9	2,382.5	71,970.9	-76,168.1	41.1%	51.4%

		classes: 100% switch)						
		50% switch of LAMA/LABA/ICS to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	148,138.9	2,382.5	25,867.1	-122,271.8	5.5%	82.5%

CO_2e, carbon dioxide equivalent; DPI, dry powder inhaler; ICS, inhaled corticosteroid; LABA; long-acting beta-agonists; LAMA, long-acting muscarinic antagonist; pMDI, pressurised metered dose inhalers.

Supplementary Table 15. Sensitivity analysis: Sweden

Model parameter	Variable	Scenario	Before Respimat Reusable switch		After Respimat Reusable switch			
			Cumulative CO_2e emissions (tonnes)	Difference with base case	Cumulative CO_2e emissions (tonnes)	Change in CO_2e emissions after intervention (tonnes)	Difference vs. base case (%)	Decrease in carbon footprint after switch (%)
Sensitivity analysis for the main analyses								
LAMA								
		Base case	**713.1**		**507.5**	**-205.6**	**-**	**28.8%**
Re-usability	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	713.1	-	1,001.1	288.0	240.0%	-40.4%
		12 devices/year	713.1	-	1,741.5	1,028.4	600.1%	-144.2%
	Number of LAMA devices used	*Base case: 3.91 devices/year*						
		6 devices/year	966.5	253.4	507.5	-459.0	-123.2%	47.5%
		12 devices/year	1,695.6	982.5	507.5	-1,188.1	-477.8%	70.1%
CO_2 data	**CO_2 data of Respimat Reusable**	*Base case: (data)*						
		+20% for Respimat Reusable	713.1	-	608.6	-104.5	49.2%	14.7%
		-20% for Respimat Reusable	713.1	-	406.3	-306.8	-49.2%	43.0%
	CO_2 data of LAMA devices	*Base case: (data)*						
		+20% for LAMA devices	856.7	143.6	507.5	-349.3	-69.8%	40.8%
		-20% for LAMA devices	571.5	-141.6	507.5	-64.0	68.9%	11.2%
LAMA/LABA								

		Base case	**448.8**		**182.0**	**-266.8**		**59.4%**
Re-usability	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	448.8	-	359.1	-89.7	66.4%	20.0%
		12 devices/year	448.8	-	624.6	175.8	165.9%	-39.2%
	Number of LAMA/LABA devices used	*Base case: 6.25 devices/year*						
		6 devices/year	432.1	-16.7	182.0	-250.1	6.3%	57.9%
		12 devices/year	828.1	379.3	182.0	-646.1	-142.2%	78.0%
CO_2 data	**CO_2 data of Respimat Reusable**	*Base case: (data)*						
		+20% for Respimat Reusable	448.8	-	218.3	-230.5	13.6%	51.4%
		-20% for Respimat Reusable	448.8	-	145.7	-303.1	-13.6%	67.5%
	CO_2 data of LAMA/LABA devices	*Base case: (data)*						
		+20% for LAMA/LABA devices	538.6	89.8	182.0	-356.5	-33.6%	66.2%
		-20% for LAMA/LABA devices	359.0	-89.8	182.0	-177.0	33.6%	49.3%
Sensitivity analysis for the scenario analyses								
		Base case	**18,741.4**		**2,680.5**	**-16,060.9**	**-**	**85.7**
Extent of inhaler reuse in practice	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	18,741.4	-	5,287.8	-13,453.6	16.2%	71.8
		12 devices/year	18,741.4	-	9,198.7	-9,542.7	40.6%	50.9
	Number of DPIs	*Base case: 9.71 devices/year*						
		6 devices/year	16,377.7	-3,819.5	2,680.5	-13,697.3	14.7%	83.6
		12 devices/year	20,197.2	1,455.8	2,680.5	-17,516.7	-9.1%	86.7
	Number of pMDI	*Base case: 12 devices/year*						
		6 devices/year (theoretical)	12,599.0	-6,142.4	2,680.5	-9,918.5	38.2%	78.7
CO_2 data	**CO_2 data of**	*Base case: (data)*						

	Respimat Reusable	+20% for Respimat Reusable	18,741.4	-	3,216.6	-15,524.8	3.3%	82.8
		-20% for Respimat Reusable	18,741.4	-	2,144.4	-16,597.0	-3.3%	88.6
	CO_2 data of DPI	*Base case: (data)*						
		+20% for DPI	20,032.7	1,291.3	2,680.5	-17,352.2	-8.0%	86.6
		-20% for DPI	17,450.0	-1,291.3	2,680.5	-14,769.6	8.0%	84.6
	CO_2 data of pMDI	*Base case: (data)*						
		+20% for pMDI	21,198.3	2,457.0	2,680.5	-18,517.8	-15.3%	87.4
		-20% for pMDI	16,284.4	-2,457.0	2,680.5	-13,603.9	15.3%	83.5
Market share	**Current prescription of devices**	Base case:						
		Total patients on DPI and pMDI in 2020: - 10%	16,867.2	-1,874.1	2,412.4	-14,454.8	10.0%	85.7
		Total patients on DPI and pMDI in 2020: + 10%	20,615.5	1,874.1	2,948.5	-17,667.0	-10.0%	85.7
		Total patients on DPI in 2020: - 10%; Total patient on pMDI in 2020: +20%	18,804.2	62.8	3,088.0	-15,716.2	2.1%	83.6
		Total patients on DPI in 2020: - 20%; Total patient on pMDI in 2020: +10%	18,678.5	-62.8	2,273.0	-16,405.5	-2.1%	87.8
		Total patients on DPI in 2020: -10%; Total patient on pMDI in 2020: +20%	20,552.7	1,811.3	2,541.0	-18,011.6	-12.1%	87.6
		Total patients on DPI in 2020: +10%; Total patient on pMDI in 2020: -20%	16,930.1	-1,811.3	2,819.9	-14,110.1	12.1%	83.3
	Currently prescribed class	Base case						
		LAMA: +20%; other classes: -5%	13,801.0	-4,940.4	2,673.3	-11,127.7	30.7%	80.6
		LAMA: -20%; other classes: +5%	13,062.7	-5,678.7	2,687.6	-10,375.1	35.4%	79.4
		LABA/ICS: +20%; other classes: -5%	14,251.4	-4,490.0	3,006.1	-11,245.3	30.0%	78.9
		LABA/ICS: -20%; other classes: +5%	12,612.3	-6,129.0	2,354.9	-10,257.5	36.1%	81.3

		LAMA/LABA: +20%; other classes: -5%	12,868.3	-5,873.1	2,592.0	-10,276.3	36.0%	79.9
		LAMA/LABA: -20%; other classes: +5%	13,995.4	-4,745.9	2,769.0	-11,226.4	30.1%	80.2
		LAMA/LABA/ICS: +20%; other classes: -5%	13,478.3	-5,263.0	2,584.6	-10,893.8	32.2%	80.8
		LAMA/LABA/ICS: -20%; other classes: +5%	13,385.4	-5,356.0	2,776.4	-10,609.0	33.9%	79.3
Extent of the switch	**Switch of devices**	*Base case: 100% switch DPI and pMDI to Respimat Reusable*						
		50% switch of DPI to Respimat Reusable (100% for pMDI)	18,741.4	-	4,782.9	-13,958.5	13.1%	74.5
		50% switch of pMDI to Respimat Reusable (100% for DPI)	18,741.4	-	8,608.5	-10,132.8	36.9%	54.1
		50% switch of DPI and pMDI to Respimat Reusable	18,741.4	-	10,710.9	-8,030.4	50.0%	42.8
	Switch of therapeutic classes	*Base case: 100% switch all therapeutic classes to Spiriva/Spiolto Respimat Reusable*						
		50% switch of LAMA (excluding Spiriva Respimat Reusable) to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	13,431.8	-5,309.5	4,508.2	-8,923.6	44.4%	66.4
		50% switch of LAMA/LABA (excluding Spiolto Respimat Reusable) to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	13,431.8	-5,309.5	2,805.5	-10,626.3	33.8%	79.1
		50% switch of LABA/ICS to Spiriva/ Spiolto Respimat Reusable (other	13,431.8	-5,309.5	4,743.4	-8,688.4	45.9%	64.7

		classes: 100% switch)						
		50% switch of LAMA/LABA/ICS to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	13,431.8	-5,309.5	4,040.4	-9,391.4	41.5%	69.9

CO_2e, carbon dioxide equivalent; DPI, dry powder inhaler; ICS, inhaled corticosteroid; LABA; long-acting beta-agonists; LAMA, long-acting muscarinic antagonist; pMDI, pressurised metered dose inhalers.

Supplementary Table 16. Sensitivity analysis: United Kingdom

Model parameter	Variable	Scenario	Before Respimat Reusable switch		After Respimat Reusable switch			
			Cumulative CO_2e emissions (tonnes)	Difference with base case	Cumulative CO_2e emissions (tonnes)	Change in CO_2e emissions after intervention (tonnes)	Difference vs. base case (%)	Decrease in carbon footprint after switch (%)
Sensitivity analysis for the main analyses								
LAMA								
		Base case	**8,835.1**		**5,788.2**	**-3,046.9**	**-**	**34.5%**
Re-usability	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	8,835.1	-	11,418.4	2,583.3	184.8%	-29.2%
		12 devices/year	8,835.1	-	19,863.6	11,028.5	462.0%	-124.8%
	Number of LAMA devices used	*Base case: 4.69 devices/year*						
		6 devices/year	10,642.5	1,807.5	5,788.2	-4,854.3	-59.3%	45.6%
		12 devices/year	18,918.2	10,083.1	5,788.2	-13,130.0	-330.9%	69.4%
CO_2 data	**CO_2 data of Respimat Reusable**	*Base case: (data)*						
		+20% for Respimat Reusable	8,835.1	-	6,945.9	-1,889.2	38.0%	21.4%
		-20% for Respimat Reusable	8,835.1	-	4,630.6	-4,204.5	-38.0%	47.6%
	CO_2 data of LAMA devices	*Base case: (data)*						
		+20% for LAMA devices	10,602.1	1,767.0	5,788.2	-4,813.9	-58.0%	45.4%
		-20% for LAMA devices	7,068.1	-1,767.0	5,788.2	-1,279.9	58.0%	18.1%
LAMA/LABA								

		Base case						
Re-usability	**Number of Respimat Reusable used**	*Base case: 2 devices/year*	**5,853.3**		**2,229.6**	**-4,379.4**		**66.3%**
		6 devices/year	5,853.3	-	4,398.3	-1,455.0	59.8%	24.9%
		12 devices/year	5,853.3	-	7,651.3	1,798.0	149.6%	-30.7%
	Number of LAMA/LABA devices used	*Base case: 10.03 devices/year*						
		6 devices/year	3,564.0	-2,289.3	2,229.6	-1,334.4	63.2%	37.4%
		12 devices/year	6,976.3	1,123.0	2,229.6	-4,746.7	-31.0%	68.0%
CO_2 data	**CO_2 data of Respimat Reusable**	*Base case: (data)*						
		+20% for Respimat Reusable	5,853.3	-	2,675.5	-3,933.5	10.2%	59.5%
		-20% for Respimat Reusable	5,853.3	-	1,783.7	-4,825.3	-10.2%	73.0%
	CO_2 data of LAMA/LABA devices	*Base case: (data)*						
		+20% for LAMA/LABA devices	7,023.9	415.0	2,229.6	-4,794.4	-9.5%	68.3%
		-20% for LAMA/LABA devices	4,682.6	-1,926.3	2,229.6	-2,453.1	44.0%	52.4%
Sensitivity analysis for the scenario analyses								
		Base case	**661,365.87**		**36,529.33**	**-624,836.54**	**-**	**94.5**
Re-usability	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	661,365.87	-	72,061.18	-589,304.69	5.7%	89.1
		12 devices/year	661,365.87	-	125,358.96	-536,006.91	14.2%	81.0
	Number of DPIs	*Base case: 9.67 devices/year*						
		6 devices/year	640,406.55	-34,280.90	36,529.33	-603,877.22	3.4%	94.3
		12 devices/year	674,687.45	13,321.58	36,529.33	-638,158.12	-2.1%	94.6
	Number of pMDI	*Base case: 12 devices/year*						
		6 devices/year (theoretical)	359,562.33	-301,803.54	36,529.33	-323,033.00	48.3%	89.8
CO_2 data	**CO_2 data of**	*Base case: (data)*						

	Respimat Reusable	+20% for Respimat Reusable	661,365.87	-	43,835.20	-617,530.67	1.2%	93.4
		-20% for Respimat Reusable	661,365.87	-	29,223.47	-632,142.40	-1.2%	95.6
	CO_2 data of DPI	*Base case: (data)*						
		+20% for DPI	672,917.63	11,551.76	36,529.33	-636,388.30	-1.8%	94.6
		-20% for DPI	649,814.11	-11,551.76	36,529.33	-613,284.78	1.8%	94.4
	CO_2 data of pMDI	*Base case: (data)*						
		+20% for pMDI	782,087.29	120,721.42	36,529.33	-745,557.95	-19.3%	95.3
		-20% for pMDI	540,644.45	-120,721.42	36,529.33	-504,115.12	19.3%	93.2
Market share	**Current prescription of devices**	Base case:						
		Total patients on DPI and pMDI in 2020: - 10%	595,229.28	-66,136.59	32,876.40	-562,352.88	10.0%	94.5
		Total patients on DPI and pMDI in 2020: + 10%	727,502.46	66,136.59	40,182.27	-687,320.19	-10.0%	94.5
		Total patients on DPI in 2020: - 10%; Total patient on pMDI in 2020: +20%	612,556.92	-48,808.95	38,887.33	-573,669.60	8.2%	93.7
		Total patients on DPI in 2020: - 20%; Total patient on pMDI in 2020: +10%	710,174.82	48,808.95	34,171.34	-676,003.48	-8.2%	95.2
		Total patients on DPI in 2020: -10%; Total patient on pMDI in 2020: +20%	776,311.41	114,945.54	37,824.27	-738,487.14	-18.2%	95.1
		Total patients on DPI in 2020: +10%; Total patient on pMDI in 2020: -20%	546,420.33	-114,945.54	35,234.39	-511,185.94	18.2%	93.6
	Currently prescribed class	Base case						
		LAMA: +20%; other classes: -5%	632,516.02	-28,849.85	36,149.92	-596,366.10	4.6%	94.3
		LAMA: -20%; other classes: +5%	694,446.60	33,080.73	36,908.74	-657,537.86	-5.2%	94.7
		LABA/ICS: +20%; other classes: -5%	762,107.66	100,741.79	40,952.61	-721,155.05	-15.4%	94.6
		LABA/ICS: -20%; other classes: +5%	564,854.96	-96,510.91	32,106.06	-532,748.90	14.7%	94.3

		LAMA/LABA: +20%; other classes: -5%	631,770.57	-29,595.30	35,260.26	-596,510.31	4.5%	94.4
		LAMA/LABA: -20%; other classes: +5%	695,192.05	33,826.18	37,798.40	-657,393.65	-5.2%	94.6
		LAMA/LABA/ICS: +20%; other classes: -5%	660,705.06	-660.81	35,581.01	-625,124.05	0.0%	94.6
		LAMA/LABA/ICS: -20%; other classes: +5%	666,257.56	4,891.69	37,477.66	-628,779.90	-0.6%	94.4
Extent of the switch	**Switch of devices**	*Base case: 100% switch DPI and pMDI to Respimat Reusable*						
		50% switch of DPI to Respimat Reusable (100% for pMDI)	661,365.87	-	55,390.52	-605,975.35	3.0%	91.6
		50% switch of pMDI to Respimat Reusable (100% for DPI)	661,365.87	-	330,086.42	-331,279.45	47.0%	50.1
		50% switch of DPI and pMDI to Respimat Reusable	661,365.87	-	348,947.60	-312,418.27	50.0%	47.2
	Switch of therapeutic classes	*Base case: 100% switch all therapeutic classes to Spiriva/Spiolto Respimat Reusable*						
		50% switch of LAMA (excluding Spiriva Respimat Reusable) to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	663,481.31	2,115.44	38,052.77	-625,428.54	-0.1%	94.3
		50% switch of LAMA/LABA (excluding Spiolto Respimat Reusable) to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	663,481.31	2,115.44	38,341.19	-625,140.12	0.0%	94.2
		50% switch of LABA/ICS to Spiriva/ Spiolto Respimat Reusable (other	663,481.31	2,115.44	287,630.68	-375,850.63	39.8%	56.6

		classes: 100% switch)						
		50% switch of LAMA/LABA/ICS to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	663,481.31	2,115.44	95,568.67	-567,912.63	9.1%	85.6

CO_2e, carbon dioxide equivalent; DPI, dry powder inhaler; ICS, inhaled corticosteroid; LABA; long-acting beta-agonists; LAMA, long-acting muscarinic antagonist; pMDI, pressurised metered dose inhalers.

Supplementary Table 17. Sensitivity analysis: United States of America

Model parameter	Variable	Scenario	Before Respimat Reusable switch		After Respimat Reusable switch			
			Cumulative CO_2e emissions (tonnes)	Difference with base case	Cumulative CO_2e emissions (tonnes)	Change in CO_2e emissions after intervention (tonnes)	Difference vs. base case (%)	Decrease in carbon footprint after switch (%)
Sensitivity analysis for the main analyses								
LAMA								
		Base case	**13,743.6**		**7,515.3**	**-6,228.3**	**-**	**45.3%**
Re-usability	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	13,743.6	-	14,825.5	1,081.9	117.4%	-7.9%
		12 devices/year	13,743.6	-	25,790.6	12,047.0	293.4%	-87.7%
	Number of LAMA devices used	*Base case: 5.79 devices/year*						
		6 devices/year	14,148.4	404.8	7,515.3	-6,633.1	-6.5%	46.9%
		12 devices/year	25,544.7	11,801.1	7,515.3	-18,029.4	-189.5%	70.6%
CO_2 data	**CO_2 data of Respimat Reusable**	*Base case: (data)*						
		+20% for Respimat Reusable	13,743.6		9,018.4	-4,725.2	24.1%	34.4%
		-20% for Respimat Reusable	13,743.6		6,012.3	-7,731.3	-24.1%	56.3%
	CO_2 data of LAMA devices	*Base case: (data)*						
		+20% for LAMA devices	16,506.0	2,762.4	7,515.3	-8,990.7	-44.4%	54.5%
		-20% for LAMA devices	11,004.0	-2,739.6	7,515.3	-3,488.7	44.0%	31.7%
LAMA/LABA								

		Base case	**54,929.8**		**4,087.2**	**-50,842.6**		**92.6%**
Re-usability	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	54,929.8	-	8,062.9	-46,866.9	7.8%	85.3%
		12 devices/year	54,929.8	-	14,026.3	-40,903.5	19.5%	74.5%
	Number of LAMA/LABA devices used	*Base case: 12 devices/year*						
		6 devices/year	27,464.9	-27,464.9	4,087.2	-23,377.7	54.0%	85.1%
		12 devices/year	54,929.8	-	4,087.2	-50,842.6	0.0%	92.6%
CO_2 data	**CO_2 data of Respimat Reusable**	*Base case: (data)*						
		+20% for Respimat Reusable	54,929.8		4,904.7	-50,025.1	1.6%	91.1%
		-20% for Respimat Reusable	54,929.8		3,269.8	-51,660.0	-1.6%	94.0%
	CO_2 data of LAMA/LABA devices	*Base case: (data)*						
		+20% for LAMA/LABA devices	65,914.6	10,984.8	4,087.2	-61,827.4	-21.6%	93.8%
		-20% for LAMA/LABA devices	43,943.1	-10,986.7	4,087.2	-39,855.9	21.6%	90.7%
Sensitivity analysis for the scenario analyses								
		Base case	**969,441.5**		**55,893.2**	**-913,548.3**	**-**	**94.2**
LAMA	**Number of Respimat Reusable used**	*Base case: 2 devices/year*						
		6 devices/year	969,441.5	-	110,260.2	-859,181.3	6.0%	88.6
		12 devices/year	969,441.5	-	191,810.6	-777,630.9	14.9%	80.2
	Number of DPIs	*Base case: 9.37 devices/year*						
		6 devices/year	931,473.4	-58,167.8	55,893.2	-875,580.2	4.2%	94.0
		12 devices/year	989,641.2	20,199.7	55,893.2	-933,748.0	-2.2%	94.4
	Number of pMDI	*Base case: 12 devices/year*						
		6 devices/year (theoretical)	534,875.5	-434,565.9	55,893.2	-478,982.3	47.6%	89.6
CO_2 data	**CO_2 data of**	*Base case: (data)*						

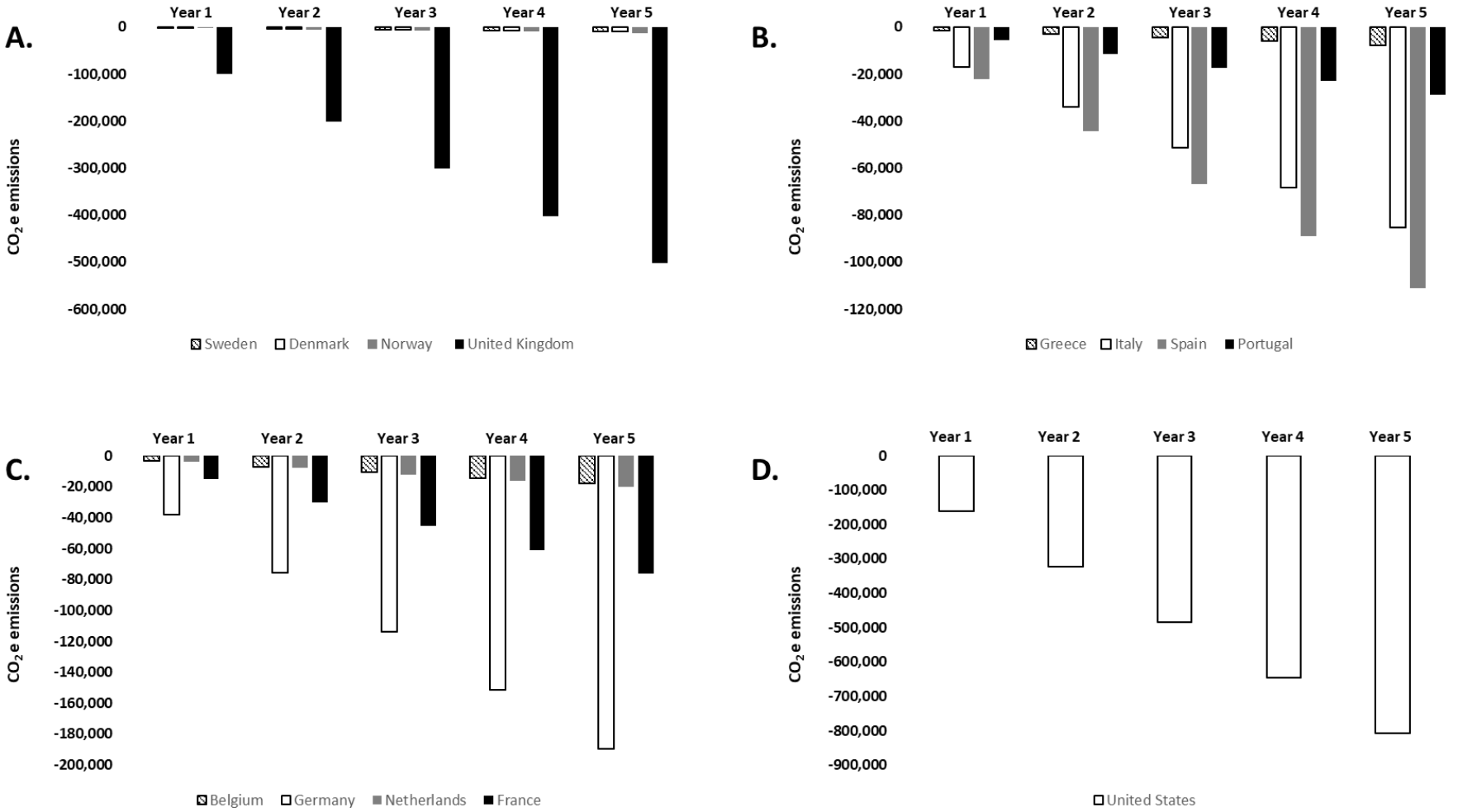
	Respimat Reusable	+20% for Respimat Reusable	969,441.5	-	67,071.8	-902,369.6	1.2%	93.1
		-20% for Respimat Reusable	969,441.5	-	44,714.6	-924,726.9	-1.2%	95.4
	CO_2 data of DPI	*Base case: (data)*						
		+20% for DPI	989,503.4	20,061.9	55,893.2	-933,610.2	-2.2%	94.4
		-20% for DPI	949,379.6	-20,061.9	55,893.2	-893,486.4	2.2%	94.1
	CO_2 data of pMDI	*Base case: (data)*						
		+20% for pMDI	1,143,267.9	173,826.4	55,893.2	-1,087,374.7	-19.0%	95.1
		-20% for pMDI	795,615.1	-173,826.4	55,893.2	-739,721.9	19.0%	93.0
Market share	**Current prescription of devices**	Base case:						
		Total patients on DPI and pMDI in 2020: - 10%	872,497.3	-96,944.1	50,303.9	-822,193.5	10.0%	94.2
		Total patients on DPI and pMDI in 2020: + 10%	1,066,385.6	96,944.1	61,482.5	-1,004,903.1	-10.0%	94.2
		Total patients on DPI in 2020: - 10%; Total patient on pMDI in 2020: +20%	902,590.2	-66,851.3	60,496.6	-842,093.6	7.8%	93.3
		Total patients on DPI in 2020: - 20%; Total patient on pMDI in 2020: +10%	1,036,292.7	66,851.3	51,289.8	-985,002.9	-7.8%	95.1
		Total patients on DPI in 2020: -10%; Total patient on pMDI in 2020: +20%	1,133,236.9	163,795.4	56,879.1	-1,076,357.8	-17.8%	95.0
		Total patients on DPI in 2020: +10%; Total patient on pMDI in 2020: -20%	805,646.1	-163,795.4	54,907.3	-750,738.8	17.8%	93.2
	Currently prescribed class	Base case						
		LAMA: +20%; other classes: -5%	889,961.8	-79,479.7	54,977.4	-834,984.4	8.6%	93.8
		LAMA: -20%; other classes: +5%	976,408.5	6,967.0	56,809.0	-919,599.5	-0.7%	94.2
		LABA/ICS: +20%; other classes: -5%	1,098,305.0	128,863.5	63,108.4	-1,035,196.6	-13.3%	94.3
		LABA/ICS: -20%; other classes: +5%	768,065.3	-201,376.2	48,677.9	-719,387.4	21.3%	93.7

		LAMA/LABA: +20%; other classes: -5%	900,258.4	-69,183.1	54,120.3	-846,138.0	7.4%	94.0
		LAMA/LABA: -20%; other classes: +5%	966,112.0	-3,329.5	57,666.0	-908,445.9	0.6%	94.0
		LAMA/LABA/ICS: +20%; other classes: -5%	890,874.7	-78,566.7	54,161.3	-836,713.4	8.4%	93.9
		LAMA/LABA/ICS: -20%; other classes: +5%	975,495.6	6,054.1	57,625.1	-917,870.5	-0.5%	94.1
Extent of the switch	**Switch of devices**	*Base case: 100% switch DPI and pMDI to Respimat Reusable*						
		50% switch of DPI to Respimat Reusable (100% for pMDI)	969,441.5	-	89,060.1	-880,381.3	3.6%	90.8
		50% switch of pMDI to Respimat Reusable (100% for DPI)	969,441.5	-	479,500.4	-489,941.1	46.4%	50.5
		50% switch of DPI and pMDI to Respimat Reusable	969,441.5	-	512,667.3	-456,774.1	50.0%	47.1
	Switch of therapeutic classes	*Base case: 100% switch all therapeutic classes to Spiriva/Spiolto Respimat Reusable*						
		50% switch of LAMA (excluding Spiriva Respimat Reusable) to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	933,185.2	-36,256.3	59,007.3	-874,177.8	4.3%	93.7
		50% switch of LAMA/LABA (excluding Spiolto Respimat Reusable) to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	933,185.2	-36,256.3	81,314.5	-851,870.7	6.8%	91.3
		50% switch of LABA/ICS to Spiriva/ Spiolto Respimat Reusable (other	933,185.2	-36,256.3	459,431.6	-473,753.6	48.1%	50.8

		classes: 100% switch)						
		50% switch of LAMA/LABA/ICS to Spiriva/Spiolto Respimat Reusable (other classes: 100% switch)	933,185.2	-36,256.3	62,465.4	-870,719.8	4.7%	93.3

CO_2e, carbon dioxide equivalent; DPI, dry powder inhaler; ICS, inhaled corticosteroid; LABA; long-acting beta-agonists; LAMA, long-acting muscarinic antagonist; pMDI, pressurised metered dose inhalers.

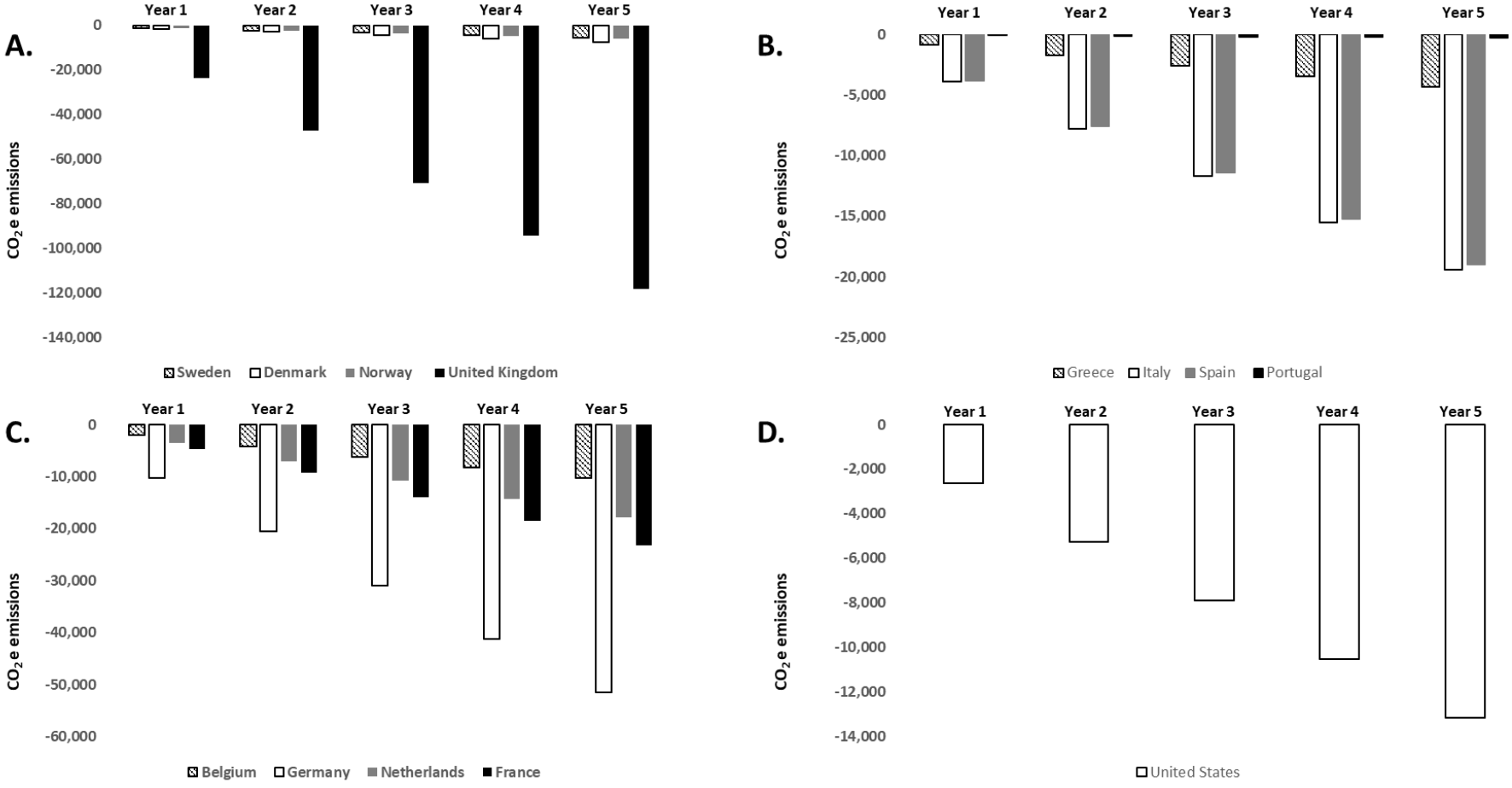
Supplementary Figure 1. Cumulative reduction in CO_2e emissions over five years using Spiolto Respimat Reusable inhalers over LABA/ICS inhalers in



Northern Europe (A), Southern Europe (B), Western Europe (C), and United States (D)

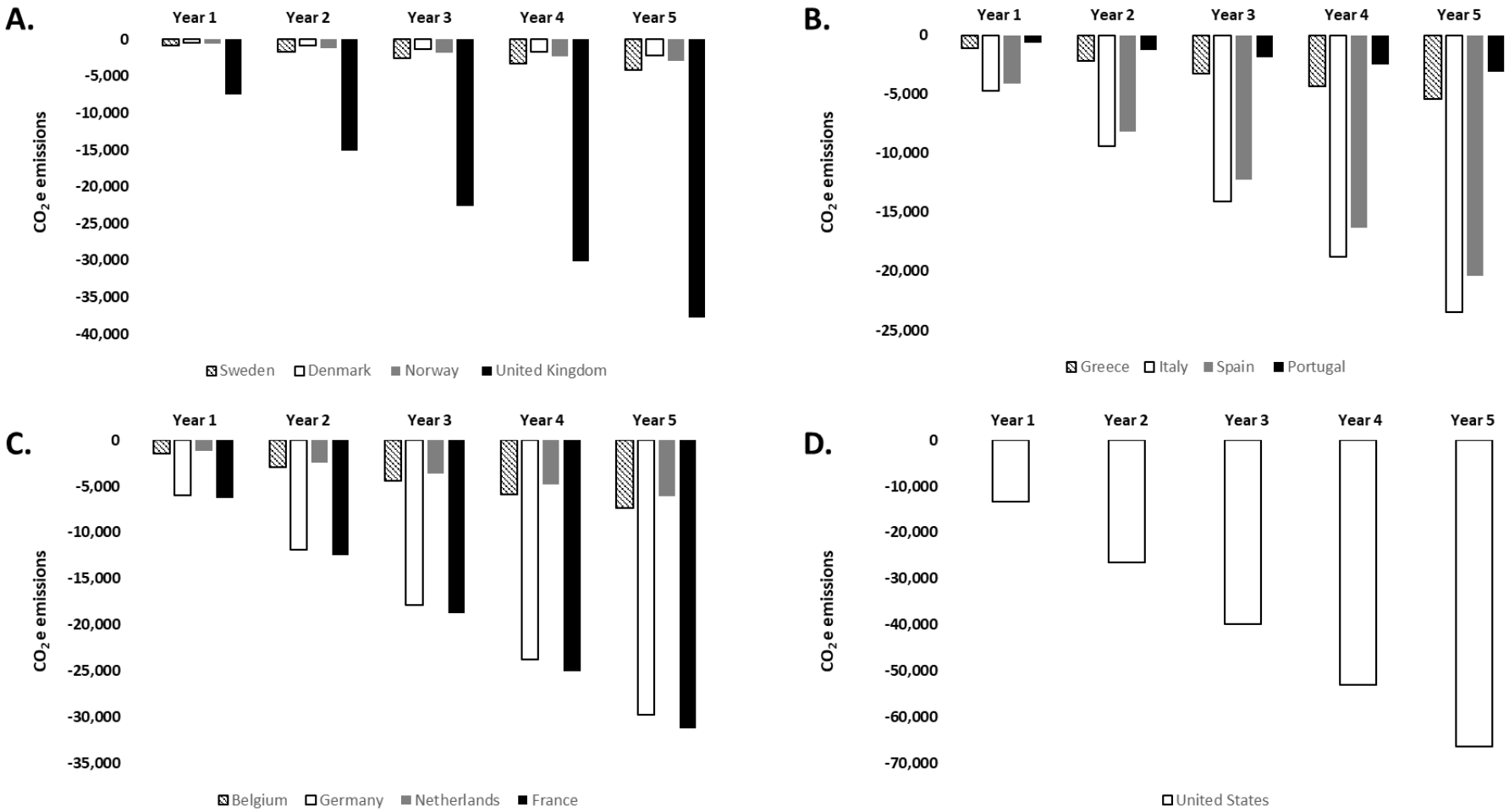
CO_2e, carbon dioxide equivalent; ICS, inhaled corticosteroid; LABA; long-acting beta-agonists. A. Northern Europe: Denmark, Norway, Sweden, and United Kingdom; B. Southern Europe: Greece, Italy, Portugal, and Spain; C. Western Europe: Belgium, France, Germany, the Netherlands; D. United States.

Supplementary Figure 2. Cumulative reduction in CO_2e emissions over five years using Spiolto Respimat Reusable inhalers over triple therapy inhalers in Northern Europe (A), Southern Europe (B), Western Europe (C), and United States (D)



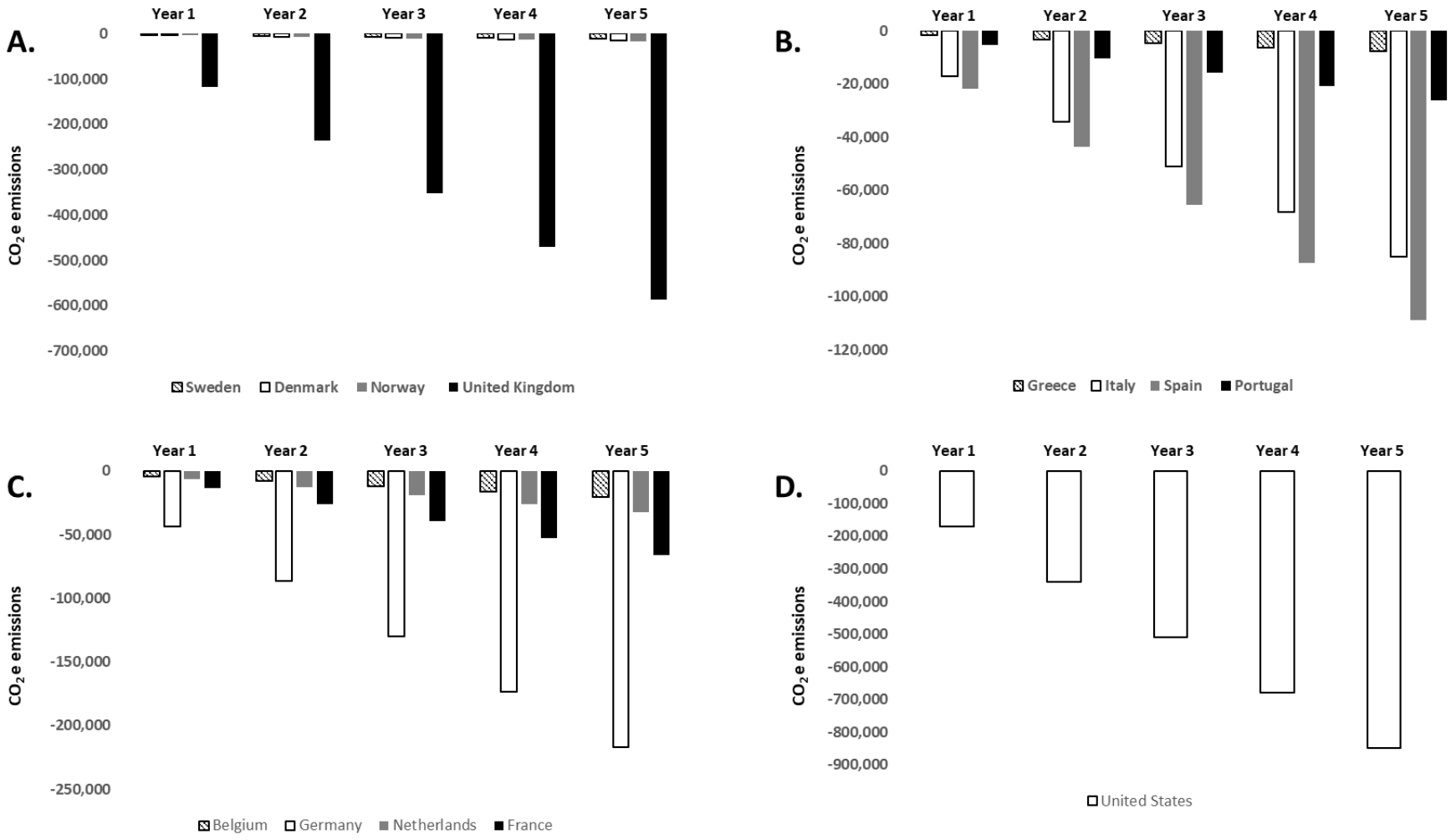
CO_2e, carbon dioxide equivalent; A. Northern Europe: Denmark, Norway, Sweden, and United Kingdom; B. Southern Europe: Greece, Italy, Portugal, and Spain; C. Western Europe: Belgium, France, Germany, the Netherlands; D. United States.

Supplementary Figure 3. Cumulative reduction in CO_2e emissions over five years using Respimat Reusable inhalers over DPIs in Northern Europe (A), Southern Europe (B), Western Europe (C), and United States (D)



CO_2e, carbon dioxide equivalent; DPIs, dry powder inhalers. A. Northern Europe: Denmark, Norway, Sweden, and United Kingdom; B. Southern Europe: Greece, Italy, Portugal, and Spain; C. Western Europe: Belgium, France, Germany, the Netherlands; D. United States.

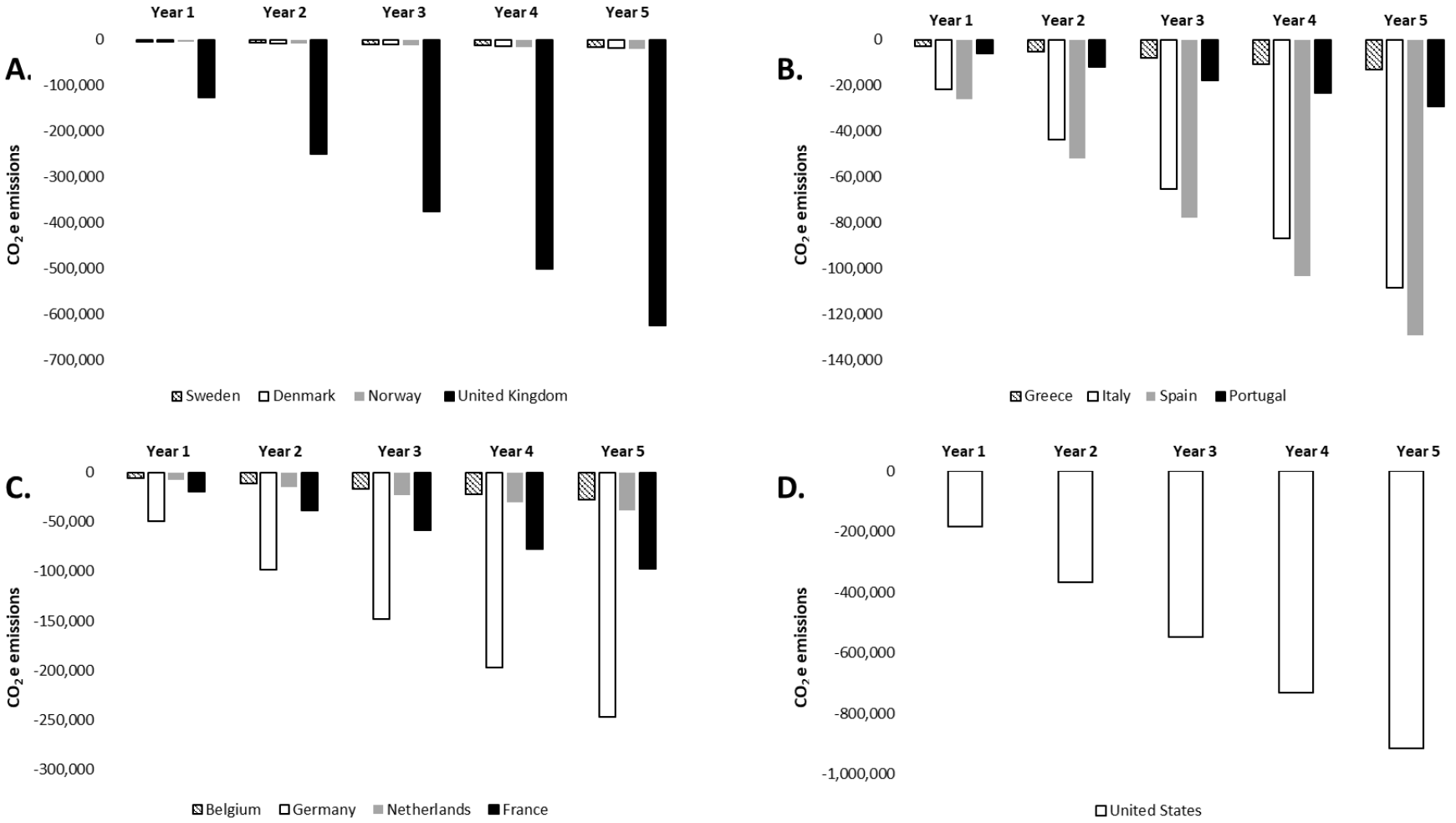
Supplementary Figure 4. Cumulative reduction in CO_2e emissions over five years using Respimat Reusable inhalers over pMDIs in Northern Europe (A),



Southern Europe (B), Western Europe (C), and United States (D)

CO_2e, carbon dioxide equivalent; pMDIs, pressurised metered dose inhalers. A. Northern Europe: Denmark, Norway, Sweden, and United Kingdom; B. Southern Europe: Greece, Italy, Portugal, and Spain; C. Western Europe: Belgium, France, Germany, the Netherlands; D. United States.

Supplementary Figure 5. Cumulative reduction in CO_2e emissions over five years using Respimat Reusable inhalers over DPIs and pMDIs in Northern



Europe (A), Southern Europe (B), Western Europe (C), and United States (D)

CO_2e, carbon dioxide equivalent; DPI, dry powder inhalers; pMDI, pressurised metered dose inhalers. A. Northern Europe: Denmark, Norway, Sweden, and United Kingdom; B. Southern Europe: Greece, Italy, Portugal, and Spain; C. Western Europe: Belgium, France, Germany, the Netherlands; D. United States.