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ORIGINAL RESEARCH ARTICLE

# Incorporating the Environmental Impact into a Budget Impact Analysis: The Example of Adopting RESPIMAT® Re-usable Inhaler

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## Abstract

**Background** RESPIMAT® re-usable enables patients to re-use the inhaler and its availability therefore reduces the number of inhalers and associated wastage.

**Objective** The objective of this study was to perform an economic evaluation that incorporates the ecological impact of adopting RESPIMAT re-usable into the healthcare system in Germany.

**Methods** Inhaler costs and environmental impact over 5 years in Germany in a scenario with RESPIMAT re-usable compared to a scenario without RESPIMAT re-usable were estimated using a budget impact model. The carbon emissions were derived for each treatment pattern considering the whole life cycle (cradle-to-grave) of the inhaler product. The cost of carbon emissions was estimated using a societal cost per ton of carbon emission.

**Results** By introducing RESPIMAT re-usable in Germany, it was estimated that by 2023, the number of inhalers used would have decreased by 5,748,750 compared to a scenario without RESPIMAT re-usable. In addition, this measure would reduce the environmental burden of inhaler use while at the same time reducing medical cost of inhalers.

**Conclusions** Adopting RESPIMAT® re-usable to the national healthcare services may be a cost-saving option, which has the additional benefit of reducing the societal cost of carbon emissions.

**JEL Classification** Q51 · Q58

**Key Points for Decision Makers**

The healthcare sector is a major contributor to emissions of global greenhouse gases

A broader approach to include the environmental effect when evaluating new health technologies may better capture the true value of a new product

RESPIMAT re-usable reduces the societal cost of carbon emissions

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## 1 Introduction

The World Health Organization (WHO) estimates that chronic respiratory diseases represent 5% of total disease burden and 8.3% of chronic disease burden worldwide and account for more than 4 million deaths each year [1], 150,000 of which occur in the European Union [2]. About 210 million people are estimated to have chronic obstructive pulmonary disease (COPD) worldwide [3] and an estimated 300 million people suffer from asthma [4, 5]. The economic burden, including productivity losses, of these diseases in the EU has been estimated to €33.9 billion and €48.4 billion for asthma and COPD, respectively [2].

Inhalation therapy is the cornerstone of COPD and asthma management [6] to reduce symptoms and the risk of severe exacerbations. There is a variety of different inhalers which can be grouped into three main categories: (1) breath-actuated or pressurised metered-dose inhalers (MDI, pMDI), (2) dry powder inhalers (DPIs) and (3) liquid multi-dose spray propellant-free devices, such as the soft mist inhaler (SMI™), RESPIMAT.

Innovation in the management of respiratory diseases has traditionally focused on the development of new molecules, but the choice of inhaler is as important as the selection of drug for inhaling in achieving an optimal treatment outcome [7]. Poor adherence to therapy is common among patients with asthma and COPD and is partly associated with difficulties in managing the inhaler device [7–10]. Patients have expressed preference for inhalers which are easy to use in episodes of breathing difficulties and provide reassurance about the inhaled dose being taken, e.g. a precise dose counter and dose confirmation mechanisms [11]. Hence, patient satisfaction with the inhaler device is expected to enhance treatment adherence and ultimately improved clinical outcomes and quality of life. However, the value of an innovation may extend beyond improvements in clinical outcomes and quality of life. Lately, other innovations aimed at avoiding propellants, reducing drug waste and disposable inhalers have been perceived as an additional benefit with the potential of reducing carbon dioxide ($CO_2$) emissions and thereby having a positive environmental impact. While the current regulated model of health technology assessment (HTA) captures the two former values (improved clinical outcomes and quality of life), it needs to be expanded to capture the latter (environmental impact) [12].

In total, the healthcare sector contributes to 5%–8% of the global greenhouse gas (GHG) emissions [13] and in Germany, the healthcare sector contributes to almost 7% of the national carbon footprint [14]. Global and regional organisations and governments have started to design and implement measures to reduce GHG emissions in the healthcare sector, by green public procurement policies and inclusion of ecological considerations in the decision-making process for purchasing and funding of healthcare technologies. $CO_2$ reduction targets have become part of corporate goals and sustainability reporting by healthcare companies. In a more patient-centric healthcare eco system, patients increasingly act as consumers and prefer eco-friendly products [15, 16].

Whilst several national and methodological guidelines encourage the inclusion of the societal perspective into the economic analyses, only a minority of analyses do so [17]. There is currently a discussion in the scientific and policy community regarding the need for re-defining what value means [18–24]. More holistic frameworks are being proposed and piloted that aim to better capture the total value and to better consider the diverse needs of stakeholders [25–27]. Comprehensive "cradle-to-grave" mapping of the product carbon footprint (PCF) expressed as carbon dioxide equivalents ($CO_2$e) is the first step to quantify the ecological impact of a health technology. $CO_2$e is a term for describing different greenhouse gases in a common unit. For any quantity and type of greenhouse gas, $CO_2$e signifies the amount of $CO_2$, which would have the equivalent global warming impact [28]. The second step is to assess the potential ecological benefits of replacing or improving the current technology. This could be done using common health economic evaluation methods such as budget impact analysis (BIA) or cost-effectiveness analysis (CEA). Currently, however, there are few examples where product-related $CO_2$ burden to society has been quantified.

Pressurised metered-dose inhalers (pMDIs) with propellants (HFA) are the most widely used inhalers in COPD and asthma. The National Health Service (NHS) in the UK reports that propellants from inhalers account for 8% of the NHS's entire carbon footprint [2]. Globally, 630 million HFA-based pMDIs are used annually resulting in an estimated $CO_2$e burden of 13 million t$CO_2$e [3], equal to the carbon footprint of 2 million EU citizens.

RESPIMAT re-usable is a propellant-free inhaler which is novel in the sense that it is re-usable and has the potential to reduce the $CO_2$ burden and the social cost of carbon emissions (SCC) by replacing its predecessor RESPIMAT disposable. The objective of this study was to perform an economic evaluation that incorporates the ecological impact of adopting RESPIMAT re-usable into the healthcare system in Germany.

## 2 Methods

### 2.1 Technologies

RESPIMAT re-usable is a newly developed inhaler with identical performance in efficacy and safety as its predecessor, RESPIMAT disposable [29]. However, RESPIMAT re-usable includes a reversible device lock mechanism which makes it re-usable.

### 2.2 Target Patient Population

The drugs Spiriva® (tiotropium bromide), Striverdi® (olodaterol) and Spiolto® (tiotropium-olodaterol) developed for use with RESPIMAT re-usable inhalers are indicated for the treatment of patients with respiratory diseases, such as COPD and asthma. They represent different drug classes (long-acting beta2 agonist and long-acting muscarinic antagonist) and are recommended as an option for maintenance therapy in mild-to-severe patients [30, 31].

### 2.3 Model Design

Given that RESPIMAT re-usable has identical performance levels as RESPIMAT disposable, no direct efficacy gain was expected from switching patients from RESPIMAT disposable to RESPIMAT re-usable. Although it would be theoretically possible to incorporate possible gains in quality of life due to environmental improvements, currently robust

data are missing for this to be a feasible approach. Also, it is plausible that RESPIMAT re-usable could provide an improved treatment compliance compared other type of inhalers. However, there are currently no data that would allow a quantification of such a benefit. For these reasons, a budget impact model was therefore chosen over a cost-effectiveness model to quantify the budget and environmental impact of RESPIMAT re-usable. A budget impact analysis was chosen ahead of a cost–benefit analysis, which is often used when taking into account a societal perspective given that the latter is rejected by most HTA-agencies [12]. The budget impact model calculates the number of inhalers and refill packages used annually in the study population over 5 years (between 2019 and 2023). The model horizon was set to 5 years, which is a relevant time perspective to the budget holder [32]. Two types of inhalers (RESPIMAT disposable and RESPIMAT re-usable) and three types of drugs (Spiriva, Spiolto, and Striverdi) were included in the analysis. Central to the model design and outcomes is the treatment pattern, i.e. how often inhalers are replaced by new ones in a scenario without RESPIMAT re-usable.

## 2.4 Treatment Patterns

RESPIMAT disposable comes in two pack sizes, either as a single disposable (D1) pack (containing one inhaler and one cartridge) or as a triple disposable pack (containing three inhalers and three cartridges). In either case, in a scenario without RESPIMAT re-usable, 12 inhalers would be used per patient per year.

RESPIMAT re-usable comes in a similar pack sizes as Respimat disposable but both the single pack (N1) and the triple pack (N3) contain one single re-usable inhaler. Available RESPIMAT re-usable pack sizes enable a patient to cover their yearly usage using fewer inhalers. Table 1 outlines the different possible combinations of N1 and N3 and saved inhalers (per patient per year) per different treatment pattern.

In the base case, 45%, 45% and 10% of patients followed Pattern 1, Pattern 2 and Pattern 3, respectively. This was assumed to reflect the variability of inhaler prescribing patterns which is partly explained by health policies, economic considerations, health insurance issues, prescribers' and patients' preferences [33]. In sensitivity analysis 1, the number of inhalers used per year is minimised (Optimal pattern) to show the potential maximum impact of RESPIMAT re-usable. Also, this treatment pattern is expected to raise over time as physicians and patients will become more familiar in prescribing and using re-usable inhalers. In sensitivity analysis 2, all patients were assumed to follow pattern 1, the least favourable pattern. No difference in usage patterns was assumed between the brands included in the model.

## 2.5 Economic Valuation

Direct medical costs in terms of inhaler costs were calculated per scenario. Inhaler costs were derived from ex-factory prices of each brand and inhaler. All costs are expressed in euros (€) 2019 and assumed to be constant throughout the model horizon. The inhaler price by brand is presented in Table 2. Prices are equal between RESPIMAT re-usable N1

**Table 1** Inhalers per year by pattern label

| Pattern opportunities | Value | Treatment pattern (12 months) | Saved inhalers per year with respect to RESPIMAT® disposable | Expected annual cost (€) per pattern |
|---|---|---|---|---|
| | Current pattern with RESPIMAT disposable | 12 × Single disposable package | | 567.62 |
| Pattern 1 | Least favourable pattern | 12 × single packs with one re-usable inhaler | 0 | 567.62 |
| Pattern 2 | Improved pattern | 3 × single pack with one re-usable inhaler + 3 × triple pack with one re-usable inhaler | 6 | 561.33 |
| Pattern 3 | Optimal pattern | 4 × triple pack with one re-usable inhaler | 8 | 559.23 |

**Table 2** Ex-factory price [34] in 2019 € per treatment pattern and brand

| | Spiriva | Spiolto | Striverdi |
|---|---|---|---|
| RESPIMAT® disposable (single disposable package) | 44.83 | 51.00 | 30.86 |
| RESPIMAT re-usable (single pack with one re-usable inhaler) | 44.83 | 51.00 | 30.86 |
| RESPIMAT re-usable (triple pack with one re-usable inhaler) | 130.75 | 153.00 | 98.13 |

and RESPIMAT disposable D1. The triple pack of Spiriva has a marginally lower price per month than RESPIMAT disposable D1, while the triple pack of Striverdi has a marginally higher price than RESPIMAT disposable D1. No discount factor was applied as is recommended in budget impact models [32]. No other costs to the healthcare system are included given that substituting RESPIMAT disposable for RESPIMAT re-usable is not assumed to affect healthcare consumption.

### 2.6 Environmental Impact

The lifecycle PCF measured as kilos of $CO_2$ equivalents was calculated for RESPIMAT disposable using primary data collected from relevant members of the supply chain via email using customised data collection templates. Returned data were cross-checked for completeness and plausibility using mass balance (accounting for material entering and leaving the system), stoichiometry (where the total mass of the reactants equals the total mass of the products) and internal/external benchmarking. The calculation took into account the PCF of the whole life cycle (cradle-to-grave) of the inhaler product [35]. RESPIMAT re-usable was not included in this study. However, since RESPIMAT re-usable is similar to RESPIMAT disposable, a similar PCF of RESPIMAT re-usable could be assumed [29]. To take a conservative approach, this study assumed that RESPIMAT re-usable has 3% higher PCF than RESPIMAT disposable. The whole life cycle is typically divided into five stages: (1) material acquisition and pre-processing, (2) production, (3) distribution and storage, (4) use and (5) end of life. Material acquisition and pre-processing starts at the extraction of the raw materials and ends before filling of the containers/capsules. It covers the extraction of materials, production and assembly of the inhaler subparts and treatment of waste created during this stage. The production stage starts at the assembly of the final product and ends before the distribution to the consumer. It includes the mixing of the formulation ingredients, assembly and package of the inhaler product plus treatment of waste created during this process. The distribution and storage stage starts at the gate of the manufacture's production facilities and ends at the point of sale. The stage covers the PCF created by distribution of the product taking into account average shipping distance and transportation methods. The use stage typically includes the processes associated with actuation of the inhaler but was ignored in this study as the inhaled formulation was assumed to stay in the lungs. The end-of-life stage starts after use by the consumer and includes the disposal and waste management of the used inhaler and the inhaler packaging and incineration, energy recovery and land filling. The amount of $CO_2$ equivalents of each process was calculated according to Eq. 1. The global warming potential (GWP) is set to 100 as recommended by Green Gas Protocol Product Life Cycle Accounting and Reporting Standard [36].

Equation 1: Calculation of $CO_2$ equivalents:

$$\text{kg } CO_2\text{e} = \text{Activity Data (unit)} \times \text{emission factor}\left(\frac{\text{kg GHG}}{\text{unit}}\right) \times \text{GWP}\left(\frac{CO_2\text{e}}{\text{kg GHG}}\right). \quad (1)$$

The estimate was complying with the requirements of the Green Gas Protocol Product Life Cycle Accounting and Reporting Standard [37] as well as the specific sector guidance for pharmaceutical products [38]. The estimated PCF of inhalers and refill is listed in Table 3. Since a package with one inhaler and three refill packages have a lower PCF per administration than single pack inhalers, savings in $CO_2$ arose when RESPIMAT re-usable refill packages were used instead of RESPIMAT disposable.

The SCC was set to €40 per ton of $CO_2$. This estimate was derived from three economic climate impact models, which translate missions into changes in atmospheric carbon concentrations, atmospheric concentrations into temperature changes, and temperature changes into economic damages [36]. This estimate is in the lower range of available estimates from the literature, which reflects the existing uncertainty around modelling the social cost of environmental outcomes. The impact of a higher estimate (€160) was tested in a sensitivity analysis [39].

The approach of SCC was preferred to others such as carbon intensity (amount of $CO_2$ due to a certain activity) since the former leaves the interpretation of the environmental impact on the reader [12].

### 2.7 Study Population

The baseline population in 2019 was based on market data and is assumed to reflect the current use of the three brands included in the model (Spiriva, Spiolto, and Striverdi) in Germany and was set to 365,000 patients. Of these, 209,000 (57%) were assumed to use Spiriva, 153,000 (42%) to use Spiolto and 3000 (1%) to use Striverdi. The size of the population and the distribution between brands were assumed to be constant throughout the model horizon.

### 2.8 Scenario Analysis

Two scenarios were analysed and compared in terms of costs of inhalers and environmental impact; one scenario (without RESPIMAT re-usable) in which the three brands were used together with a Respimat disposable inhaler and another scenario (with RESPIMAT re-usable) in which RESPIMAT disposable was replaced by a RESPIMAT re-usable inhaler. Given that RESPIMAT re-usable were launched in April

**Table 3** Product carbon footprint (kilos of $CO_2$) by treatment pattern

| | Activity data (units) | Emission factor (kg GHG/unit) | GWP ($CO_2$e/kg GHG) | Total |
|---|---|---|---|---|
| RESPIMAT® disposable (single disposable package) | | | | |
| Material acquisition and preprocessing | 1 | 0.00456 | 100 | 0.456 |
| Production | 1 | 0.00245 | 100 | 0.245 |
| Distribution | 1 | 0.00005 | 100 | 0.005 |
| Use | 60 | 0.00000 | 100 | 0 |
| End of life | 1 | 0.00069 | 100 | 0.069 |
| Total | | | | **0.775** |
| RESPIMAT re-usable (triple pack with one re-usable inhaler) | | | | |
| Material acquisition and preprocessing | 1 | 0.00618 | 100 | 0.618 |
| Production | 1 | 0.00300 | 100 | 0.300 |
| Distribution | 1 | 0.00006 | 100 | 0.006 |
| Use | 180 | 0.00000 | 100 | 0 |
| End of life | 1 | 0.00081 | 100 | 0.081 |
| Total | | | | **1.035*** |
| RESPIMAT re-usable (single pack with one re-usable inhaler) | | | | **0.798*** |

*RESPIMAT re-usable was assumed to have 3% higher PCF than RESPIMAT disposable

2019, it was assumed that in the first year (2019), 50% of patients switched to RESPIMAT re-usable while from 2020 and onwards, all patients would have switched to RESPIMAT re-usable. The budget impact of treatment pattern was explored in three sensitivity analysis. In a first sensitivity analysis, all patients using RESPIMAT re-usable were assumed to use only three inhalers per year compared to 12 inhalers per years for patients using Respimat disposable, while in the second sensitivity analysis, all patients using RESPIMAT re-usable were assumed to continue to use 12 inhalers per year. In a third sensitivity analysis, the SCC was set to €160 rather than €40. All other assumptions were kept equal to the base case analysis.

## 3 Results

### 3.1 Base Case

By progressively introducing RESPIMAT re-usable in Germany, it was estimated that by 2023, the number of inhalers used would have decreased by 5,748,750 compared to a scenario without RESPIMAT re-usable. In addition, this measure would reduce both inhaler costs and the environmental burden of inhaler-use. Figure 1 shows the annual number of inhalers used in the two scenarios. Given that only 50% of patients switch from RESPIMAT disposable to RESPIMAT re-usable, the difference in number of inhalers used between the two scenarios is smaller in the first year compared with subsequent years where all patients are assumed to have switched to RESPIMAT re-usable. Figure 2 shows the annual cost of carbon emission in the two scenarios analysed. Cumulative results (between 2019 and 2023) are presented in Table 4.

### 3.2 Sensitivity Analysis

In a first sensitivity analysis, all patients using RESPIMAT re-usable were assumed to use only four inhalers per year. The details of this analysis are shown in Table 4. Compared to a scenario without RESPIMAT re-usable, 13,140,000 fewer inhalers would have been used by 2023. This is a further decrease of more than seven million inhalers compared to the base case analysis. Consequently, savings on cost of inhalers are enhanced and the environmental impact is further eased. In the second sensitivity analysis, all patients using RESPIMAT re-usable were assumed to continue to use 12 inhalers per year. Therefore, the number of inhalers and inhaler costs were equal between the two scenarios. Rather, carbon emissions would increase by 458 tons of $CO_2$ equivalents by 2023 by introducing RESPIMAT re-usable.

In the third sensitivity analysis, the social cost of carbon emissions was set to €160 keeping all other assumptions from the base case constant. Under this assumption, the cumulative cost of carbon emission between 2019 and 2023 would decrease by €551,959 if RESPIMAT re-usable were adopted into the German healthcare system. The annual cost-saving of this analysis is shown in Fig. 3.

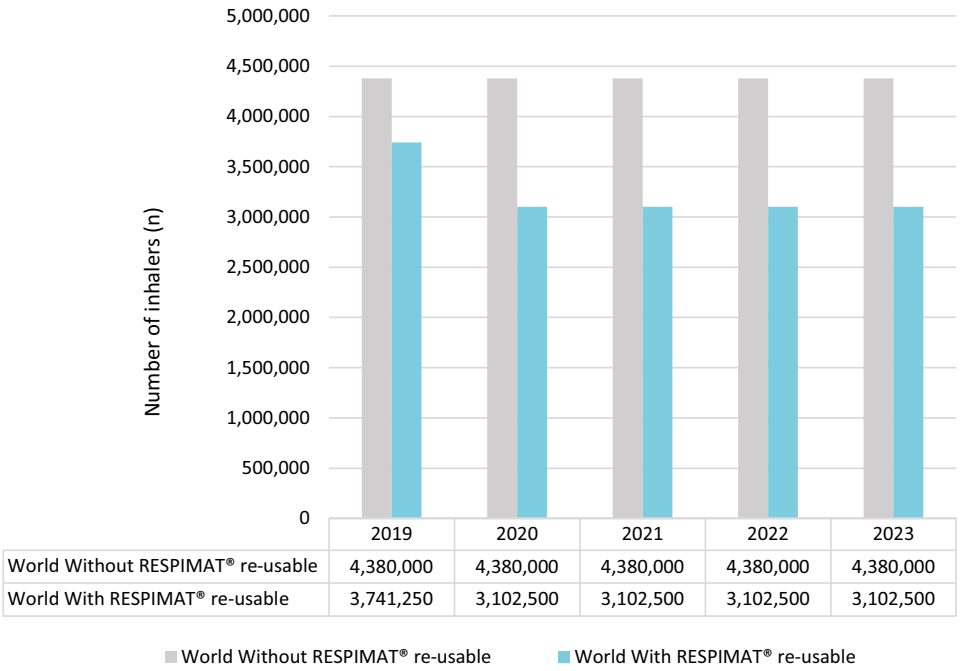


**Fig. 1** Number of inhalers used by year

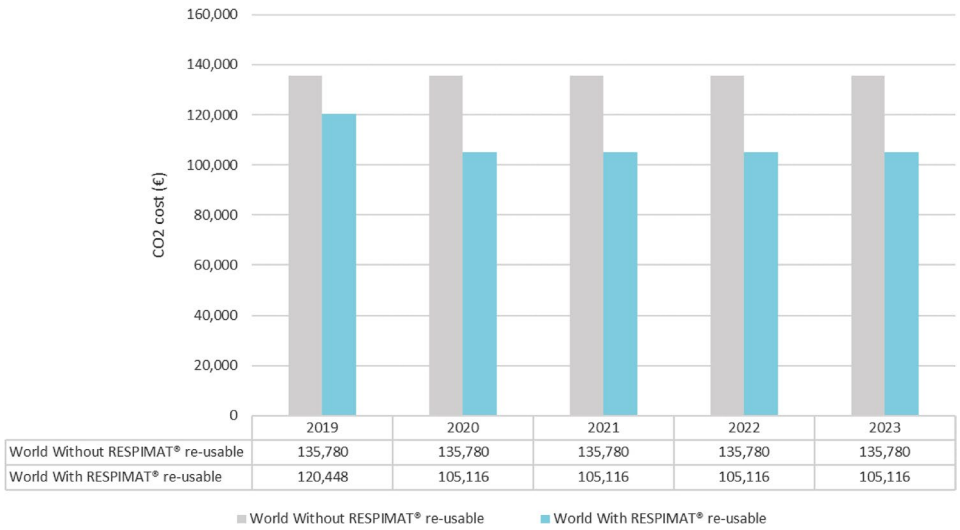


**Fig. 2** Societal cost of carbon emission by year

## 4 Discussion

### 4.1 Summary of Findings

The objective of this study was to perform an economic evaluation of adopting RESPIMAT re-usable in Germany that considered both the traditional healthcare costs as well as the environmental impact. The results showed that replacing RESPIMAT disposable with RESPIMAT re-usable would lead to both a reduction in inhaler-related costs as well as a reduction in $CO_2$ emissions. In the base-case analysis it was indicated that more than 5.7 million inhaler devices were saved implying that carbon emissions were reduced by 3450 tons and the societal cost of carbon emissions was reduced by approximately €130,000. The relatively small impact (approximately 0.2% reduction of total carbon footprint per capita) is due to the benign carbon footprint of the disposable version RESPIMAT [14].

### 4.2 Previous Economic Evaluations of Inhalers and Other Literature

Economic analyses comparing effectiveness and cost-effectiveness of inhalers are rare and existing evidence is not consistent regarding the advantages and disadvantages of

**Table 4** Cumulative results between 2019 and 2023 – base case and sensitivity analysis

| | Scenario with RESPIMAT® re-usable | Scenario without RESPIMAT re-usable | Incremental |
|---|---|---|---|
| Base case analysis—In the scenario with RESPIMAT re-usable, 45%, 45% and 10% of patients were assumed to use Pattern 1, Pattern 2 and Pattern 3, respectively | | | |
| No. of inhalers (*n*) | 16,151,250 | 21,900,000 | − 5,748,750 |
| Carbon emissions (tons) | 13,523 | 16,973 | − 3450 |
| Inhaler cost (€) | 1,029,878,546 | 1,035,903,000 | − 6,024,454 |
| Cost of carbon emissions (€) | 540,910 | 678,900 | − 137,990 |
| Sensitivity analysis (1)—In the scenario with RESPIMAT re-usable, all patients were assumed to use Pattern 3 | | | |
| No. of inhalers (*n*) | 8,760,000 | 21,900,000 | − 13,140,000 |
| Carbon emissions (tons) | 8498 | 16,973 | − 8474 |
| Inhaler cost (€) | 1,022,132,820 | 1,035,903,000 | − 13,770,180 |
| Cost of carbon emissions (€) | 339,927 | 678,900 | − 338,973 |
| Sensitivity analysis (2)—In the scenario with RESPIMAT re-usable, all patients were assumed to use Pattern 1 | | | |
| Carbon emissions (tons) | 17,431 | 16,973 | 458 |
| Cost of carbon emissions (€) | 697,230 | 678,900 | 18,330 |

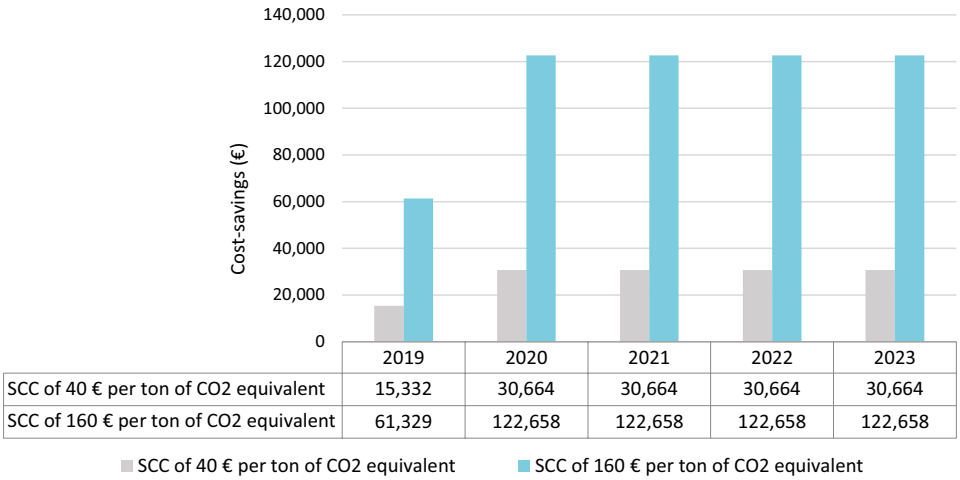


**Fig. 3** Cost-savings from reduced carbon emissions of adopting RESPIMAT re-usable

different inhalers [5, 40, 41]. In a systematic review by the UK NHS, costs and outcomes of different inhalers (nebuliser, DPI, pMDI) were compared [41]. The study found no differences between inhalers regarding costs, clinical outcomes and inhaler technique while another retrospective multicentre study found that adherence was better with pMDI compared to PDI [36]. However, another international, randomised, open study found that the effectiveness in terms of number of exacerbations was significantly better in patients using a PDI compared to patients using a pMDI [42].

This study differs significantly from previous economic evaluations in the sense that it does not compare two different inhalers and hence assumes that no difference exists between RESPIMAT disposable and RESPIMAT re-usable in terms of inhaler technique, adherence, efficacy or safety. Moreover, this study uses a budget impact model which simulates a cohort of patients.

To date, very few published health economic studies include the environmental aspect of health technologies. In one recent publication (Marsh et al. 2017) the environmental impact of treatment was included to an existing cost-utility analysis which evaluated the consequences of adding insulin to an oral diabetic [43]. The model estimated the generation of carbon emission both as a result of the production, distribution and consumption of the treatment in itself plus the emissions that are generated as a result of the treatment's health outcome. However, the carbon intensity applied in the model was not product-specific

(insulin and oral diabetic) but rather represented an average of pharmaceutical products purchased by the NHS.

To our knowledge, this study is the first budget impact model which incorporates the environmental impact of a health technology. In addition, the inputs used to estimate the environmental impact of each treatment pattern are based on product-specific estimates of the carbon footprint of each brand, which adds reliance to the estimated results. This is considered to be one of the main strengths of this study.

### 4.3 Relevance/Importance of Considering Environmental Impact

Since 1993, decision-making bodies in Canada, Australia, the EU have formally incorporated economic analyses into national HTAs to inform coverage and reimbursement decisions [19, 20]. Today more than 52 HTA agencies in 33 countries assess the value of health technologies and inform P&R decisions [44]. Yet, no defined pathway exists on how to include the environmental value of drugs and medical devices into HTAs and as a consequence, the potential ecological benefit or value created by a novel health technology will not be considered by payers in their decision making. The other side of this argument is obviously that manufactures of health technologies have no incentives to improve their products in areas other than those captured by today's HTA framework. This is problematic from both a theoretical and policy perspective. From a theoretical standpoint, all consequences of an intervention should be considered when conducting a health economic evaluation from a societal perspective. The environmental consequence is no exception and ought to be considered as an equally important component when performing health economic analysis. From a policy perspective, the omission of ecological value is equally troublesome. Industrial countries, including the EU, have committed themselves to binding targets for curbing GHG emissions [45, 46]. Studies from the USA report that healthcare contributes 8%–10% of the nation's GHG emissions from both healthcare activities and from indirect activities associated with the supply chain of healthcare-related goods and services [47, 48]. Hence, the impact of the healthcare sector on global $CO_2$ emissions is significant and the sector must collectively take steps towards reducing the environmental impact and contribute to reach the targets set out by their respective national governments. Thus, a more holistic approach in the HTA-process to better capture the total value could be possible. It could be based on the theoretical framework that all consequences, including environmental, of an intervention should be considered while at the same time align with the commitments of national governments to reduce the environmental impact [12]. Such framework would create a broader spectrum for market access in which manufactures could be rewarded—potentially as a price premium or some other market access—for products with a more benign environmental profile compared to competitors.

### 4.4 Limitations of the Study

Despite its strengths, we also acknowledge that the study proposed in this study also has some limitations. Foremost, data on product-specific $CO_2$ emissions are limited and may be time consuming to derive. In this sense, using an estimate on average carbon intensity of pharmaceutical products as in Marsh et al. may be a pragmatic approach [43]. Moreover, the results in this study are based on a modelled cohort of patients rather than an observed patient cohort. As is common in health economic models, several simplifications have been made. The study is limited in the sense that it does not take into account the dynamic effect the introduction of RESPIMAT re-usable may have on patients using inhalers of other manufactures. The study also assumes that the patient population remains constant throughout the model horizon, which is a simplification given mortality rates and increasing prevalence in respiratory symptoms [49]. Despite these limitations, the study provides valid insights on the effect of replacing RESPIMAT disposable with RESPIMAT re-usable and, as stressed previously, gives a novel example on how the environmental effect can be incorporated into a health economic model.

In addition to the limits of data, the value of $CO_2$ emissions is uncertain due to several factors including discount rate, valuation of nonmarket damages, population growth and weights given to different geographical regions [30]. Currently, no generally accepted method exists and needs to be determined to reach a consensus.

### 4.5 Conclusions

In conclusion, adopting RESPIMAT re-usable to the national healthcare services may be a cost-saving option which has the additional benefit of reducing the societal cost of carbon emissions.

**Data Availability Statement** The data that support the findings of this study are available from the corresponding author upon reasonable request.

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## Compliance with Ethical Standards

**Funding** GO and FB are employed by Quantify Research and were funded by Boehringer Ingelheim to conduct this study. CM is an independent consultant and was funded by Boehringer Ingelheim to conduct this study. MB is employed by Boehringer Ingelheim.

**Ethical approval** Ethics committee approval was not required as this article does not contain any studies with human participants performed by any of the authors.

**Author contributions** FB, MB and CM conceived this research and designed experiments; All authors participated in the design and interpretation of the data; GO and FB performed the analysis and wrote the paper. All authors participated in the revisions of it. All authors read and approved the final manuscript.



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