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ORIGINAL RESEARCH

A Budget Impact Model to Estimate the Environmental Impact of Adopting RESPIMAT® Re-usable in the Nordics and Benelux

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ABSTRACT

Introduction: The healthcare sector contributes 5–8% of the global greenhouse gas emissions. Global and regional organizations and governments have started to design and implement measures to reduce global greenhouse gas emissions in the healthcare sector, e.g. by green public procurement policies and inclusion of ecological considerations in the decision-making process for purchasing and funding of healthcare technologies. The objective of this study was to perform budget impact analysis of adopting RESPIMAT re-usable in the Nordics and Benelux that considered both the traditional healthcare costs as well as the environmental impact.

Methods: Inhaler costs and environmental impact over 5 years in the Nordics and Benelux in a scenario with RESPIMAT re-usable compared to a scenario without RESPIMAT re-usable were estimated using an budget impact model. RESPIMAT re-usable enables patients to re-use the inhaler device and its availability therefore reduces the number of inhalers and associated wastage. 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: Progressively introducing RESPIMAT re-usable in the Nordics and Benelux was estimated to decrease the number of inhalers used by 2023 by 7,466,621 compared to a scenario without RESPIMAT re-usable, which would result in a reduction of the environmental burden of inhaler use of 4717 tCO_2e and a decrease in societal cost of €205,888.

Conclusions: Adopting RESPIMAT re-usable would lead to a substantial reduction in CO_2 emissions, leading to savings from a societal perspective.

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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, accounting for more than 4 million deaths each year [1] of which 28,000 occur in the Nordics, Belgium, Netherlands and Luxembourg (Benelux) [2, 3]. About 210 million people are estimated to have chronic obstructive pulmonary disease (COPD) worldwide [4] and an estimated 300 million people suffer from asthma [5, 6]. The economic burden, including productivity losses, of these diseases in the European Union (EU) has been estimated to be €33.9 billion and €48.4 billion for asthma and COPD, respectively [2].

Inhalation therapy is the cornerstone of COPD and asthma management [7] to reduce symptoms and the risk of severe exacerbations. There are a variety of different inhalers which can be grouped into three main categories: (1) breath-actuated or pressurized 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 [8]. Poor adherence to therapy is common among patients with asthma and COPD and partly associated with difficulties in managing the inhaler device [8–11]. 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 [12, 13]. Hence, patient satisfaction with the inhaler device is expected to enhance treatment adherence and ultimately improve 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 to reduce carbon dioxide (CO_2) emissions and thereby have a positive environmental impact. While the current regulated model of health technology assessment (HTA) captures the first two values (improved clinical outcomes and quality of life), it needs to be expanded to capture the last one (environmental impact). For example, 70% of the inhaler users in the UK are on pMDI [14]. Yet, the UK Treasury estimates that for each pMDI inhaler with a unit cost of 2–4 GBP there is an environmental damage cost of 1–3 GBP [14].

In total, the healthcare sector contributes 5–8% of the global greenhouse gas (GHG) emissions [15]. Global and regional organizations and governments have started to design and implement measures to reduce GHG emissions in the healthcare sector, e.g. 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 ecosystem, patients increasingly act as consumers and prefer eco-friendly products [16, 17].

pMDIs with propellants (hydrofluoroalkane, 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_2e burden of 13 million tCO_2e [4], equal to the carbon footprint of 2 million EU citizens [14].

Whilst several national and methodological guidelines encourage the inclusion of the societal perspective in the economic analyses, only a minority of analyses do so [18]. There is currently a discussion in the scientific and policy community regarding the need for redefining what value means [19–25]. More holistic

frameworks are being proposed and piloted which aim to better capture the total value and to better consider the diverse needs of stakeholders [26–28]. Comprehensive "cradle-to-grave" mapping of the product carbon footprint (PCF) expressed as CO_2e is the first step to quantify the ecological impact of a health technology. 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.

RESPIMAT® re-usable is a new type of inhaler that is propellant free and re-usable which has the potential to reduce the CO_2 burden and the social cost of carbon emissions (SCC) by replacing conventional pMDIs. The objective of this study was to perform a budget impact analysis that incorporates the ecological impact of substituting Respimat disposable with RESPIMAT re-usable in the healthcare system in the Nordics (Denmark, Iceland, Finland, Norway and Sweden) and Benelux.

METHODS

Technologies/Interventions

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.

Target Patient Population

The drugs developed for use with the Respimat disposable and RESPIMAT re-usable inhalers are indicated for the treatment of patients with respiratory diseases, such as COPD and asthma. Today, approximately 3 million inhalers are used annually together with Spiriva®, Spiolto® and Striverdi® in the studied countries.

Model Design

Given that RESPIMAT re-usable has identical performance levels as Respimat disposable, no direct efficacy gain is expected from switching patients from Respimat disposable to RESPIMAT re-usable [30]. And although it would be theoretically possible to incorporate possible gains in quality of life due to environmental improvements, currently robust data is missing for this to be a feasible approach and the potential gain in Quality of life would probably be negligible. Also, it is plausible that RESPIMAT re-usable could provide an improved treatment compliance compared to 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 (BIM) was chosen over a cost-effectiveness model to quantify the budget and environmental impact of RESPIMAT re-usable. The BIM calculates the number of inhalers and refill packages used annually in the study population over 5 years (between 2019 and 2023). 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 BIM design and outcomes is the treatment pattern, i.e. how often inhalers are replaced by new ones in a scenario RESPIMAT re-usable. This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

Treatment Patterns

Respimat disposable comes in two pack sizes, either as a single disposable 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 and year.

RESPIMAT re-usable comes in similar pack sizes as Respimat disposable but both the single pack (N1) and the triple pack (N3) contain one single re-usable inhaler, for 1 month and 3 months of treatment, respectively. In

Table 1 Inhalers per year by pattern label

Treatment pattern	Treatment pattern (12 months)	Saved inhalers per year with respect to Respimat disposable
Current	12 × D1	
Moderately optimised	6 × N1 + 6 × R1	6
Highly optimised	4 × N1 + 8 × R1	8
Most optimal	2 × N3 + 2 × R3	10

addition, two refill packs (without inhalers) are also available containing one refill (R1) and three refills (R3), respectively. 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 pack sizes and saved inhalers (per patient and year) per different treatment pattern.

In analysis 1, all patients switching to RESPIMAT re-usable were assumed to follow the "Moderately optimised pattern". In analysis 2, all patients switching to RESPIMAT re-usable were assumed to follow the "Highly optimised pattern". In analysis 3, all patients were assumed to follow the "Most optimal pattern". RESPIMAT re-usable is only available as N1 for Striverdi and hence these patients were excepted from these rules and were assumed to use 12 single packs (N1) per year. In addition, input values were tested in a one-way sensitivity analysis and results are presented in Table 5 in the supplementary material.

Economic Valuation

Direct medical costs in terms of treatment costs were calculated per scenario. Treatment costs were derived from ex-factory prices or pharmacy purchasing price of each brand and inhaler and assumed to be constant throughout the BIM horizon. The treatment cost by country and brand is presented in Table 6 in the supplementary material. Price parity between RESPIMAT re-usable and Respimat disposable was assumed in analyses 1 and 2 but an explorative analysis was undertaken in analysis 4 in which a price discount of 2% was applied to the pack size R1. No annual discount factor was applied as is recommended in BIMs [31]. No other costs to the healthcare system are included given the equivalence in effect and safety between Respimat disposable and RESPIMAT re-usable [30]. Therefore, substituting the former with the latter is not assumed to affect healthcare consumption. All costs are expressed in 2018 euros. Treatment costs in Sweden, Norway and Denmark were converted to euro using the average exchange rate between euro and respective currency during 2018 [32–34].

Environmental Impact

The life cycle PCF measured as kilos of CO_2 equivalents was derived for each treatment pattern taking into account the PCF of the whole life cycle (cradle-to-grave) of the inhaler product (Table 2). 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

Table 2 Product carbon footprint (kilos of CO_2) by treatment pattern

Treatment pattern	PCF (kilos of CO_2 equivalents)
Respimat disposable (D1)	0.775
RESPIMAT re-usable (N1)	0.798
RESPIMAT re-usable (N3)	1.035
RESPIMAT re-usable refill 1 month (R1)	0.119
RESPIMAT re-usable refill 3 months (R3)	0.358

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 begins 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.

$$\begin{aligned} \text{kg } CO_2\text{e} = {} & \text{Activity Data (unit)} \\ & * \text{Emission Factor}\left(\frac{\text{kg GHG}}{\text{unit}}\right) \\ & * \text{GWP}\left(\frac{CO_2\text{e}}{\text{kg GHG}}\right) \end{aligned} \quad (1)$$

The global warming potential (GWP) is set to 100 as recommended by the Green Gas Protocol Product Life Cycle Accounting and Reporting Standard [35].

The estimate complied with the requirements of the Green Gas Protocol Product Life Cycle Accounting and Reporting Standard [35] as well as the specific sector guidance for pharmaceutical products [36]. The SCC was set to US$50 (43.65€) 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 [37]. 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 [38].

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 to the reader [39].

Study Population

The baseline population in 2019 was assumed to reflect the current use of the three brands included in the BIM (Spiriva, Spiolto and Striverdi) in the Nordics and Benelux and was set to 261,980 patients. Of these, 176,642 (67%) were assumed to use Spiriva, 81,909 (31%) to use Spiolto and 3429 (1%) to use Striverdi. The evolution of both the size of the population and the distribution between brands throughout the BIM horizon was based on forecasted market shares. As the focus of this study was on the environmental impact of replacing Respimat disposable with RESPIMAT re-usable, potential dynamic changes in market shares and competitors' reactions were not considered.

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 progressively replaced by a RESPIMAT re-usable inhaler. Market penetration rates of RESPIMAT re-usable varied by country in 2019 (21–70%); from 2020 and onwards, all patients were assumed to have switched to RESPIMAT re-usable. The treatment pattern for patients switching to RESPIMAT re-usable is described in Table 1.

Compliance with Ethics Guidelines

Since this study did not involve any human subject, ethics committee approval was not required.

RESULTS

Base Case

Progressively introducing RESPIMAT re-usable in the Nordics and Benelux was estimated to decrease the number of inhalers used by 2023

by 7,466,621 compared to a scenario without RESPIMAT re-usable. In addition, this measure would reduce the environmental burden of inhaler use by 4717 tCO_2e which translates into a reduced societal cost of €205,888. Figure 1 shows the annual number of inhalers used in the two scenarios. Given that only a fraction of patients switch from Respimat disposable to RESPIMAT re-usable in 2019, the difference in number of inhalers used between the two scenarios is smaller than the 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 Tables 2 and 3.

Sensitivity Analysis

In two sensitivity analyses, all patients using RESPIMAT re-usable (with the exception of patients on Striverdi) were assumed to follow the "Highly optimised" and "Most optimal" treatment pattern plus an analysis in which patients followed the moderately optimised pattern but a 2% discount for R1 was applied. The details of this analysis are shown in Table 4. In the "most optimal" pattern, 12,444,368 fewer inhalers would have been used by 2023 compared to a scenario without RESPIMAT re-usable. This is a further decrease of almost 5 million inhalers compared to analysis 1. Consequently, the environmental impact is further eased.

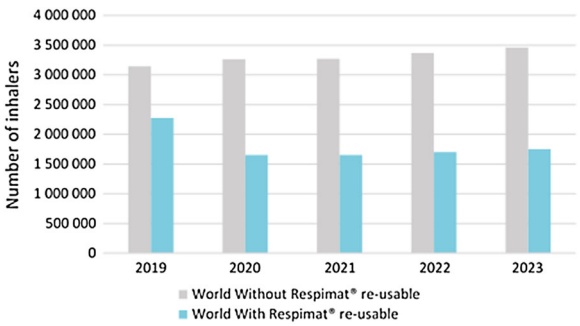

Fig. 1 Number of inhalers used by year

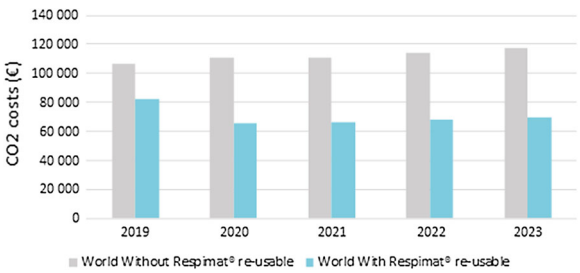

Fig. 2 Societal cost of carbon emission by year

DISCUSSION

Summary of Findings

The objective of this study was to perform an economic evaluation of adopting RESPIMAT re-usable in the Nordics and Benelux 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 a reduction in CO_2 emissions. In analysis 1 in which patients follow a moderately optimised pattern of inhaler use, more than 7 million inhaler devices were saved implying that the societal cost of carbon emissions was reduced by approximately €200,000 over 5 years. If patients were to follow the most optimal treatment pattern (analysis 3), an additional 5 million inhaler devices would be saved compared to the moderately optimised pattern. In addition, the societal cost of carbon emission would decrease further by €150,000 and amount to approximately €350,000 over 5 years.

Potential of RESPIMAT Re-usable

The relatively small estimated impact on carbon emission of switching patients from Respimat disposable to RESPIMAT re-usable is due to the benign carbon footprint of the former. However, pressurized metered dose inhalers, which are the most common inhaler device used in COPD and asthma, have a much more unfavourable carbon footprint. Whereas the PCF of RESPIMAT re-usable is 0.798 kilos of CO_2 equivalents, the PCF of a typical pMDI may be up to 20 times higher, driven mainly by the

Table 3 Cumulative results between 2019 and 2023: analysis 1—"Moderately optimised"

	Scenario with RESPIMAT re-usable*	Scenario without RESPIMAT re-usable	Incremental
No. of inhalers (*n*)	9,029,599	16,496,220	− 7,466,621
Carbon emissions (tons)	8068	12,785	− 4717
Treatment cost (€)*	630,680,087	630,680,087	0
Cost of carbon emissions (€)	352,159	558,047	− 205,888

*Given price parity between Respimat disposable and RESPIMAT re-usable, the treatment cost is equal between the two scenarios

Table 4 Cumulative results between 2019 and 2023: sensitivity analysis

	Scenario with RESPIMAT re-usable*	Scenario without RESPIMAT re-usable	Incremental
Analysis 2: highly optimised			
No. of inhalers (*n*)	6,540,726	16,496,220	− 9,955,494
Carbon emissions (tons)	6378	12,785	− 6406
Total costs			
Treatment cost (€)*	630,680,087	630,680,087	0
Cost of carbon emissions (€)	278,418	558,047	− 279,629
Analysis 3: most optimal			
No. of inhalers (*n*)	4,051,852	16,496,220	− 12,444,368
Carbon emissions (tons)	4684	12,785	− 8101
Total costs			
Treatment cost (€)*	630,680,087	630,680,087	0
Cost of carbon emissions (€)	204,453	558,047	− 353,594
Analysis 4: moderately optimised with 2% discount for R1			
No. of inhalers (*n*)	9,029,599	16,496,220	− 7,466,621
Carbon emissions (tons)	8068	12,785	− 4717
Total costs			
Treatment cost (€)	624,921,020	630,680,087	− 5,759,066
Cost of carbon emissions (€)	352,159	558,047	− 205,888

*Given price parity between Respimat disposable and RESPIMAT re-usable, the treatment cost is equal between the two scenarios

emission of the HFA gas during use as well as the emissions of leftover propellant gas during waste treatment. RESPIMAT re-usable, on the other hand, has no propellant. Hence, replacing pMDIs with RESPIMAT re-usable would correspond to an annual reduction of 186 tons CO_2 (corresponding to an SCC of €8122) per 1000 replacements. This is the equivalent of the annual CO_2 footprint of 29 EU citizens [40]. The introduction of RESPIMAT re-usable is not expected to lead to any price reduction or increase with respect to Respimat disposable and is therefore not expected to lead to any incremental costs or savings to the healthcare sector. However, treatment costs may be reduced as a result of other initiatives aiming to reduce the overall cost of inhalers which now represents one of the highest expenditures within ambulatory care [41].

An ideal inhaler device combines a series of characteristics including ease of use, capable of delivering a predictable and consistent lung dose, minimal side effects and a reasonable cost [41, 42]. Hence, therapeutic success in COPD and asthma is not limited to the efficacy of the drug but depends largely on the characteristics and the ability of patients to handle the inhaler correctly [43, 44]. Large variation in the use of inhaler device exists between countries. For example, in the UK, pMDIs encompasses as much as 70% of the market, while in Sweden, only 10% use pMDIs [14]. The benign carbon footprint of RESPIMAT re-usable makes it an attractive alternative to pMDIs.

Limitations

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 of average carbon intensity of pharmaceutical products like in Marsh et al. may be a pragmatic approach [45]. Moreover, the value of CO_2 emissions is uncertain because of several factors including discount rate, valuation of nonmarket damages, population growth and weights given to different geographical regions [39]. Currently, no generally accepted method exists and one is needed to reach a consensus.

In addition, the assumed treatment patterns in this study may be guided by other factors than the availability; doctors and/or patients may have preference for regular medical visits and therefore continue to prescribe RESPIMAT re-usable containing one inhaler only (N1). However, as the use of RESPIMAT re-usable extends, countries may introduce prescribing cost-containment measures, similar to what is expected to occur in inhaled medications [46]. Moreover, the estimated treatment cost in each scenario could potentially be overestimated because of existing mechanisms to decrease the prices of treatments in each national healthcare service. However, the budget impact of these mechanisms is anticipated to be null since their effect would be equal on RESPIMAT re-usable and Respimat disposable. An additional limitation of this study is the effect of introducing RESPIMAT re-usable on the market share of other manufactures which has not been considered in this analysis.

CONCLUSION

The introduction of RESPIMAT re-usable leads to a substantial reduction in CO_2 emissions, leading to savings from a societal perspective.

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Compliance with Ethics Guidelines. This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

Data Availability. Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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