Exploring Environmental Impacts of Switching salmeterol/fluticasone propionate (SAL/FP) from Metered Dose Inhaler (MDI) to Dry Powder Inhaler (DPI) in respiratory Illness in the United Kingdom

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Introduction and objectives

> In 2019, chronic respiratory diseases ranked as the third leading cause of death worldwide, with asthma being the most prevalent respiratory disease at 264.4 million cases, followed by chronic obstructive pulmonary disease (COPD) at 212.3 million cases.[1] A survey revealed that there were 5.4 million asthma cases in 2022 making it the most common respiratory condition in the United Kingdom (UK).[2] This led to an annual associated cost of £1.1 billion, with £666 million spent on prescriptions alone.[3]

> Inhalers play a vital role in managing respiratory conditions and improving quality of life for millions of patients worldwide.[4] However, there is a growing concern about the environmental impact of inhalers, particularly due to their carbon footprint and contribution to climate change.

> Annually, 61 million inhalers are prescribed in the UK, resulting in a carbon footprint of 1.3 mega tonnes carbon dioxide equivalent (CO2e) emissions, with pressurised metered dose inhalers (pMDI) responsible for 70% of these emissions.[5] This accounts for 3.2% of the National Health Service's (NHS) total medicine-related greenhouse gas (GHG) emissions.[6,7]

> Alternatives to pMDIs are readily available, such as dry power inhalers (DPIs) and soft-mist inhalers (SMIs). DPIs have significantly less global warming potential (GWP) producing around 20g CO2e per dose as opposed to the carbon footprint of pMDIs (500g CO2e/dose).[8]

> Globally, the NHS was the first to set the target of net zero carbon by 2050 and took measures to achieve it.[7] The study aimed to assess the potential environmental impacts of transitioning from pMDI to DPI as a delivery method for salmeterol/fluticasone propionate (SAL/FP) by using carbon footprint of different brands of SAL/FP. A secondary aim of the study was to evaluate the budgetary implication of this transition, to help provide policymakers with additional insights into reducing GHG emissions and effectively managing financial decision.

Methods

> An environmental and budget impact model was developed for a five-year period to estimate the reduction in GHG emissions resulting from the transition of SAL/FP pMDIs to SAL/FP DPIs.

> Efficacy was not factored into the model due to the uniform composition of all brands studied. It was assumed that the safety and efficacy of inhalers from different manufacturers remain constant. This was based on the understanding of uniform clinical effectiveness among inhaler types, provided patients utilize proper inhalation technique.[9]

> SAL/FP was divided into three treatment mixes based on the strength of their dose (**Table 1**).

Table 1. Treatment mix based on formulation type of salmeterol/ fluticasone propionate.

Treatment mixes	Salmeterol/ fluticasone propionate (SAL/FP) formulation	
	Pressurised metered dose inhalers (pMDIs)	Dry powder inhalers (DPIs)
Treatment mix 1	Salmeterol 25mcg, fluticasone propionate 250mcg	Salmeterol 50mcg, fluticasone propionate 500mcg
Treatment mix 2	Salmeterol 25mcg, fluticasone propionate 125mcg	Salmeterol 50mcg, fluticasone propionate 250mcg
Treatment mix 3	Salmeterol 25mcg, fluticasone propionate 50mcg	Salmeterol 50mcg, fluticasone propionate 100mcg

> Prescription Cost Analysis (PCA) was used from the NHS to identify the number of inhalers being prescribed in 2022-2023.[10-13] This was used to derive the number of patients using pMDI or DPI, assuming 100% medication adherence. The proportion of patients were then used to identify the market share of each brand.

> Product carbon footprint (PCF) measured in CO2e emissions and cost of SAL/FP were retrieved from a report published by PrescQIPP.[5]

> Discount rates were not applied to the costs in compliance with the ISPOR best practices for budget impact analysis (BIA).[14]

> Population growth of -0.1% was taken from the World Bank and the growth rate was assumed to be constant for 5 years.[15]

> When we considered the market without DPI (referred as reference scenario), the market shares of pMDI was assumed to be 100%.

> In the new scenario DPIs were introduced to the patient population proportionally over 70% as replacing the entire population with DPIs is realistically challenging and not feasible. This is due, in part, to the requirement for patients using DPIs to have adequate peak inspiratory flow and sufficient manual and cognitive capacity.[16]

> The model's trade-off ratio between budget and carbon impact was then calculated.

> Multiple scenario analyses were conducted to validate the robustness of our findings such as switching the patient population to lowest carbon footprint DPI alternative to identify optimal emission reduction, switching to the cheapest DPI alternative to overcome the fiscal challenges as opposed to base case, and applying no population growth by hypothetically replacing 100% MDI with DPI in the UK and its constituent countries.

Results

> In 2022/23, 18,157,095 SAL/FP inhalers were prescribed, emitting 0.35 mega tonnes of CO2e emissions at a cost of £443 million (assuming 100% market share for pMDIs).

Base case

> Shifting over 70% pMDIs to DPIs reduced CO2e emissions by 47.07% (yearly average of 0.16 mega tonnes) annually over 5 years (2023-27), with a yearly average cost of £54.6 million (£330.56/ton of CO2e emissions) (**Table 2**, **Figure 1** and **Figure 2**). This represents the cost to save a ton of CO2e emission. However, the absence of an official willingness to pay (WTP) threshold for achieving the NHS's net-neutral target makes it challenging for the decision-makers to assess the decision.[17]

Sensitivity analyses

> Deterministic sensitivity analysis (DSA) analysis revealed the top ten parameters influencing environmental and economic outcomes, includes pMDI and DPI carbon footprints and NHS inhaler costs.

> CO2e reduction ranged from 0.15 to 0.17 mega tonnes annually, primarily influenced by Seretide Evohaler 25/250 pMDI's carbon footprint, while budget impacts ranged from £30M to £79M yearly, mainly driven by NHS cost fluctuations of Seretide Accuhaler 50/250 DPI (**Figure 3** and **Figure 4**).

Results

Scenario analyses

> Scenario analyses provided insights into potential trade-offs between carbon emissions and the cost incurred by the transition.

> **Lowest product carbon footprint (PCF)**
- Replacing over 70% of pMDIs with DPIs featuring lowest PCF reduced CO2e emissions by 47.71% (0.16 mega tonnes), similar to the base case. However, this had an opposite effect on costs, savings £10.2 million (**Figure 5** and **Figure 6**). This favourable outcome accompanied with cost saving, highlights a positive impact.

> **Cheapest DPI alternative**
- Replacing pMDIs with cheapest DPI alternative reduced CO2e emissions by 46.44% (0.16 mega tonnes) yearly, incurring a yearly average cost of £380 million, saving approximately £64 million (**Figure 5** and **Figure 6**).
- Although the lowest PCF scenario slightly outperforms in emissions reduction, the cheapest DPI alternative offers substantial cost savings despite marginally lower emission reductions.
- This comparison (47.71% vs 46.44% reduction in CO2e emissions and cost saving of £10.2 million vs £64 million) will assist decision-makers in weighing the trade-off between environmental impact of financial efficiency.

> **No population growth**
- Replacing pMDIs with no population growth throughout the time horizon reduced CO2e emissions by 55.79% (0.19 mega tonnes), costing £509 million annually, an additional £65 million (**Figure 5** and **Figure 6**).

> **Regional impact without population growth**
- Northern Ireland had the highest environmental and budget impact, saving 154,335 tonnes CO2e, accounting for 80% of the total cost, due to high inhalers prescription rate (**Figure 7** and **Figure 8**).

> The treatment mixes consistently demonstrated carbon impacts across scenarios, with treatment mix 1 having the highest carbon impact, followed by treatment mix 2 and 3. A similar trend was observed for budget impact, except in base case and the scenario where no population growth was applied, where treatment mix 2 had the highest impact, followed by 1 and 3.

Table 2. Carbon and budget impact over 5-year time horizon by treatment mixes

Treatment mixes	Year 1	Year 2	Year 3	Year 4	Year 5	Yearly average
Carbon impact of Switching from pMDI to DPI (t CO2e)						
Treatment Mix 1	19,822	52,248	76,505	94,642	108,195	70,282
Treatment Mix 2	24,509	51,876	72,348	87,653	99,086	67,094
Treatment Mix 3	12,642	22,407	29,710	35,168	39,246	27,834
Total	56,974	126,531	178,562	217,463	246,526	165,211
Budget impact of Switching from pMDI to DPI (£)						
Treatment Mix 1	£3.9M	£10.2M	£15.0M	£18.5M	£21.2M	£13.7M
Treatment Mix 2	£14.9M	£31.5M	£43.9M	£53.1M	£60.1M	£40.7M
Treatment Mix 3	£71.9K	£127.5K	£169.0K	£200.1K	£223.3K	£158.4K
Total	£18.8M	£41.8M	£59.0M	£71.9M	£81.5M	£54.6M

Figure 1. Carbon impact of treatment mix of SAL/FP (t CO2e)

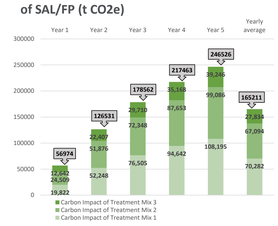


Figure 2. Budget impact by treatment mix of SAL/FP (£)

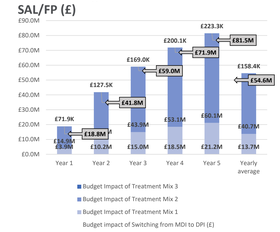


Figure 3. Univariate DSA of carbon impact

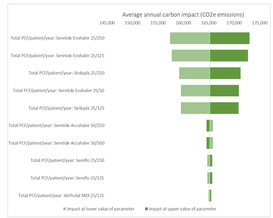


Figure 4. Univariate DSA of budget impact

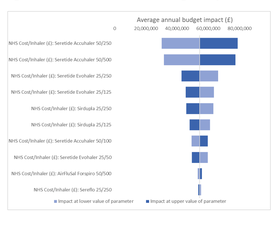


Figure 5. Carbon impact: Scenario analyses

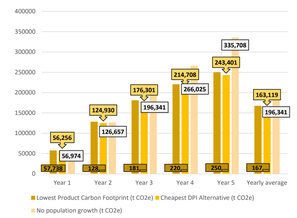


Figure 6. Budget impact: Scenario analyses

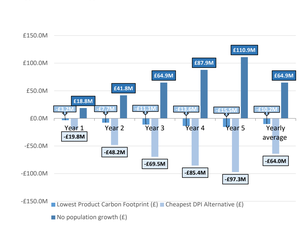


Figure 7. Environmental impact of displacing DPI based on region.

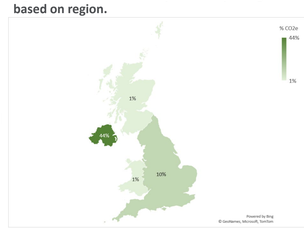
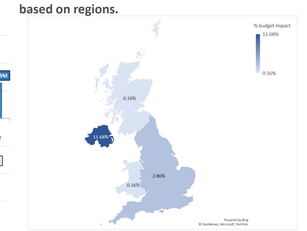


Figure 8. Economic impact of displacing DPI based on regions.



Conclusion

> The results suggest that transitioning from pMDIs to DPIs has the potential to reduce GHG emissions, aligning with broader sustainability goals.

> However, it is also important to acknowledge that such a transition will not be without its financial costs and challenges.

> When considering such a shift in inhaler usage, policymakers and healthcare executives must carefully assess the positive environmental impacts against the fiscal implications.

> A balanced approach that accounts for both environmental sustainability and economic feasibility, is in line with the principles of healthcare sustainability should be promoted by the healthcare authorities.

> Additionally, geographical differences in impact should be considered when planning and executing such reforms to guarantee equitable outcomes.

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