Treatment with dual and triple therapy in chronic obstructive pulmonary disease in line with current guidelines reduces the carbon footprint

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Background

- International guidelines recommend triple therapy with long-acting antimuscarinic antagonists (LAMA), long-acting β-agonists (LABA), and inhaled corticosteroids only for patients with chronic obstructive pulmonary disease (COPD) who continue to exacerbate despite treatment with dual therapy (LAMA/LABA).[1]
- In clinical practice, triple therapy is often overprescribed. Real-world evidence suggests that triple therapy is being over-utilised in patients for whom international guidelines would not recommend.[2–4]
- Triple therapy in the form of fixed dose combinations (FDC) is available in two inhaler types: pressurised metered-dose inhalers (pMDIs) and dry powder inhalers (DPIs).
- Dual therapy (LAMA/LABA) is available as a reusable (Europe) or disposable (US) soft mist inhaler (SMI).
- The carbon footprint, expressed in carbon dioxide equivalent (CO_2e), of the three inhaler devices differ, with pMDIs having a higher carbon footprint due to use of powerful greenhouse gases, hydrofluorocarbon (HFC) propellants, that have a high global warming potential.
- While pMDIs are only available as single-use inhalers, DPIs and SMIs are also available in reusable forms, which further reduces their carbon footprints.
- As each inhaler type has different carbon footprints, with SMIs having the lowest carbon footprint, some national governments and organisations have introduced targets to reduce high carbon footprint inhaler use, as part of their efforts in the fight against global warming.[5,6]

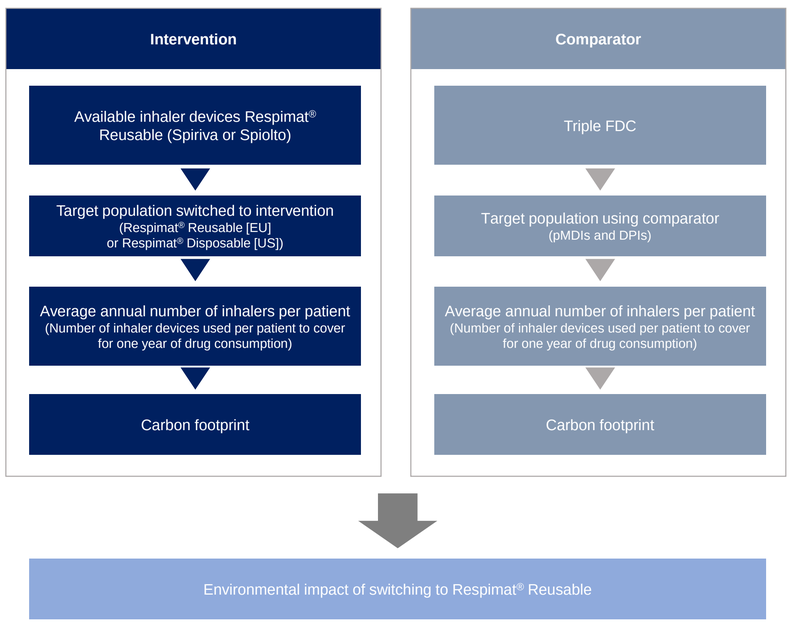
Objective

- This study aimed to assess the change in carbon footprint of hypothetically redistributing COPD patients currently treated with triple FDC to LAMA/LABA SMI (Respimat® Reusable in Europe and Respimat® Disposable in the United States), in line with international guidelines.[1]

Methods

- An environmental impact model was established to assess the change in carbon footprint of replacing different types of pMDIs or DPIs with a reusable SMI, Respimat® Reusable, across 12 European countries and Respimat® Disposable in the United States over 5 years (**Figure 1**). Respimat® Reusable is not available in the United States.

Figure 1: Model structure



- The model was developed in accordance with ISPOR best practice guidelines for budget impact modelling, deemed to be the most appropriate guidance for model development.[7]
- The eligible population was adults with COPD on triple FDC.
- Inhaler use per country was derived from IQVIA MIDAS® international data (2021)[8] and inhaler carbon footprints were identified from published sources.[9–14] To estimate the carbon footprint of those inhalers with no available data, an average, by inhaler type, was taken between the available estimates and attributed to those inhalers with no available data on carbon footprint (**Table 1**).

Table 1. Carbon footprint of the triple fixed dose combination and dual therapy inhalers used as model inputs

Device type	Class	Product	Reusable?	CF-Inhaler*,†	CF-Refill*,†	Reference
pMDI	Triple FDC	Trimbow	No	14.5		Panigone et al. (2020)[9]
		Breztri Aerosphere	No	25.3		Janson et al. (2020),[10] Panigone et al. (2020),[9] Wilkinson et al. (2019),[11] NICE[12]
DPI	Triple FDC	Trelegy Ellipta	No	0.8		Janson et al. (2020)[10]
		Elebrato Ellipta	No	0.8		Janson et al. (2020)[10]
		Enerzair	Yes	0.4	0.1	Novartis (2021)[13]
SMI	LAMA/LABA	Spiolto Respimat® Reusable	Yes	0.7	0.1	Hänsel et al. (2019)[14]

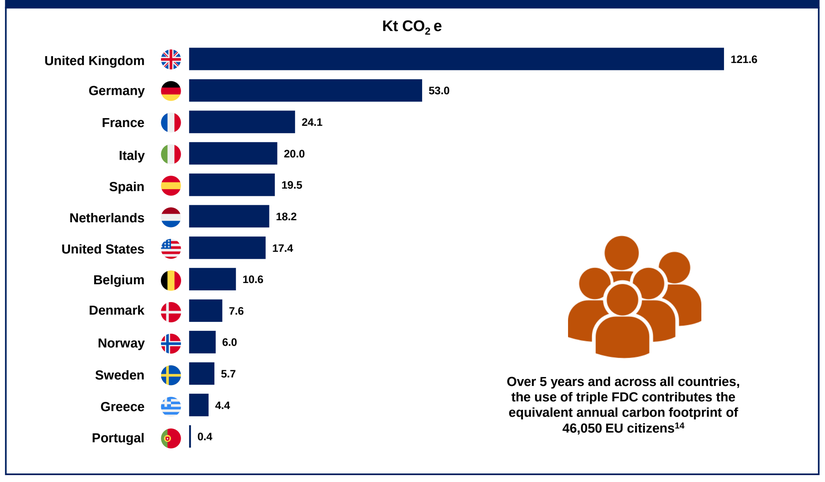
*The proportion of CF (~17%) attributed to the refill was based on the proportion of active pharmaceutical ingredients and distribution as the total carbon footprint per package in Janson et al.(2020)[10] with the exception of SMIs (in which case Hänsel et al. 2019[14] provided this data); † for products/inhalers with no available CF-estimate, an average of all available evidence was used. CF, carbon footprint; DPI, dry powder inhaler; FDC, fixed dose combination; LABA; long-acting beta-agonists; LAMA, long-acting muscarinic antagonist; pMDI, pressurised metered dose inhaler; SMI, soft mist inhaler.

- For each country, the size of the eligible population was estimated as the sold yearly dosages based on market share data.
- The proportion of patients overprescribed according to international guidelines was based on published UK data,[3] and applied to all European countries, or published data from the United States.[2]

Results

- Based on current clinical practice, the use of triple FDC inhalers contribute 308.5 kilo tonnes (kt) of CO_2e across all countries over 5 years (**Figure 2**).

Figure 2. Carbon footprint of patients currently prescribed triple FDC

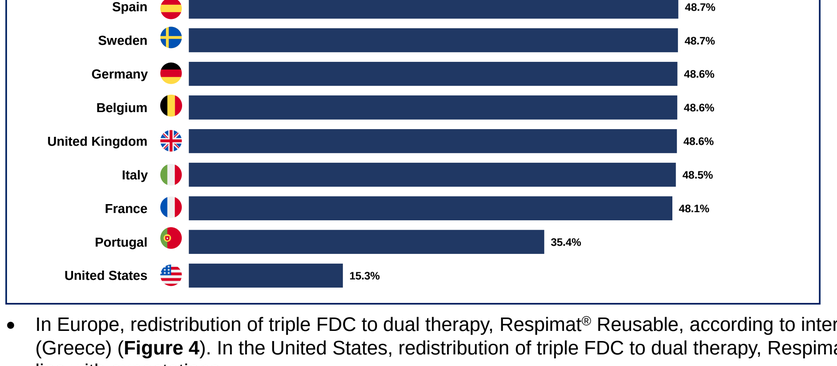


- Based on published data, 50% of patients in Europe and 95% in the United States were assumed to be prescribed triple therapy FDC not in line with international recommendations (**Table 2**). This difference in proportions is attributable to the data being based on different sources.

Table 2. Change in proportion of patients with COPD treated with triple therapy following redistribution in accordance with GOLD recommendations

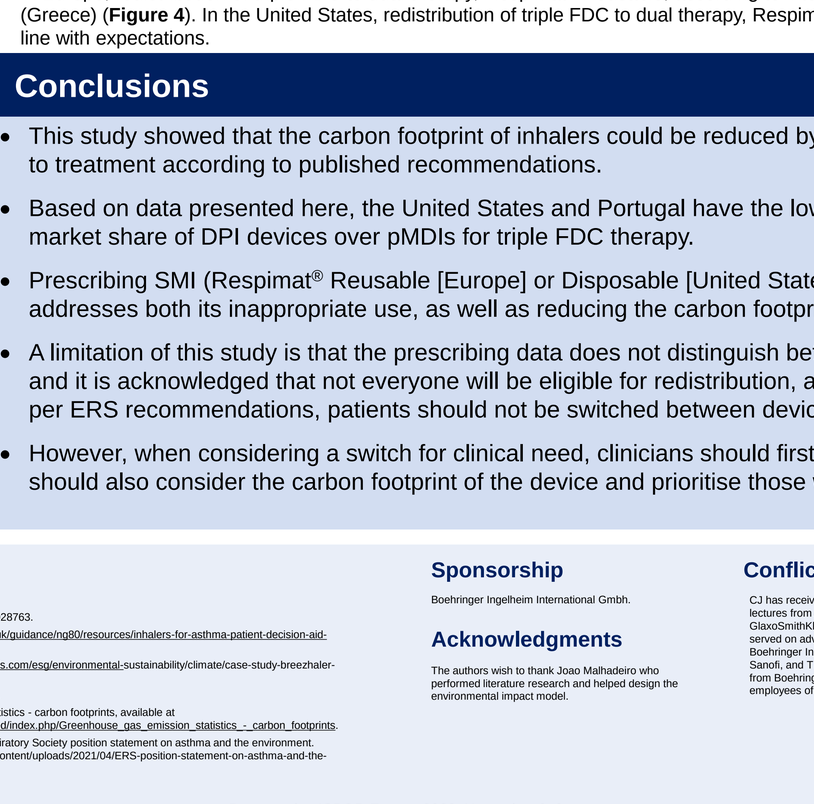
Country	Current treatment	Proposed treatment	Relative change	Reference
United Kingdom	55.6%	27.7%	-49.8%	3
United States	11.5%	0.6%	-94.6%	2

Figure 3. Reduction in carbon footprint of patients after redistribution of patients according to international guidelines, to LAMA/LABA, Respimat® Reusable (Europe) or Respimat® Disposable (US)



- In Europe, over 5 years, hypothetical redistribution of triple therapy FDC to dual therapy Respimat® Reusable, in line with international recommendations, reduced CO_2 emissions to 150.4 kt of CO_2e **(Figure 3**). In the US, redistribution of inhaler devices reduced CO_2 emissions to 14.7 kt of CO_2e (**Figure 3**), this lower rate is in line with expectations for the US.

Figure 4. Redistribution of triple FDC therapy to dual therapy, Respimat® Reusable, according to international guidelines, reduces the carbon footprint by up to 49.2% in Europe; redistribution to Respimat® Disposable in the United States reduces the carbon footprint by 15.3%



- In Europe, redistribution of triple FDC to dual therapy, Respimat® Reusable, according to international recommendations decreased the carbon footprint by 35.4% (Portugal) to 49.2% (Greece) (**Figure 4**). In the United States, redistribution of triple FDC to dual therapy, Respimat® Disposable, reduced CO_2 emissions by 15.3% **(Figure 4).** The lower rate for the US is in line with expectations.

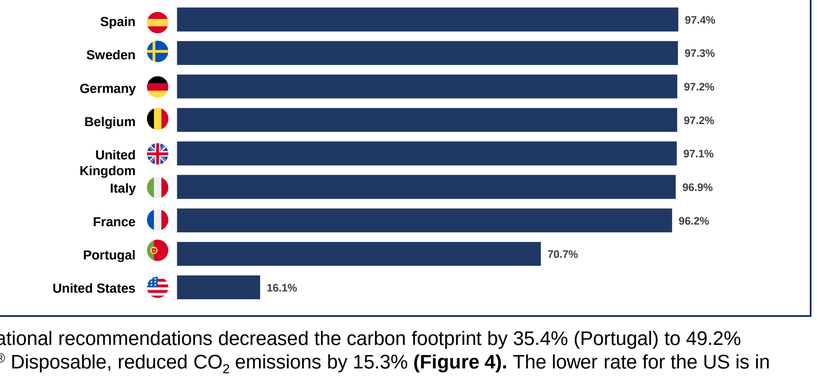
- Based on this data, market shares of patients receiving triple FDC were redistributed between triple FDC and Respimat® Reusable (Europe) or Respimat® Disposable (United States) to reflect the recommended treatment pattern by international guidelines (**Table 3**) and the change in carbon footprint was assessed.

Table 3. Change in proportion of patients with COPD treated with triple therapy following redistribution in accordance with GOLD recommendations

Country	Pre-redistribution	Post-redistribution	
	Number of patients on triple FDC	Number of patients remaining on triple FDC	Number of patients switched to dual LAMA/LABA therapy
Belgium	21,970	10,985	10,985
Denmark	13,076	6,538	6,538
France	67,401	33,701	33,701
Germany	108,339	54,170	54,170
Greece	5,070	2,535	2,535
Italy	45,458	22,729	22,729
Netherlands	24,901	12,451	9,110
Norway	11,445	5,723	5,723
Portugal	8,458	4,229	4,229
Spain	37,142	18,571	18,571
Sweden	11,253	5,627	5,627
United Kingdom	259,230	129,615	129,615
United States	313,726	15,686	298,040

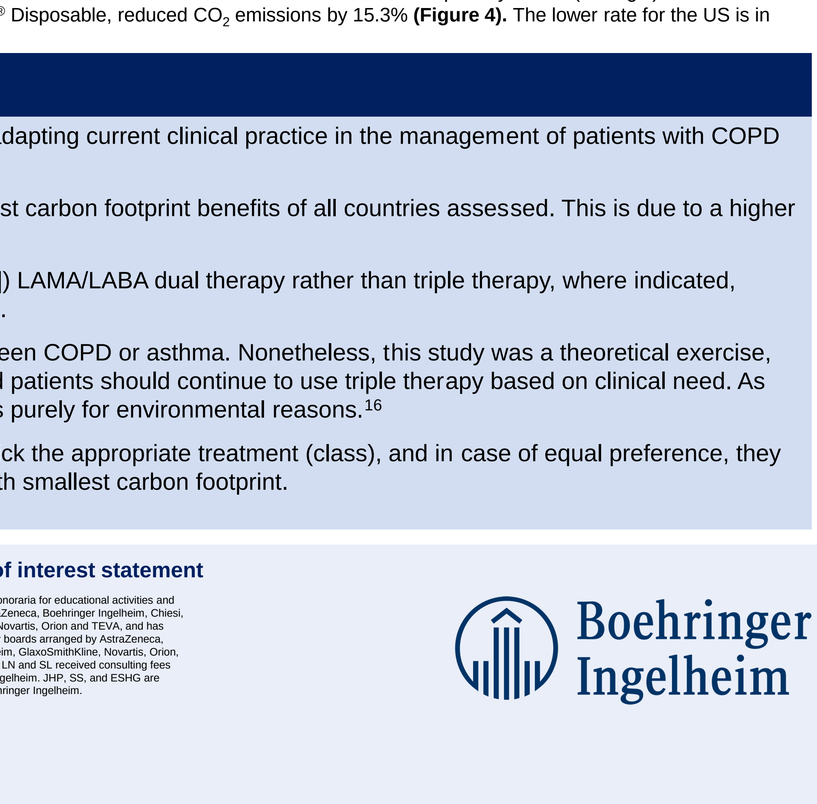
- Over 5 years and across all countries, redistribution of inhaler devices according to international guidelines could save the equivalent annual carbon footprint of 21,408 EU citizens.[15]
- Over 5 years and across all countries, redistribution of all patients currently on triple FDC therapy to dual therapy, Respimat® Reusable (Europe) or Disposable (US) reduced the CO_2 emissions to 22.9 kt of CO_2e (**Figure 5**).

Figure 5. Reduction in carbon footprint if all patients using triple therapy were redistributed to LAMA/LABA, Respimat® Reusable (Europe) or Respimat® Disposable (US)



- In Europe, redistribution of all patients currently on triple FDC to dual therapy, Respimat® Reusable, decreased the carbon footprint by 70.7% (Portugal) to 98.4% (Greece) (**Figure 6**). In the United States, redistribution of triple FDC to dual therapy, Respimat® Disposable, reduced CO_2 emissions by 16.1% (**Figure 6**).

Figure 6. Redistribution of all patients currently receiving triple FDC therapy to dual therapy, Respimat® Reusable, reduces the carbon footprint by up to 98.4% in Europe; redistribution to Respimat® Disposable in the United States reduces the carbon footprint by 16.1%



Conclusions

- This study showed that the carbon footprint of inhalers could be reduced by adapting current clinical practice in the management of patients with COPD to treatment according to published recommendations.
- Based on data presented here, the United States and Portugal have the lowest carbon footprint benefits of all countries assessed. This is due to a higher market share of DPI devices over pMDIs for triple FDC therapy.
- Prescribing SMI (Respimat® Reusable [Europe] or Disposable [United States]) LAMA/LABA dual therapy rather than triple therapy, where indicated, addresses both its inappropriate use, as well as reducing the carbon footprint.
- A limitation of this study is that the prescribing data does not distinguish between COPD or asthma. Nonetheless, this study was a theoretical exercise, and it is acknowledged that not everyone will be eligible for redistribution, and patients should continue to use triple therapy based on clinical need. As per ERS recommendations, patients should not be switched between devices purely for environmental reasons.[16]
- However, when considering a switch for clinical need, clinicians should first pick the appropriate treatment (class), and in case of equal preference, they should also consider the carbon footprint of the device and prioritise those with smallest carbon footprint.

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Conflict of interest statement

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