Climate-conscious prescription of inhaled medications

DEGAM S1-Guideline

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Background

In Germany, the health care system is responsible for about 5% of carbon dioxide (CO$_2$) emissions [1], in other countries this number is between 4% (England) [2] and 10% (USA) [3]. The biggest contributor to the carbon footprint caused by ambulatory primary care is the prescription of medications, followed by emissions from transportation (of patients and staff) and heating [2,4].

Chronic respiratory diseases such as bronchial asthma and chronic obstructive bronchitis (COPD) can be fostered by climate change itself or the causes thereof (such as particulate matter pollution). These conditions are already among the most common diseases and their prevalence is increasing [5]. Various types of inhalers are used in the treatment of asthma and COPD. The extent to which these inhalers contribute to climate changes varies depending on their method of functioning.

The two main categories of inhalers are dry powder inhalers and metered-dose inhalers.

**Dry powder inhalers** (DPIs) contain an active substance in powder form. The active ingredient is released and distributed by inhalation, requiring a sufficiently strong inhale to ensure effective therapy.

In contrast, **metered dose inhalers** (MDIs) use propellants to transport the active substance into the deep sections of the lungs.

The chlorofluorocarbons (CFCs) that were used as propellants for MDIs in the past have been largely banned due to their impact on the ozone layer and have been replaced since 1989 by hydrofluoroalkanes (fluranes) [6]. While these do not damage the ozone layer, they are powerful greenhouse gases. Compared with DPIs, MDIs therefore have more potential to damage the atmosphere (global warming potential - GWP).

While CO$_2$ has a GWP of 1, norflurane (HFA 134a), which is used in most MDIs, has a GWP of 1,430 and apaflurane (HFA-227ea) has a GWP of 3,220 [7].

In the UK, MDIs are responsible for 3.5% of the greenhouse gas emissions of the entire UK health system [8].

At the same time, the market share of MDIs varies significantly around the world (from 34% in Japan to 88% in the US) [9].

Health care situation in Germany

According to data from the Central Institute for Statutory Health Insurance Physicians (Zentralinstitut für die Kassenärztliche Versorgung (ZI)), 48% of all inhalers are MDIs. The short-ac-
ting drug salbutamol, which is mainly used as an acute treatment, represents 46.3 % of all prescribed MDIs [10].

According to prescription data, between 13-94 % of all inhalers for bronchial asthma/COPD on the German market are MDIs [11].

Clinical aspects of therapy with inhaled medications

The choice of inhaler used or prescribed is mainly based on the patient’s ability to properly implement the inhaler and to reproduce the necessary breathing technique. In general, DPIs are not recommended for children <5 years of age, in geriatric patients or patients with acute exacerbations.

Despite this, a switch to more climate-friendly DPI is possible for many patients.

In a randomised trial, switching to more climate-friendly DPIs led to a substantial reduction in greenhouse gas emissions without adverse effects on asthma control [12]. According to a systematic review from 2001, there were no clinically relevant differences between MDI and other types of inhalers [13].

Objective of the guideline

This guideline aims to support a shift in prescribing patterns of inhalers to reduce the carbon footprint of the health care system. It addresses those involved in prescribing inhalers and counselling patients with asthma/COPD. This includes doctors and their practice teams as well as pharmacists and other health professionals.

The guideline supports climate-conscious prescription of inhalers by

- summarising existing evidence on the decision between DPIs and MDIs

- explicitly addressing the climate damage caused by propellants

Guideline recommendations for differentiated use

Using a systematic guideline search, explicit recommendations on the use of specific inhalers were extracted from current German and international guidelines for the treatment of bronchial asthma/COPD.

The following evidence-based recommendations are representative of the recommendation statements found.
<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Source</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>In children under 5 years of age, for inhalation of beta-2 sympathomimetics or glucocorticosteroids, an MDI with spacer (= inhalation aid) should be prioritised.</td>
<td>NVL Asthma</td>
<td>↑↑</td>
</tr>
<tr>
<td>Children and adults with mild and moderate asthma attacks should be treated with an MDI with a spacer.</td>
<td>SIGN Asthma</td>
<td>A</td>
</tr>
<tr>
<td>For stable asthma: For children aged 5-12 years, an MDI with a spacer is as effective as any other inhaler.</td>
<td>SIGN Asthma</td>
<td>A</td>
</tr>
<tr>
<td>For adults with stable asthma, an MDI with or without a spacer is as effective as any other inhaler.</td>
<td>SIGN Asthma</td>
<td>A</td>
</tr>
<tr>
<td>Prescribers, pharmacists and patients should be aware of the significant differences in the global warming potential of different MDIs and that inhalers with low global warming potential should be used when they are likely to be equally effective.</td>
<td>SIGN Asthma</td>
<td>A</td>
</tr>
</tbody>
</table>

For the treatment of acute asthma attacks/exacerbation of COPD, MDIs are presumed to be more appropriate and should be implemented accordingly.
Figure 1: Algorithm for climate-conscious prescription of inhaled medications

- Therapy with inhaled medication needed
  - Powerful intake of breath and expiration over 2-3 sec. is possible
    - Exclusion criteria for DPI?
      - no
        - DPI not appropriate, MDI with/without spacer recommended
          - See Decision Aid 3
      - yes
        - Establish patient preferences
          - Exclusion criteria
            - Children under 5 years
            - Proper implementation of inhaler not feasible / spacer needed
            - Patient preference
          - Establish patient preferences
            - Presentation of suitable inhaler systems
            - Previous experiences
            - Balancing advantages/disadvantages
            - Explicit mention of the carbon footprint
            - See Decision Aid 1 and 2
          - Prescription and training in use of DPI
          - Prescription and training in use of MDI

Climate-conscious prescription of MDIs:
- Prescription of MDIs with lower global warming potential (norfluran as propellant of choice)
- Preference of MDIs with dose counter
  - See Decision Aid 3
Decision aid 1 for climate-conscious prescription of inhalers

Distinction between metered dose inhaler and powder inhaler

This decision aid summarises the essential differences between MDIs and DPIs to enable optimal therapy. For additional material, please refer to the patient information of the National Asthma Care Guideline at www.atemwegsliga.de/richtig-inhalieren.html. Video instructions for each type of inhaler are also available.

Table 1: Differences between metered dose inhalers and dry powder inhalers

<table>
<thead>
<tr>
<th>Inhaler</th>
<th>Metered dose inhalers (MDIs)</th>
<th>Dry powder inhalers (DPIs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breathing</td>
<td>Require coordination of actuation and inhalation if not used with a spacer (not applicable to breath-actuated devices)</td>
<td>Release of medication is triggered by intake of breath (breath-actuated)</td>
</tr>
<tr>
<td>Method of breathing</td>
<td>Slow, deep inhalation</td>
<td>strong inhalation</td>
</tr>
<tr>
<td>Spacer</td>
<td>possible</td>
<td>not possible</td>
</tr>
<tr>
<td>Dose counter</td>
<td>sometimes available</td>
<td>almost always possible</td>
</tr>
<tr>
<td>Risk of climate damage due to propellant</td>
<td>very high</td>
<td>low</td>
</tr>
</tbody>
</table>
Decision aid 2 for climate-conscious prescription of inhalers

Carbon footprint of therapies with inhaled medicines

Comparison of the carbon footprints of MDIs vs. DPIs and potential methods to reduce environmental impact.

Figure 2: Carbon footprint / potential methods to reduce carbon consumption in kg CO$_2$
For data basis see methods section
Decision aid 3 for climate-conscious prescription of inhalers

Differences between types of metered dose inhalers

Despite the harmful effects on the climate caused by the propellants contained in MDIs, a prescribing decision may be made in favour of an MDI.

There exist relevant differences between the MDIs in terms of their potential to damage the atmosphere (global warming potential - GWP). Whereas the norflurane used in most MDIs has a GWP of 1.430, very few MDIs use the even more climate-damaging propellant gas apaflurane (GWP 3.220). MDIs with apaflurane should be avoided whenever possible.

The following list provides an overview of all MDIs available in Germany which use the propellant apafluran [14] (Yellow List, active ingredient: apaflurane).

Table 2: Inhalers with the propellant apaflurane available in Germany

<table>
<thead>
<tr>
<th>Active ingredient</th>
<th>Product</th>
<th>Alternatives/Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cromoglicic/Reproterol</td>
<td>Aarane®</td>
<td>The combination is of limited benefit; for recommendation see Guideline NVL Asthma</td>
</tr>
<tr>
<td>Cromoglicic/Reproterol</td>
<td>Allergospasmin®</td>
<td>The combination is of limited benefit; for recommendation see Guideline NVL Asthma</td>
</tr>
<tr>
<td>Fluticasone/Formoterol</td>
<td>Flutiform®</td>
<td>Different product with a combination of Formoterol and inhaled steroid</td>
</tr>
<tr>
<td>Budesonide, Formoterol</td>
<td>Symbicort® (160/4)</td>
<td>Also available as a DPI (Turbohaler®)</td>
</tr>
</tbody>
</table>

Methodology

In 10/2021, the search for guidelines for „asthma“/“COPD“/“chronic bronchitis“ was performed on Guideline Network International (https://guidelines.ebmportal.com/).

Inclusion criteria: Language: German + English, publication year 2016 or later.

A total of 24 guidelines for asthma and 7 for COPD/chronic bronchitis were found.
After review of the search results based on the inclusion criteria, 10 guidelines on asthma and 7 on COPD/chronic bronchitis remained. Five papers were not evaluated as they were either duplicates or addressed an irrelevant subject. The relevant German-language guidelines NVL Asthma, NVL COPD, S2k-Leitlinie on the diagnosis and treatment of patients with chronic obstructive bronchitis and emphysema (COPD) are included in the review.

All statements in the included guidelines regarding the selection/differentiation between MDIs/DPIs were extracted and summarised in a synopsis.

The literature search for the background text was carried out in the form of a narrative review and via feedback from the guideline reviewer and the DEGAM working group on climate change and health.

**Sources for the calculation of the carbon footprint:**
Switching from an MDI to DPI assuming daily use and 2 doses/day. Per dose 0.026 kg CO\textsubscript{2} for DPI and 0.65 kg CO\textsubscript{2} for MDI = difference of 18.98 kg versus 474.5 = 455 kg

Savings according to [16]

Change of diet from mixed diet to vegetarian diet = 440 kg/year,

Calculated according to https://uba.co2-rechner.de/de_DE/sc-food#panel-scenario

A short-range flight (1000 km), 1000 km by car (single rider) calculated according to: https://www.quarks.de/umwelt/klimawandel/co2-rechner-fuer-auto-flugzeug-und-co/

Planting a tree: average amount of carbon absorption by a beech tree/year = 12.5 kg
https://www.co2online.de/service/klima-orakel/beitrag/wie-viele-baeume-braucht-es-um-eine-tonne-co2-zu-binden-10658/

**Included guidelines**


Literature


