National Institute for Public Health
and the Environment
Ministry of Health, Welfare and Sport

The impact of Dutch healthcare on the environment

Environmental footprint method, and examples for a health-promoting healthcare environment

RIVM report 2022-0159

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Synopsis

The impact of Dutch healthcare on the environment.

Environmental footprint method, and examples for a health-promoting healthcare environment

Climate change is having a major impact on health and the environment. That makes it important to have an overview of all the sources that contribute to climate change. One of these sources is the healthcare sector. The Ministry of Health, Welfare and Sports, therefore, wants to know the impact of the Dutch care sector on the environment. Among other things, it turns out that the care sector is responsible for about 7 percent of the emission of greenhouse gases. This number confirms previous estimates and is now better substantiated.

RIVM has developed a method to calculate the environmental impact of healthcare. This is the first time that scientific knowledge about multiple impact categories of healthcare on the environment has been mapped out for the Netherlands. Next to the method development, practical examples were gathered on how to support good health for clients and patients in health care facilities.

The method calculates the environmental impact of medical procedures, such as the use of anaesthetics (that can be greenhouse gases) in operations, as well as the impact of the production of goods and services used in health care. The footprint has been calculated for more than just climate change (emissions of greenhouse gases). It has also been calculated for the use of water and raw materials (metals and minerals), for land use and for the amount of waste produced. If required, more impact categories can be added to the method.

Roughly speaking, the production of chemical products such as pharmaceuticals, soaps and solvents causes most - about 40 percent - of the greenhouse gas emissions and the use of raw materials by the healthcare sector. Exactly which products and processes cause this is not yet clear and requires more research.

Additionally, various care organisations were interviewed, such as hospitals, geriatric care and mental health care (GGZ) institutes, to look for practical examples of how to improve a health promoting environment in and around health care provider facilities. The examples concern practices that keep people in care institutions - such as the elderly and disabled - healthy, for example by giving them healthier food and by planting greenery. Such a healthy 'care environment' can help to prevent illness and contributes to good and sustainable health care.

RIVM makes recommendations to further improve the environmental footprint method. For example, a plan can be made on how to determine the present situation and how to monitor future developments.

Collecting more practical examples is also recommended, because these are very much asked for by healthcare professionals.

Keywords: sustainable healthcare, environmental footprint, health promoting care environment, impact of pharmaceuticals, climate change, circular economy, biodiversity, environment and health, environmental impact, sustainability

Publieksamenvatting

Het effect van de Nederlandse zorg op het milieu.

Methode voor milieuvoetafdruk en voorbeelden voor een gezonde zorgomgeving

Klimaatverandering heeft grote gevolgen voor de gezondheid en het milieu. Het is dan ook belangrijk om alle bronnen die aan klimaatverandering bijdragen in beeld te hebben. Een daarvan is de zorgsector. Het ministerie van VWS wil daarom weten wat de effecten van de Nederlandse zorgsector op het milieu zijn. De zorgsector blijkt onder meer voor zo'n 7 procent bij te dragen aan de uitstoot van broeikasgassen. Dit bevestigt eerdere schattingen uit onderzoek van anderen, en is nu beter onderbouwd.

Het RIVM ontwikkelde een methode om de effecten op het milieu te berekenen. Hiermee is de wetenschappelijke kennis over meerdere effecten van de Nederlandse zorg op het milieu voor het eerst in kaart gebracht. Daarnaast is naar voorbeelden in de praktijk gezocht die de gezondheid verbeteren.

De methode berekent zowel de effecten van medische handelingen, zoals het gebruik van narcosemiddelen bij operaties (die sterke broeikasgassen kunnen zijn), als de effecten van de productie van goederen en diensten die in de zorg worden gebruikt. De voetafdruk is berekend voor meer dan alleen klimaatverandering (de uitstoot van broeikasgassen). De berekening is ook gemaakt voor het gebruik van water en grondstoffen (metalen en mineralen), het landgebruik en de hoeveelheid afval. Zo nodig kunnen aan de methode meer effecten worden toegevoegd.

Grofweg veroorzaakt de productie van chemische producten, waaronder geneesmiddelen en producten als zeep en oplosmiddelen, het grootste deel (ongeveer 40 procent) van de uitstoot van broeikasgassen en het grondstoffengebruik door de zorg. Het is nog niet precies duidelijk welke producten en processen die uitstoot en dat gebruik veroorzaken. Daarvoor is meer onderzoek nodig.

Met verschillende zorgsectoren, zoals ziekenhuizen, ouderenzorg en de geestelijke gezondheidszorg (GGZ), is gezocht naar de praktijkvoorbeelden. Het gaat om voorbeelden die mensen in zorginstellingen, zoals ouderen en mensen met een beperking, gezond houden, bijvoorbeeld door hen gezond eten te geven en door planten en bomen aan te leggen. Zo'n gezonde 'zorgomgeving' kan helpen ziekte te voorkomen, en draagt bij aan goede en duurzame zorg.

RIVM doet aanbevelingen om de methode te verbeteren. Zo kan bijvoorbeeld een plan worden gemaakt om de situatie zoals die nu is te bepalen, en de ontwikkeling ervan in de toekomst te kunnen volgen. Ook wordt aangeraden om meer praktijkvoorbeelden te verzamelen, omdat zorgprofessionals daar veel behoefte aan hebben.

Kernwoorden: milieuvoetafdruk, duurzame zorg, gezondheidsbevorderende leefomgeving, impact van geneesmiddelen, klimaatverandering, circulaire economie, biodiversiteit, milieu en gezondheid, milieueffecten, duurzaamheid

Contents

Summary

Climate change has a major impact on health and the environment. Like other sectors, the healthcare sector can also help to mitigate climate change and other environmental impacts by providing more sustainable products and services. The Ministry of Health, Welfare and Sport therefore commissioned RIVM to develop and apply a method to gauge the environmental impact – including climate change – of the Dutch healthcare sector. The aim of the method is to identify topics that require further attention. In determining the footprint, the following environmental impact categories were specifically considered: greenhouse gas emissions (also known as the climate footprint), blue water consumption, use of abiotic raw materials and land use. Total waste production was examined as well. If desired, more impact categories can be added in the future.

This report calculates the first national environmental footprint for the healthcare sector. The calculations show that the Dutch healthcare sector is responsible for approximately 7% of the national climate footprint. This figure is in line with previously published estimates. The most recent available data and key figures were used to calculate the national environmental footprint. By combining generic analyses (input-output analysis) with specific analyses (life cycle analyses), the foundation has been laid for a future baseline measurement. It can be seen that chemical products (including consumables and pharmaceuticals) are a major contributor to the healthcare sector's environmental impact. It is not yet possible to obtain a complete picture of exactly which products or parts of the chain are responsible for which percentage of the calculated impact. To better specify the environmental impact of pharmaceuticals, for example, more data must be made available via methods such as life cycle analyses (LCA). Product-specific data and analyses could then contribute to the sector-wide impact calculations.

This study also highlights practical examples for a good and health-promoting healthcare environment, also known as a health-promoting care environment. Background documents and 'What Works Files' have been drawn up based on a literature review of interventions for a good care environment.

Healthcare practice was examined as well, and concrete examples were gathered for the themes of nature, architecture and food. These themes are important for a health-promoting care environment. We have seen positive effects of changes in the care environment that improve the well-being of patients, visitors and staff and can contribute to health and sustainability. There is a great need for more practical examples for the health-promoting care environment, as well as for the climate and the circular economy. This was expressed in webinars and interviews that were held, and this wish is in line with findings in the previous RIVM report 'Verkenning Monitoringsopties Green Deal Duurzame Zorg' [Survey of Monitoring Options for Green Deal for Sustainable Healthcare] (2021). Furthermore, there is a specific demand for more

examples from and for long-term care, such as mental health services. Notably, nearly all professionals state that an institution should have a vision for a healthy living and working environment. Support from management is crucial to the success and continuity of initiatives. Scientific substantiation and the structuring of practical examples leads to concrete and effective practical examples. These are then more reliable and accessible for various healthcare organisations, which in turn makes it easier for such organisations to work towards a more sustainable healthcare sector.

To improve the method and insights and contribute to concrete potential actions for both policy and practice, recommendations have been formulated for the Ministry and relevant parties. One of the recommendations is to develop an approach for a baseline measurement and follow-up monitoring of the environmental footprint of the healthcare sector in the Netherlands. This report provides the initial background knowledge for developing this approach. A baseline measurement will also enable the Ministry of Health, Welfare and Sport to fulfil one of its commitments to the 26th United Nations Climate Change Conference of the Parties (COP26) held in Glasgow in 2021, and to monitor the progress of the circular economy objectives.

The environmental footprint of the Dutch healthcare sector shows where attention and actions are needed to make treatments, products and services more sustainable. This will reduce emissions in the chain, which will help to improve public health and the climate. Sustainable healthcare not only serves today’s patients, but will protect the environment and public health in the future as well.

1 Introduction

1.1 Green Deal for Sustainable Healthcare and knowledge base

Climate change has a major impact on health and the environment.[1] Institutions and service providers in the healthcare sector are therefore being confronted with the effects that climate change has on public health. Increasing greenhouse gas emissions cause more heat to be retained in the atmosphere. This warming effect leads to changes in the climate, such as milder winters, hotter summers and more extreme weather patterns, including heat waves and heavy rainfall. These changes can cause increased heat stress, longer and more intense hay fever seasons and outbreaks of (new) diseases and pests (Figure 1).[2] Added pressure has also been placed on the international healthcare system due to various challenges, such as scarcity of resources, decreased supply security and the COVID-19 pandemic.[3]

Like other sectors, the healthcare sector itself contributes to environmental impact– including climate change – by providing products and services (Figure 1). Earlier studies estimate that the healthcare sector in the Netherlands is responsible for 6 to 8% of the national climate footprint.[4-6] Combating or preventing climate and environmental impact helps to improve public health and living conditions, both now and in the long term.[7] The healthcare sector can therefore make a significant contribution to achieving the national climate targets[8] and circular economy objectives.

To reduce the healthcare sector's environmental impact – including greenhouse gas emissions – and improve collaboration and knowledge sharing between care institutions in this regard, the first Dutch Green Deal for Sustainable Healthcare was drawn up in 2015, followed by another in 2018.[9] These deals have been signed by various parties, including care providers, suppliers and patient organisations. A third covenant is expected in the autumn of 2022. The agreements in the Green Deal for Sustainable Healthcare (2018-2022) are currently still divided into themes: climate, circularity, reducing pharmaceutical residues in surface water, and the health-promoting care environment. The latter theme concerns an environment that enables residents, staff and users of healthcare institutions to behave in a healthy manner. In addition, during the international UN climate summit COP26 in Glasgow in 2021, the Minister of Health, Welfare and Sport at the time, Hugo de Jonge, announced a commitment to emissions reduction initiatives for the healthcare sector. This includes regularly monitoring of the ecological footprint (also known as the environmental footprint), supporting the healthcare sector in providing sustainable care, and facilitating the development of sustainable and low-carbon supply chains for the healthcare sector.[10]

To determine the Dutch healthcare sector's current impact on the environment and identify hotspots and knowledge gaps, the Ministry of Health, Welfare and Sport commissioned the RIVM to choose and, where necessary, further develop a method for this purpose. This method, called 'Knowledge Base Green Deal for Sustainable Healthcare', contributes to a knowledge base on sustainable healthcare. Its aim is to identify topics that require further attention, and to provide support in making decisions and setting priorities.[11,12] The healthcare sector is coming under increasing pressure, after all, and resources and time must therefore be spent in a targeted manner.[13,14] This report focuses primarily on developing the method and identifying the environmental impact – or environmental footprint – of the Dutch healthcare sector. The footprint has been calculated for the following environmental impacts: climate change (greenhouse gas emissions), blue water consumption (freshwater from surface- and groundwater sources), use of raw materials (metals and minerals), land use and amount of waste produced. If necessary, more impact categories can be added in future studies.

This method reflects the overall situation in the Netherlands based on a macro-economic overview and is therefore general. A sector-wide environmental footprint calculation helps to guide sustainability efforts in healthcare by:

- understanding how the environmental impact of the healthcare sector are structured;
- identifying focus areas for making healthcare more sustainable;
- gaining insights into which data is available or lacking;
- providing structure for the collection of new data;
- contributing to a harmonised vocabulary and methodology;
- generally monitoring the sustainability of the healthcare sector in the Netherlands in the future.

In the years ahead, the method can be further expanded and updated for sub-sectors, product groups and services. The method is a supplement to the existing CO_2 road maps for real estate in care and cure, designed by the Expertise Centre for Sustainable Healthcare.[15,16] While this method is more general (i.e. national), it does examine a range of environmental impact categories and topics. It therefore does not provide insights for specific institutions and products, but can nevertheless be helpful in drawing up annual or policy plans since key themes have been identified.[12] Furthermore, a separate chapter is dedicated to practical examples of sustainable healthcare based on the themes of nature, food and architecture, which helps to define more concrete potential actions.[17]

The aim of this report is to contribute to scientific, qualitative and quantitative knowledge about the environmental impact of the healthcare sector. The aim is also that this knowledge, together with quality of care and socio-economic aspects, will provide a more complete picture of sustainable and high-quality healthcare, both now and in the long term. The results therefore additionally contribute to the knowledge that is needed to achieve national and international climate targets and circular economy objectives.

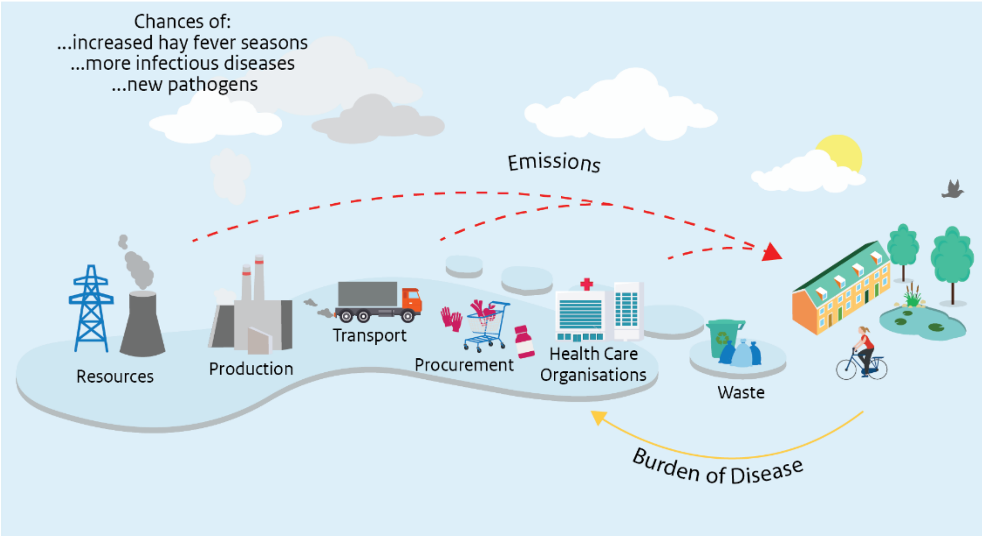

Figure 1 Diagram of the environmental footprint of a chain, with the self-reinforcing effects on public health and the living environment. Institutions and service providers in the healthcare sector are being confronted with the impacts of climate change on public health. Increased greenhouse gas emissions and fine particulates cause more heat to be retained in the atmosphere. This warming effect leads to climate change, which in turn causes increased heat stress, longer hay fever seasons, and the emergence of new diseases and pests [1, 2]

1.2 Structure of the document

This report consists of various parts. These parts build upon each other, but they can also be read separately.

The largest component of this project involved developing and refining a technical method. Chapters 2 and 3 have therefore been written by experts in the field, such as industrial ecologists. The other chapters are more broadly accessible. They have also been written for readers with some background knowledge about sustainability, environmental impacts and the healthcare sector who are interested in identifying the environmental impact of the healthcare sector in the Netherlands, the health-promoting care environment and recommendations to improve the methodology and better connect it with healthcare practice.

Chapter 2. The environmental footprint of the Dutch healthcare sector
This chapter is the main focus of this report and the largest contributor to this knowledge base project. The method for determining the environmental footprint calculations for the healthcare sector in the Netherlands is explained in this chapter. It involves a hybrid approach in which input-output analysis is combined with additional environmental impact. National statistics were used for this purpose. These statistics were supplemented with data for anaesthetic gases, pressurised metered-dose inhalers and individual travel movements. The results for the following environmental impact are discussed: greenhouse gas emissions (also known as the climate footprint), blue water consumption, extraction of abiotic raw materials and land use. Total waste production was examined as well. The results of the model with respect to the climate footprint are compared to the results of existing

studies. The results of the composition of the footprint are presented to understand the sector-wide environmental impact of the healthcare sector.

Chapter 3. In-depth analysis of the environmental footprint of chemical products, including pharmaceuticals
Chapter 3 takes an in-depth look at the category (i.e. product group) that is the largest contributor to environmental impact according to the results in Chapter 2: chemical products, including pharmaceuticals. In the generic, national overview of the environmental footprint (Chapter 2), it is not yet possible to calculate the exact percentage that can be attributed to pharmaceuticals. Chapter 3 therefore specifically discusses pharmaceuticals and what is known about their environmental impact, with a focus on the same environmental impact categories as calculated in Chapter 2. We examine what the literature says about life cycle analyses and the possibilities there might be to estimate the impact using machine learning. In this analysis, the aim is not only to attempt to specify the impact from the national environmental footprint, but also to address the challenges of combining the different data in order to create an overview.

Chapter 4. Study background and practical examples of the health promoting healthcare environment
This chapter explains how practical examples of the health promoting healthcare environment in the previous RIVM project 'Interventies Duurzame Zorg' [Interventions for Sustainable Healthcare] were collected. In addition to presenting knowledge from the more technical environmental impact analyses, this project has taken the first step in collecting and sharing practical examples of the health promoting healthcare environment, with an emphasis on the themes of climate and circular economy (Chapters 2 and 3). The practical examples can be found on the RIVM website.[17] This chapter outlines the approach to qualitatively substantiate the examples and make them as accessible and concrete as possible. General insights are discussed. The aim is to provide healthcare professionals with potential avenues for action by sharing and structuring examples of inspiring sustainable initiatives from real-world practice. Related activities and possibilities for connecting and expanding the examples are briefly discussed as well.

Chapter 5. General discussion, conclusion and recommendations
Chapter 5 consists of a general discussion, a conclusion and recommendations for the environmental footprint of the Dutch healthcare sector as well as for approaching and connecting practical examples. The possibilities for further utilising this study for a national monitor are also specifically addressed. This method can therefore be used to fulfil one of the commitments made by the Ministry of Health, Welfare and Sport in response to the UN climate summit COP26, namely to monitor the ecological footprint of the healthcare sector in the Netherlands.

2 The environmental footprint of the Dutch healthcare sector

This chapter describes how the healthcare sector's environmental impact is assessed. A sector-wide footprint method is used for this purpose, which is also applied in existing relevant studies. In addition to the interpretation of the results, the end of the chapter also includes a discussion of how the results can be used and how the model can be improved.

The content of this chapter has been published in peer-reviewed scientific journal (link[1]), with the exception of section 2.2.2.2. We have added further explanation and additional visualisations for more background information.

2.1 Introduction

In recent years, several studies have been published which include a calculation of the Dutch healthcare sector's environmental impact. According to these studies, the Dutch healthcare sector is responsible for 6 to 8% of the national climate footprint.[4-6] These studies all applied 'environmentally extended' input-output analysis (EE-IOA) or made use of EE-IOA data. EE-IOA is a method to estimate the total environmental impact (i.e. the footprint) of a sector or region. The study by Gupta Strategists[5] focuses specifically on the Dutch healthcare sector, while the studies by Pichler et al.[4] and Arup and HCWH[6] present a comprehensive footprint method for calculating the climate footprint of a national healthcare sector. Climate footprint studies on the national healthcare sector of several other countries have also been published in recent years, using EE-IOA as the primary method: Japan[18], Australia[19], the US[20], Canada[21], Austria[22], China[23], and England.[24]

Though the abovementioned studies focused on climate change as the sole impact category, EE-IOA can be valuable for broader sustainability analyses as well. The relationships between the economy, the environment and socio-economic factors are presented in a single consistent framework.[25] The importance of multiple environmental impact categories is often demonstrated through footprint analyses at product or process level, so-called life cycle analyses (LCA). LCA studies frequently cover multiple impact categories that can be taken into account in a comparison between two products or processes.

Lenzen et al.[26] were the first to include additional impacts (due to fine particulates, air pollutant, risk of malaria, reactive nitrogen in water, and scarce water use) in a footprint analysis of the healthcare sector, with the Netherlands being one of the 189 countries analysed. Their global study quantifies the footprint by country or world region to facilitate comparisons between countries. For a more accurate footprint calculation, however, it is recommended to improve data quality by using national statistics.[27] The footprint calculation can also be improved by including additional impacts that are relevant to the healthcare

[1] Steenmeijer MA, Rodrigues JFD, Zijp MC, Waaijers-van der Loop SL. The environmental impact of the Dutch health-care sector beyond climate change: an input-output analysis. The Lancet Planetary Health 2022. https://doi.org/10.1016/S2542-5196(22)00244-3

sector; the studies for England[24] and Austria[22] and the study by Gupta Strategists[5] add further sources of environmental impact to arrive at a more complete footprint. Gupta Strategists[5] states that, when included in the calculation, individual travel movements make up a large share of the total climate footprint. The studies for England and Austria also take individual travel movements into account. In addition, the impacts of anaesthetic gases and pressurised metered-dose inhalers are considered.

Although the current results are valuable for footprint calculations for the Netherlands, they do not yet provide a sufficient basis for the footprint study for the Dutch healthcare sector. The study by Gupta Strategists[5] uses impact coefficients for the EE-IOA calculations for England, but also adds more specific information such as travel movements. While the global approach in Lenzen et al.[26], Arup and HCWH[6] and Pichler et al.[4] does use EE-IOA data for the Netherlands, this is not specified based on national statistics, and no specific relevant sources of environmental impacts for this sector are provided. Nevertheless, because EE-IOA makes it possible to calculate the environmental impact of other impact categories that are relevant to the Green Deal for Sustainable Healthcare, this method will be used to determine the impact of the healthcare sector in other impact categories (besides climate change).

At the same time, EE-IOA as a macro-economic method is non-specific and can only explain results to a certain extent. EE-IOA will only give insight into how different product groups contribute to the footprint at a macro level, and can therefore help with prioritisation between these product groups. However, the results do not provide any details about impacts within the product group itself. To obtain these details, data could be collected on the impact of specific products within the product group. In the study for Austria, for instance, this was done for a number of core goods and services directly purchased by healthcare, including energy, medical gloves and some commonly used pharmaceuticals.[22] For product-specific data, a more in-depth analysis using a method such as life cycle analyses (LCAs) is needed.

The aim of Chapter 2 is to support the healthcare sector in developing a footprint model in order to understand and address the healthcare sector's impact on the environment, beyond just its contribution to climate change through greenhouse gas emissions. The model and data used are explained in Section 2.2. The results of the calculation are discussed in Section 2.3. Finally, in Section 2.4, we reflect on the results and examine the knowledge and/or data that is needed to improve the calculation in the future.

2.2 Method

This section describes the development of the model for the environmental footprint calculation for the Dutch healthcare sector. The model and references to the data used can be found on RIVM's Github page (link).

In this methodology description, the model is explained by answering the following questions:

- The sectoral environmental footprint using EE-IOA (Section 2.2.1): what is the basis for the calculation and how (and with what data) is this calculation made?
- Addition of healthcare sector-specific impact calculations (Section 2.2.2): which healthcare sector-specific impacts are not currently included in the EE-IOA footprint, and how are these calculated for the Netherlands?
- Characterisation of environmental stressors (Section 2.2.3): how are the results of the EE-IOA and the additional healthcare sector-specific impact calculations characterised according to the same impact categories as the additional estimates for healthcare-specific environmental effects?
- Uncertainties in model and data (Section 2.2.4): what can be said about the accuracy and reliability of the results based on the methodology and data used?

2.2.1 Sectoral footprint calculation for the Netherlands using EE-IOA

This section describes the footprint calculation using EE-IOA. In Section 2.2.1.1, a brief explanation of EE-IOA is provided for readers who are unfamiliar with the concept. The rest of Section 2.2.1 focuses on input-output analysts. Section 2.2.1.2 lays the initial foundation for the sectoral footprint calculation and introduces the terminology that is used throughout the remainder of the chapter. Section 2.2.1.3 then discusses the EE-IOA data and the impact categories included. Lastly, Section 2.2.1.4 outlines the steps taken to translate the national healthcare expenditure into the desired input for the EE-IOA calculation.

2.2.1.1 Brief background on EE-IOA

Input-output analysis (IOA) is a macro-economic calculation method that can be used to analyse linkages between industries. IOA is based on an input-output table (IO table). This is a matrix in which the mutual transactions between different sectors are combined; in other words, it is a way to map out the network of all sectors. IOA is used to calculate how much economic activity is required from all sectors in a value chain in order to generate a certain output. So, when there is a demand for a product or service: how much has each industry contributed to make this possible? This calculation includes the economic activity of all industries that play a role in the value chain, based on intermediary transactions in the IO table.

Economic activities (production and consumption of goods and services) are often related to the environment. During an economic activity, raw materials are extracted from the environment (e.g. extraction of resources, land use) and substances are released into the environment (e.g. greenhouse gas emissions, fine particulates). These stressors can be added to the IO table for each sector, in the same way as production factors like ‘added value’ by the sector and ‘number of employees’ in the sector. This is referred to as an *environmentally extended* IO table, or EE-IOA. Just as the total economic activity of all sectors can be calculated for a given output, the total of environmental stressors from those sectors can be calculated as well. These environmental stressors can then be characterised based on impact, such as converting kilograms of methane gas into kilograms of CO_2 equivalents, or CO_2-eq, which represent the effects on climate change. Because an IO table is structured at country and sectoral level, EE-IOA can be applied to calculate the footprint of an economy (e.g. a national footprint) and/or part of an economy (e.g. an economic sector).

For a further explanation of the basis of IOA and EE-IOA calculations, we refer the reader to the fundamental work of Leontief[28] and Miller and Blair.[29]

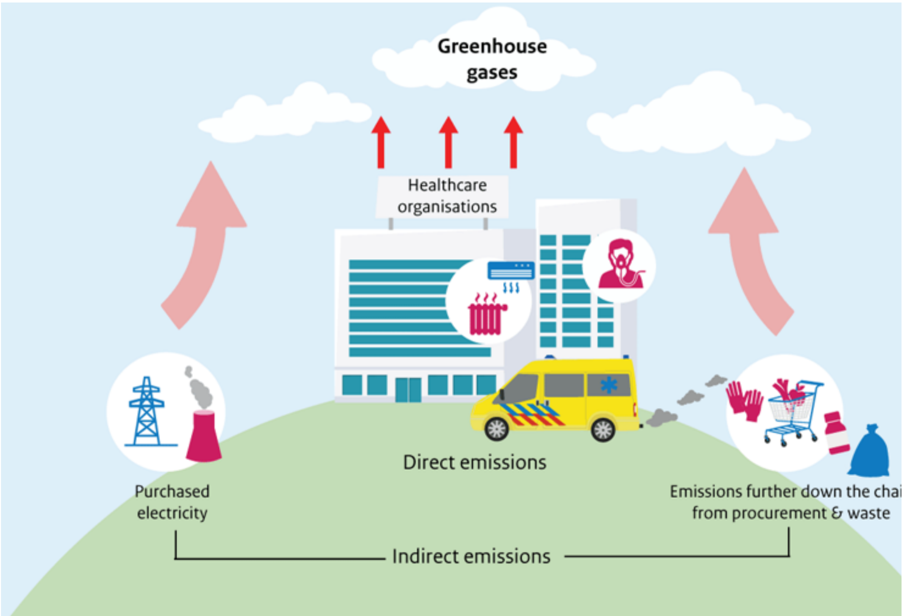

Figure 2 Visualisation of the direct and indirect environmental impact of the healthcare sector, demonstrated for the emission of greenhouse gases.

The environmental footprint for a sector is the sum of impacts from the operational phase (direct impact, e.g. from ambulance exhaust fumes) and the production and waste disposal phases (indirect impact, i.e. effects occurring in the value chain of purchased goods and services), as illustrated in Figure 2. The direct environmental impact is the same as Scope 1 in the Greenhouse Gas Protocol (GHGP)[30], a greenhouse gas accounting standard for organisations. Although the protocol is only designed for greenhouse gas emissions, it can also be applied to other environmental impact categories. The indirect environmental impact is comparable to Scopes 2 and 3 combined, where Scope 2 of the GHGP concerns the indirect impacts due to the purchase of heat and electricity, and Scope 3 concerns the purchase of all other goods and services. For example: in the case of waste production, the waste generated by the sector itself, such as waste produced in the operating rooms, falls under Scope 1. Meanwhile, all of the waste generated in the chain for production of purchased goods and services falls under Scopes 2 and 3.

2.2.1.2 Basis for calculation

The healthcare expenditure vector

The indirect impacts are calculated based on what is referred to in this study as the *healthcare expenditure vector.* In national consumption footprint calculations, this is comparable to the *final demand vector*. This vector can be used to calculate how much economic activity is needed in the entire global value chain to deliver a given product – in this case healthcare products and services.

Mathematical basis
The sectoral footprint is calculated using the following matrix calculation:

$$\mathbf{f} = \mathbf{C}(\mathbf{BLy} + \mathbf{r})$$

where:

- column vector **f** (*M* x 1): the total footprint f for the selected impact categories *M*;
- matrix **C** (*M* x *K*): characterisation factors to convert the total environmental stressors into impact for the selected impact category, where *K* is the number of environmental stressors;
- **Bly:** the calculation of the total indirect environmental stressors, where:
  - matrix **B** (*K* x *N*): the direct stressor intensity, where *N* is the number of industries;
  - matrix **L** (*N* x *N*): the Leontief inverse;
  - column vector **y** (*N* x 1): the healthcare expenditure vector;
- column vector **r** (*K* x 1): the direct environmental stressors from the sector.

In the following section (Section 2.2.1.3), the EE-IOA data are chosen (required for **B**, **L** and **r**), and the set of impact categories (*K*) are selected. The healthcare expenditure vector (**y**) is set up in Section 2.2.1.4, and the characterisation factors (**C**) are discussed in Section 2.2.3. This calculation only considers the impact of business activities and does address any activities by households, such as commuter travel. Part of the impact of households is added to this study later on (see Section 2.2.2) in order to include it in the system boundaries and the results.

The two perspectives
In this study, the indirect impacts in the footprint have been analysed in two ways. This can be done by diagonalising **BLy** in the footprint calculation in two ways (diagonalisation indicated by **^**; illustrative explanation in Figure 3):

- a so-called contribution analysis, with $\mathbf{BL\hat{y}}$. In other studies, this is also referred to as the 'footprint from the consumption perspective' (not to be confused with the consumption footprint). In a contribution analysis, the indirect impact is calculated based on the purchased goods and services (the embedded impact of the total value chain per product). The contribution analysis is comparable to the overall result of an LCA:
- a so-called hotspot analysis, with $\mathbf{B\widehat{Ly}}$. In other studies, this is also referred to as the 'footprint from the production perspective' (not to be confused with the production footprint). In a hotspot analysis, the indirect impact is calculated for the location (sector and/or geography) where the effect physically occurs. A hotspot analysis is comparable to the process-based contributions in an LCA.

In both cases, the calculation yields an $M \times N$ matrix, if it is also characterised with **C.**

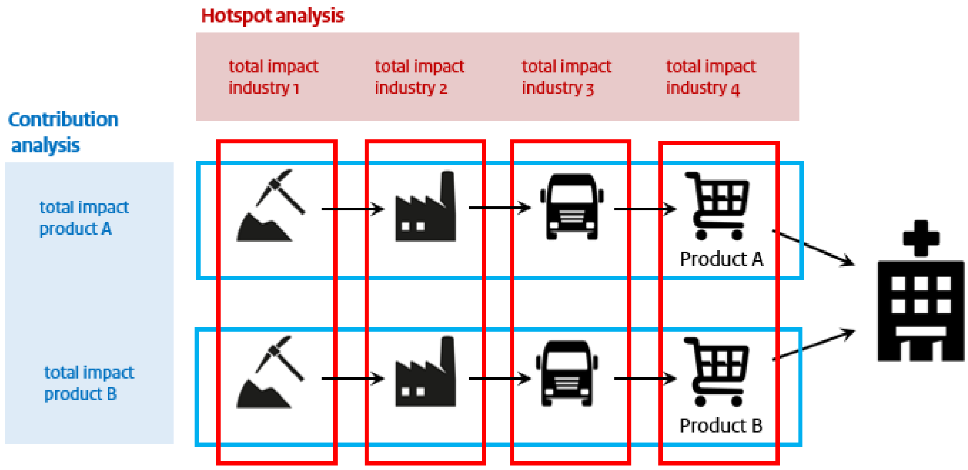

Figure 3 Visualisation of the two perspectives. In the contribution analysis (blue), the footprint is broken down into the total chain impacts per purchased product group (Products A and B here). In the hotspot analysis (red), the footprint is broken down into the industry where the effect physically takes place (fictitious Industries 1-4 here).

Both perspectives are applied for two reasons. First, the two perspectives provide greater insight into the composition of the footprint (where the impact occurs and which products cause it). Second, the results can be compared to those of other studies which use either of the two perspectives. For example, the study by Gupta Strategists[5] applies a contribution analysis, and the study by HCWH and Arup[6] presents the results as a hotspot analysis. This is not the only method to analyse the composition of the footprint. A structural path analysis (SPA)[31] could also be used for this purpose. This network analysis exposes the individual chains (i.e. the paths) that contribute to the footprint. However, we have not used SPA in this study.

2.2.1.3 IOA data and impact categories used

EE-IO data sets

A number of EE-IO data sets are available that can be used to calculate a (sector) environmental footprint, but these can differ greatly from one another. The article by Dawkins et al.[27] compares the most well-known EE-IO data sets and provides an overview of fundamental differences, which can be seen in appendix A.

To get an idea of where the effect takes place geographically in the hotspot analysis, a multi-regional IO table (MRIO) is used. Compared to a single-region table (SRIO), such as the national accounts of Statistics Netherlands, an MRIO offers greater insight into the region where the effect takes place due to activity in a particular source region (the receiving region). This allows for a better understanding of the composition of the footprint.

The industry-by-industry EE-MRIO Exiobase v3 was chosen as the basis for the calculations. The development of Exiobase v3 is described by Stadler et al.[32] At the time the footprint model for this RIVM study was developed, 2016 was the most recent available year. The choice of Exiobase v3 was based on the following reasons: first, Exiobase is a harmonised database with a relatively high resolution.[27] The MRIO is divided into 163 sectors for 49 countries and regions. Since EE-IOA is a non-specific method, it can be difficult to explain the footprint. It becomes even more difficult as the level of detail of the MRIO decreases. The relatively higher level of detail of the sectors in Exiobase compared to other harmonised MRIOs makes the footprint clearer to interpret. This reduces the need for a more extensive analysis, such as a structural path analysis[31], in order to understand the impact. Although the full version of Eora, another widely used EE-MRIO, has an even higher sector resolution, it is not harmonised and is only available for a fee, unlike Exiobase. Exiobase v3 also offers the most environmental extensions (662 categories of resource extraction and material use, 417 emissions categories)[27]. More environmental extensions can be added to the MRIO from the hybrid (i.e. containing a mix of monetary and physical IO values) Exiobase v3 multi-regional supply use table (MRSUT)[33], such as waste production and avoided emissions. Lastly, an extension of the time series was released in November 2020.[34] The macro-economic data and trade data have been updated up to and including the year 2018. Extensions have been updated where possible, and in the absence of data the impact has been 'nowcast' (extrapolated to the present) in a linear fashion, with stressor intensities remaining constant. This means Exiobase is the EE-MRIO that offers the most recent year and the longest time series. Exiobase additionally offers time series from 2019 through 2022, based on forecasts by the International Monetary Fund (IMF).

The model presented in this report can also be used with other EE-MRIOs. However, this choice will affect the availability of environmental extensions, as these differ greatly between the data sets.

Data from national statistics offices are generally preferred over data from an MRIO, since MRIO data can undergo more processing (harmonisation), with all the uncertainties that entails. In addition, national accounts are of higher quality and are regularly maintained. The national accounts from statistics agencies are primarily single-region data, however, meaning that imports and exports fall under 'the rest of the world'. Dawkins et al.[27] previously demonstrated that combining an MRIO with national statistics is a practical way to obtain multi-regional results in a footprint analysis. Several data points in the Dutch MRIO section have been replaced by statistics from Statistics Netherlands. The direct greenhouse gas emissions from the sector, as reported in Exiobase, have been replaced by more recent data from Statistics Netherlands (described earlier in this section), and the healthcare expenditure vector is also based on the healthcare expenditure reported by Statistics Netherlands (Section 2.2.1.4).

Impact categories
The following impact categories are included in this study: climate change (greenhouse gas emissions, also referred to as the climate footprint), blue water consumption, extraction of abiotic raw materials (i.e. extraction of minerals and metals), and land use. In addition, the total waste production (the sum of waste from economic activities and

waste from raw material reserves in society) has been added from the extension of the hybrid Exiobase v3 MRSUT.[33] This expansion of impacts is related to various environmental themes, namely combating climate change and promoting circularity and biodiversity (see Figure 4). For practical reasons, the expansion was limited to a set of five. These impacts could be expanded in future studies if desired. In each case, the contribution to climate change (i.e. the climate footprint) is necessary for the comparison with the other studies, which in most cases only calculate the climate footprint for the healthcare sector. As far as we know, apart from the work of RIVM, no studies have been conducted on the Dutch healthcare sector for the other impact categories.

This five-item list does not include all possible environmental impacts that could be caused by the healthcare sector. For example, the emission of substances (other than greenhouse gases) into the environment and their ecotoxicological risks and consequences have not been considered in this study.

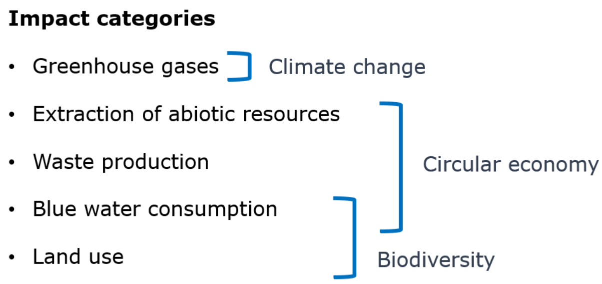

Figure 4 Environmental themes based on impact categories.

Direct emissions from national accounts

The operational greenhouse gas emissions (i.e. the direct greenhouse gas emissions from the healthcare sector) from Exiobase have been replaced by data from the environmental accounts of Statistics Netherlands.[35] These environmental accounts are compiled annually and, as in Exiobase, the environmental impacts are linked to economic activities. The sector category *Q Health and welfare care* corresponds to the sector category *Health and social work* in Exiobase v3. The greenhouse gases only include CO_2, CH_4 and N_2O, not including gases for medical use. Due to a lack of data, the direct environmental impacts for the other impact categories have not been replaced by national statistics; the direct impacts have been taken from Exiobase in this case.

Only the direct emissions data from the healthcare sector has been replaced, while that of the other sectors has not. Statistics Netherlands reports 1.58 Mt CO_2-eq for 2016, roughly double what Exiobase reports when applying the same characterisation factors (these being 1, 25 and 298 kg CO_2-eq/kg for CO_2, CH_4 and N_2O, respectively). The characterisation factors are further explained in Section 2.2.3. As indicated earlier, the Statistics Netherlands data is the most accurate and most regularly updated, which could explain this difference.

More accurate data is not available for the other environmental impact categories, so the direct environmental impacts remain as reported in Exiobase.

2.2.1.4 Construction of healthcare expenditure vector

This section describes the steps to translate the national healthcare expenditure into the desired input for the EE-IOA calculation (the healthcare expenditure vector).

Step 1: Survey of healthcare sector expenditure
Step 2: Data assessment to link healthcare expenditure and MRIO
Step 3: Link healthcare expenditure to MRIO sector classification
Step 4: Calculation of healthcare expenditure vector

Step 1: Survey of healthcare expenditure

When it comes to calculating the footprint of the healthcare sector, IOA terms refer to the footprint that is created in order to meet a 'demand for healthcare goods or healthcare services', i.e. the impact of healthcare expenditure by households and governments. Statistics Netherlands keeps track of this expenditure according to the System of Health Accounts (SHA) classification system, developed by the OECD, WHO and Eurostat.[36,37] The SHA categorises expenditure entirely by function (e.g. medical or preventive care) or by care providers (e.g. hospitals, nursing homes). Expenditure funding includes both direct expenditure by households and payments via funding schemes, such as health insurance policies.

Statistics Netherlands reports the data on expenditure for the healthcare sector according to two scopes (an expenditure overview is provided in appendix B):

- Healthcare: which covers all SHA categories;
- Health and welfare: a wider scope that combines health and welfare services. Additional categories are added on top of the existing SHA categories in this case. Welfare services include welfare care, social services, childcare and youth care.

The expenditure for these scopes is once again specified for two definitions:

- Internationally comparable: all healthcare expenditure for residents, regardless of whether the service is provided in the home country (all healthcare expenditure for Dutch residents in the Netherlands and abroad);
- Expenditure in a broad definition: all healthcare expenditure for residents and non-residents included in the Netherlands (all expenditure for the Dutch healthcare sector).

Healthcare expenditure is broken down by function into dozens of types of services (such as preventive care and home care), with the exception of two product categories: Pharmaceuticals and other medical non-durables' and 'Therapeutic applicances and other medical durables. Healthcare expenditure is simplified by dividing it into three main groups of expenditure on care services and care products (supplemented with information from the SHA manual[31]):

1) Care services:
   - Healthcare services (SHA: HC 1-4, 6, 7, 9):
     - Curatitive and rehabilitative care; long-term nursing care; ancillaryservices to healthcare; prevention and public health services; healthcare administration and health insurance; healthcare n.p.m. (not previously mentioned);
   - Welfare services (non-SHA categories):
     - Welfare care,
     - Social services,
     - Childcare
     - Youth care;

Medical goods (HC 5 – not broken down by function; outpatient expenditure, retail):

2) Pharmaceuticals and other medical non-durables (SHA: HC 51). This includes prescription drugs (generic and patented); generic and patented over-the-counter drugs; medical consumables (over-the-counter and prescribed), including bandages, syringes, first aid kits, compresses, medical stockings, condoms and other mechanical barrier contraceptives. Products for in-vitro diagnosis (IVD) also fall under this category as medical consumables;
3) Therapeutic appliances and other medical durables (HC 52). This includes eyeglasses, contact lenses and accessories; hearing aids and accessories; orthopaedic devices and prostheses; other medical devices and equipment for long-term use.

Based on the available expenditure data, the above-mentioned HC 51 and HC 52 product groups cannot be broken down any further. However, it can be stated that the expenditure for HC 51 is largely spent on medicines, as the expenditure for outpatient drugs from the Health Insurance Act alone amounted to €4,532 million euros in 2016[38], compared to the total outpatient expenditure of €5,639 million euros for medicines & consumables (see appendix B, both expenditures expressed in market price).

From this point forward, these three types of expenditure will be referred to as 1) care services, 2) pharmaceuticals & consumables (HC 51) and 3) therapeutic aids (HC 52), and the sum of the categories will be indicated as the healthcare sector.

Step 2: Data assessment to link healthcare expenditure and MRIO

To construct the healthcare expenditure vector, healthcare expenditure must be linked to the Exiobase sector categories. This requires a conversion from the purchaser price to the basic price. The MRIO is reported in basic prices, which Dutch healthcare expenditure is reported in purchaser price. The difference between the basic price and the purchaser price is the sum of transport costs, trade margins, taxes and subsidies.[39] This conversion is derived from the Supply table of the national accounts.[40] The average conversion to basic price for all sectors has been calculated from this table by dividing the basic price (supply at basic price) by the total purchaser price (Total = 'supply at basic prices + trade and transport margins + taxes on products – subsidies on products). Finally, import ratios must also be taken into account, as these are not included in the expenditure data. Because it is unlikely that the product groups of pharmaceuticals & consumables and therapeutic aids are purchased from a single country, an import ratio is derived from the MRIO as a proxy.

Step 3: Linking healthcare expenditure to MRIO sector classification

These three data sets (the healthcare expenditure, the conversions from the national accounts and Exiobase) must therefore be linked to each other. In the national account, sectors are divided using the sector classification NACE Rev. 2. Because Exiobase uses the older version of this classification (NACE Rev. 1.1), the sector categories do not fully correspond.[41] Linking the two classifications to healthcare expenditure reveals the following:

- Care services: There are two categories for care services in the national accounts (*Human health activities* and *Residential care and social work*), while care services fall entirely under *Health and social work* in Exiobase;
- Pharmaceuticals & consumables: there is a separate sector category for pharmaceuticals (*Manufacturing of pharmaceutical products and preparation*) in the national accounts, but Exiobase has a broader sector category called *Chemicals not elsewhere classified (n.e.c.)*. This means that this sector category includes the production of pharmaceuticals as well as a range of other chemical products. In Exiobase v3, this category includes all chemical products except for plastic and rubber products, semi-finished goods and fertilisers. The distribution among the different products within an aggregated product group is not known (such as the proportion of bulk chemicals and pharmaceuticals under *Chemicals n.e.c.*).
- For health expenditure on therapeutic aids, Exiobase contains a more suitable category (*Medical precision and optical instruments, watches and clocks*) than the broader sector category featured in the national accounts (*Computer, electronic and optical products*).

Table 1 shows the link between the three classifications.

Table 1 Link between healthcare expenditure based on the sector categories used in Exiobase and the national accounts. Table adapted from Steenmeijer et al. (2022) (link).

Healthcare expenditure categories according to System of Health Accounts[26]	Exiobase sector categories	Sector categories in the national accounts
HC 1-9 excl. HC 5 - Care services	85. Health and social work	83. Human health activities
Other: Welfare services (non-SHA)		84. Residential care and social work
HC 51. Pharmaceuticals & medical consumables	62. (Manufacture) of chemicals n.e.c.	28. Manufacture of pharmaceutical products and preparation
HC 52. Therapeutic aids	33. (Manufacture of) medical precision and optical instruments, watches and clocks	33. Manufacture of computer, electronic and optical products

Based on this link, the decision was made to calculate expenditure in the broad definition and for the wider scope (health and welfare). The choice of this scope is pragmatic, in order to align with the definition in Exiobase and thus facilitate integration and interpretation. In Exiobase, healthcare is aggregated with the social services/welfare services sector (*Health and social work*). The expenditure was chosen for the in the broad definition because the impact of care for residents and non-residents is not reported separately. While this may be the case for calculations using IOA, which also address the import and export of care services, it is not the case when collecting bottom-up information (as a supplement to the footprint; see Section 2.2.2). Furthermore, based on the purpose of the footprint model – that is, to determine the environmental impact of the Dutch healthcare sector – it is not useful to discount the impact of imported care (care received by Dutch residents abroad) and exported care (Dutch care received by non-residents).

Step 4: Calculation of healthcare expenditure vector
Table 2 contains the data used to calculate the conversion factor (purchaser price to basic price) for the three types of healthcare expenditure, according to the link in Table 1. Due to the minimal difference between the basic price and market price of care services, the conversion factor is negligible (i.e. equal to 1). In Table 3, this conversion factor is applied to the reported healthcare expenditure so that it can be used in the calculation with Exiobase.

Table 2 The conversion factor for the three different types of healthcare expenditure for 2016, calculated by dividing the sector's supply basic price by the purchaser price according to the supply table in the national accounts. Table adapted from Steenmeijer et al. (2022) (link).

Healthcare expenditure type	Sector categories in the national accounts	Sector supply in national accounts, purchaser price (in millions of euros)	Sector supply in national accounts, basic price (in millions of euros)	Conversion factor from purchaser price to basic price
Care services	83. Human health activities + 84. Residential care and social work	(44,635 + 36,223 =) 70,858	(44,463 + 36,223 =) 70,686	no conversion
Pharmaceuticals & medical consumables	28. Manufacture of pharmaceutical products and preparation	24,452	16,447	0.67
Therapeutic aids	33. Manufacture of computer, electronic and optical products	109,444	92,962	0.85

Table 3 The three types of healthcare expenditure in 2016, the reported expenditure in purchaser prices and the healthcare expenditure in basic prices, calculated by multiplying these expenditures by the corresponding conversion factor in Table 2. Table adapted from Steenmeijer et al. (2022) (link).

Healthcare expenditure	Healthcare expenditure in purchaser price (in millions of euros)	Conversion factor from market price to basic price (from Table 2)	Healthcare expenditure in basic price (in millions of euros)
Care services	86,096	no conversion	86,096
Pharmaceuticals & medical consumables	5,639	0.67	3,778
Therapeutic aids	3,107	0.85	2,641
Total expenditure	94,842		92,515

Section 2.2.1.2 explains that a contribution and hotspot analysis will be performed. The contribution analysis offers little detail based on current healthcare expenditure; the footprint is therefore divided into the three expenditure categories. To provide more insight into the products and services that make a large contribution to the footprint, the expenditure on care services has been made 'exogenous'. This means the intermediate use (i.e. the purchase or input) of care services is used for the healthcare expenditure vector instead of the total expenditure on care services.

With the currently selected scope, definition and perspectives, the healthcare expenditure vector is the sum of the following three elements:

1. the intermediate use of care services, driven by the final expenditure on care services;
2. the expenditure for medicines & consumables;
3. the expenditure for therapeutic aids.

For the expenditure on care services (1), the column of the inter-industry matrix (also known as the Z-matrix or transaction matrix) for Exiobase's *Health and social work* for the Netherlands was adopted. This vector was then scaled using the ratio calculated by dividing expenditure on care services by the total input from the healthcare sector. The total input is the sum of the total intermediate use (purchase/input) and the production factors (added value) of a sector. There is no conversion from purchaser price to basic price (see Table 2).

For the expenditure on Pharmaceuticals & consumables (2) and the expenditure on therapeutic aids (3), the converted basic price values from Table 3 are used. These values are then distributed across a vector for Exiobase's *Chemicals n.e.c.* and *Medical precision and optical instruments, watches and clocks*, according to the import distributions in the total Dutch final demand for these same Exiobase sectors (see Appendix C). Thus, if 10% of *Chemicals n.e.c.* consumed in the Netherlands are imported from Germany, it is also assumed that 10% of the consumption of pharmaceuticals & consumables relates to German imports.

2.2.2 Addition of healthcare sector-specific impact calculations

This section examines the healthcare sector-specific impacts that are not currently included in the EE-IOA footprint. Where possible, estimates of the additional impact sources are subsequently made so that these can be added to the EE-IOA footprint. This creates a more complete picture of the overall impact of the healthcare sector. First, existing studies are consulted (Section 2.2.2.1), and then estimates are made for emissions due to the administration of anaesthetic gases (Section 2.2.2.2), emissions due to the use of pressurised metered-dose inhalers (Section 2.2.2.3) and, lastly, the impact of individual travel movements (Section 2.2.2.4)

2.2.2.1 Additional calculations in existing studies

Previous studies on the climate footprint of the healthcare sector indicate that the top-down calculations using EE-IOA should be supplemented with additional bottom-up estimates, since otherwise important healthcare sector-specific impacts are left out. Although in reality there could be other additional sources of environmental effects, only the following three are mentioned in the literature: individual travel movements, anaesthetic gases and pressurised metered-dose inhaler. These are further explained in the discussion section of this chapter (Section 2.4.2).

Climate footprint studies for England[24] and Austria[22] and the study by Gupta Strategists[5] for the Netherlands include private travel movements in their carbon footprint calculations, with a significant estimated contribution for this source (10%, 12% 22%, respectively). The impact of individual travel movements of employees, patients and visitors is not calculated in the sectoral footprint with EE-IOA, since individual travel movements are attributed to households in the national statistics. Nevertheless, it is important to include the impact of individual travel movements in the footprint calculation, because the healthcare sector can have a substantial effect on individual travel movements, for example by regionalising healthcare or encouraging the use of public transport. In addition, commuter travel is included in Scope 3 of the Greenhouse Gas Protocol.[30]

Discussions with the sector and the literature also show that the use of pressurised metered-dose inhalers (pMDI; inhaled medication such as that delivered via inhalers) and anaesthetic gases (narcotic gases) has important healthcare-sector related climate impact. In the sectoral footprint calculation using EE-IOA, the emission of propellants from pMDI is not included since these emissions take place during home use (and are therefore regarded as consumptive emissions by households). The contribution of emissions from propellants to the healthcare sector's footprint globally[6], in Austria[22] and in England[24] is estimated at 0.35%, 0.4% and 3.4%, respectively. Finally, the release of anaesthetic gases, which are operational emissions, is often estimated separately in various studies due to the lack of emissions data on medical gases in carbon reporting. In studies for Austria[22] and England,[24] the contribution of these gases to the climate footprint is estimated at 0.3% and 2%, respectively.

The following sections describe the estimates for emissions due to the use of pMDI (Section 2.2.2.2) and the environmental impact of individual travel movements (Section 2.2.2.3). In addition, Section 2.2.1.3 shows that medical gases are not included in greenhouse gases in the national accounts, so the impacts of anaesthetic gases are also added separately to the footprint calculation (Section 2.2.2.4). As a final step, the (estimated) environmental impact of these three sources is added to the sectoral footprint as calculated using EE-IOA.

2.2.2.2 Emissions due to the use of pressurised metered-dose inhalers

The emission of greenhouse gases during the use of pMDI is calculated based on a combination of the number of pMDI canisters dispensed, as calculated from the GIPdatabank[42], and the propellant content of each canister, as provided by the Dutch Medicines Evaluation Board (MEB). See Appendix E for the complete list.

From 2016-2020, the use of pMDI increased each year compared to dry powder inhalers (see Figure 5). The number of propellent-containing pMDI packages dispensed rose as well. These propellants have a high global warming potential (GWP). Most pMDI contain norflurane (HFK-134a), with a GWP of 1,549 (with climate-carbon feedbacks, i.e. self-reinforcing changes in the carbon cycle due to a warming climate).[43] A smaller number of pMDI contain heptafluoropropane (HFK-227ea), with an ever higher GWP of 3,860 (with climate-carbon feedbacks).[43] Between 2016 and 2020, the number of pMDI canisters containing the strong greenhouse gas heptafluoropropane (HFK-227ea) increased from 1.3% to 2.4% of the total amount of pMDI dispensed (see Figure 6)

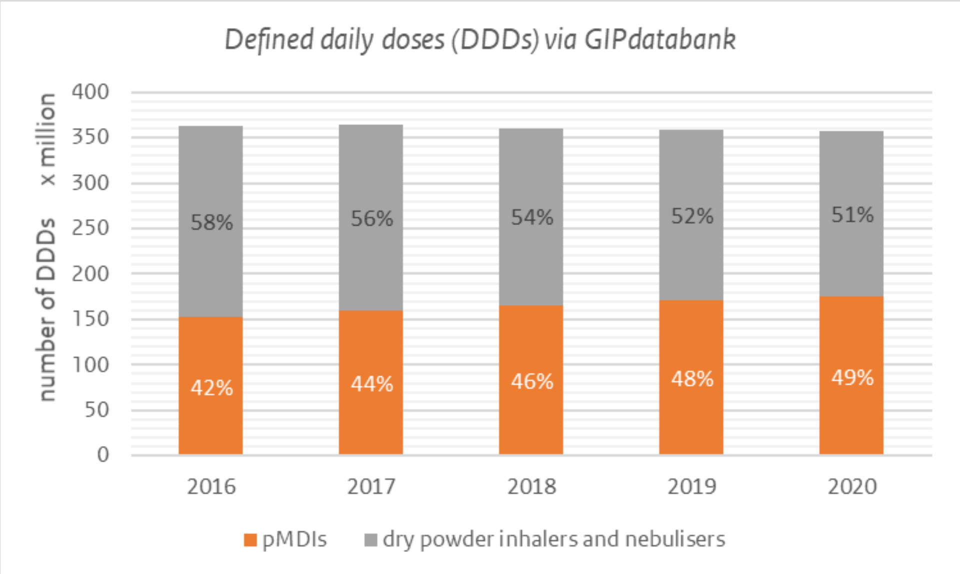

Figure 5 Development in the number of defined daily doses (DDDs) of pressurised metered-dose inhalers and dry powder inhalers and nebulisers provided to Dutch patients between 2016 and 2020.

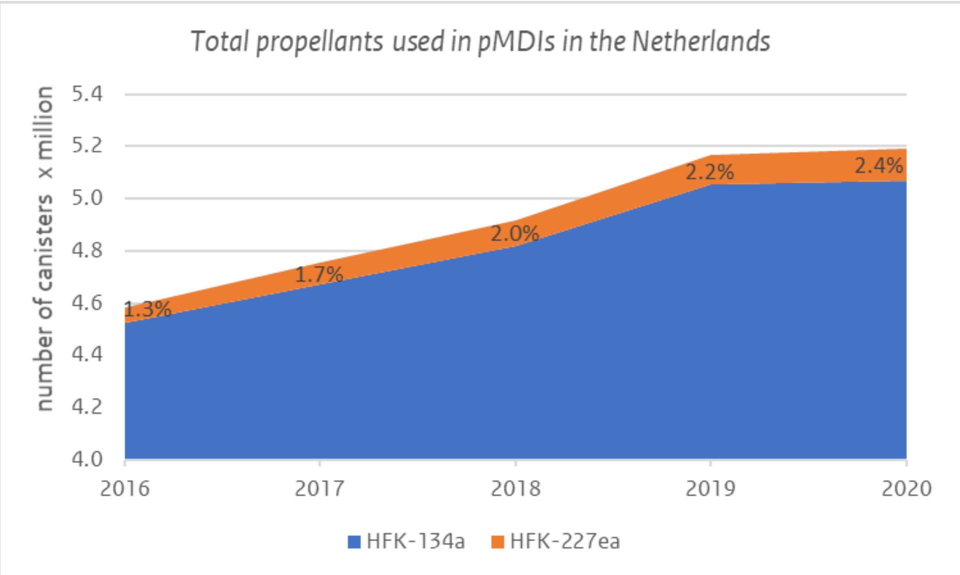

Figure 6 Use of different types of propellants in pressurised metered-dose inhalers in the Netherlands. Figure based on data from GIPdatabank regarding the number of canisters dispensed. HFK-134a = norflurane. HFK-227ea = heptafluoropropane.

While the total number of daily doses of inhalers has decreased over the years, the number of canisters used has increased, and with it the total emissions from pMDI (see Figure 5, Figure 6 and Figure 7). From 2016-2020, total direct emissions rose by 11.1% (see Figure 7). At the same time, the emissions per defined daily dose (DDD) fell by 3.3% between 2019 and 2020, possibly due to the use of more efficient pMDI with less propellant per dose.

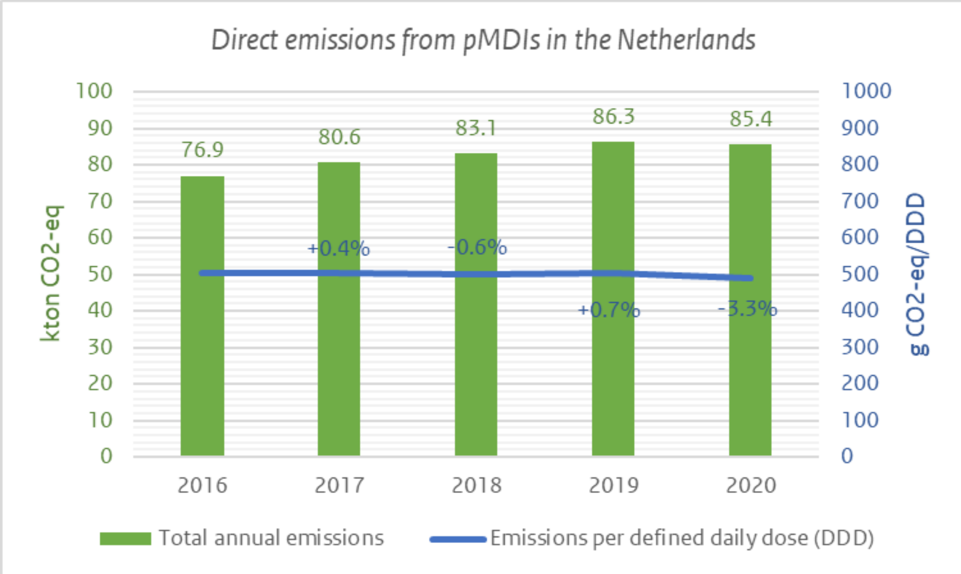

Figure 7 Development in the total direct emissions from pressurised metered-dose inhalers (pMDI) and the emissions per daily dose of pMDI. The calculations for this figure were made based on data from GIPdatabank regarding the number of canisters dispensed. The amounts of propellant per type of pMDI come from the Dutch Medicines Evaluation Board (MEB) and the global warming potential values used are from ReCiPe 2016.[43]

The direct emissions from pMDI calculated for the year 2016 (76.9 kt CO_2-eq) were used to calculate the baseline year of the Dutch healthcare sector's footprint. This result is added to the climate footprint calculated using EE-IOA. Apart from climate change, no other environmental impacts are attributed to home use of pMDI.

2.2.2.3 Impact due to individual travel movements

Approach

The approach for calculating the total distance travelled by employees, patients and visitors for each means of transport was taken from Tennison et al.[24], and was also previously applied in the study by Gupta Strategists.[5] The estimates for the distances travelled are lined to the corresponding activities in the lifecycle database Ecoinvent v3.7[44] to calculate the overall impact. The most appropriate activities provide information in person*km and calculate the impact up to and including the use phase.

The impact of individual travel movements is calculated based on LCA data, and thus concerns both the direct impacts (use phase; impacts that take place during transport such as exhaust emissions) and the indirect impacts elsewhere in the chain. The impact results of individual travel movements are broken down into a direct impact and an indirect impact. The indirect impact is added to the hotspot analysis without further specification of the originating sector or region, as it would be too time-consuming to bridge the Exiobase and Ecoinvent classifications. This extra step is not necessary for the contribution analysis.

Commuting distance travelled

According to Statistics Netherlands, an average of 1,220,750 people were employed in health and welfare services (including childcare) in 2016.[45] As far as is known, no specific information is available for employees in the healthcare sector with regard to the average number of trips between work and home per week. For this estimate, the part-time factor ('The relative working hours of the job compared to a full-time job at the same company or in the same business sector'[46]) is used; on average, this factor was 0.68 for the health and welfare sector (including childcare) in 2016.[47] In the absence of data, the results for full-time working weeks (36 hours/week) have been used in combination with the part-time factor. From this, it has been calculated that (0.68 * 36 hours/week =) 24.5 hours are worked per week. This equates to an average of 159 working days annually, and combined with an assumed 21 days of paid leave (including public holidays), the final result is 138 working days per year. This means that (138 days/year * 1,220,750 employees =) 168 million travel movements took place in 2016.

Statistics Netherlands also presents the distribution of the average number of trips to and from work and the average corresponding distance per means of transport per person per year.[48] These figures do not relate specifically to the healthcare sector. The total number of kilometres for 'other means of transport' is redistributed proportionally, as no further information about these means of transport is available. Next, the new distribution for each trip is multiplied by the average distance travelled for each means of transport, combined with the expected travel movements for commuting purposes, to calculate the total distance travelled per means of transport (see Table 4).

Table 4 The distribution of the number of trips per means of transport for commuting purposes and the average distance per trip, as provided by Statistics Netherlands, to estimate the average distance travelled by healthcare workers per means of transport in 2016. Table adapted from Steenmeijer et al. (2022) (link).

Means of transport	Number of trips per person per year	% of total trips	% of total trips redistributed	Distance of trip per person	Total distance for 168 travel movements in millions of km
Car (driver)	86	53.4%	54.3%	25.30	2,280
Car (passenger)	6	3.7%	3.8%	26.33	166
Train	7	4.3%	4.4%	39.49	280
Bus/tram/metro	7	4.3%	4.4%	13.70	100
Moped/scooter	4	2.5%	2.5%	7.74	32
Bicycle	41	25.5%	25.9%	4.68	201
Walking	7	4.3%	4.4%	2.83	21
Other means of transport	3	1.9%	Redistributed proportionally	-	-

2.2.2.4 Distance travelled by patients and visitors

Gupta Strategists applied a value of 150 km/person/year for the distance travelled by patients or visitors for personal trips for all Dutch residents, a figure that was also sourced from the same NHS data used by Tennison et al. [24]. Table S10 of Tennison et al.'s study shows that in 2016, the average distance travelled per resident for personal medical reasons in England was 159 km (99 miles). There is no similar figure for the Netherlands; Statistics Netherlands does not report on travel for the purpose of healthcare. This study did not examine whether the density of England and the Netherlands is comparable in terms of medical facilities. If this figure is adopted for the Netherlands, it results in a total of 2.7 billion kilometres travelled by patients and visitors in 2016 (159km/person/year * 16,980,000 residents). This is based on the distribution of total traveller-kilometres per means of transport for the Netherlands in 2016[49] (see Table 5).

Table 5 The distribution of the total traveller-kilometres per means of transport, provided by Statistics Netherlands, to estimate the distance travelled per means of transport for individual travel movements of patients and visitors. Table adapted from Steenmeijer et al. (2022) (link).

Means of transport	millions of traveller-kilometres in 2016	% of total traveller-kilometres	% of total traveller-kilometres redistributed	Total millions of kilometres (total = 2.7 billion kilometres)
Car (driver)	97.7	50.2%	52.9%	1,429
Car (passenger)	43.1	22.1%	23.3%	630
Train	16.9	8.7%	9.2%	247
Bus/tram/metro	5.9	3.0%	3.2%	86
Moped/scooter	1.1	0.6%	0.6%	16
Bicycle	14.6	7.5%	7.9%	213
Walking	5.3	2.7%	2.9%	76
Other means of transport	10.2	5.2%	Redistributed proportionally	-

Linking Ecoinvent processes to means of transport

It is assumed that the means of transport 'Car (passenger)' and 'Walking' have no impact. The impact of travel movements by car is attributed to the driver, since there is no information about the (average) number of passengers riding along. Next, the other five means of transport were linked to corresponding Ecoinvent v3.7 activities (see Table 6).

For the impact of travelling by train, no suitable activity for passenger trains in the Netherlands was available in Ecoinvent. If the percentage of electric railways is compared over the years, Belgian passenger train activity comes closest to the situation in the Netherlands. NS, the Dutch national railway service, states that in 2016, 75% of all electric trains were powered by wind energy. The PBL Netherlands Environmental Assessment Agency estimates that the total wind energy capacity

installed in the Netherlands for 2015 consists of approximately 10.5% offshore and 89.5% onshore. The activity is adjusted by replacing the process inputs with data from Dutch suppliers, updating the values for the electricity, and adding the electricity from offshore and onshore wind energy (assuming that in both cases the turbines are 1-3 MW).
The total distance travelled by bus/tram/metro is not further specified. Based on available suitable activities, a share of 50% of kilometres travelled is assumed for *Transport, tram (GLO)* and 50% for *Transport, regular bus (GLO)*.

As far as is known, there are no reliable sources for the percentage of electric scooters and mopeds in 2016. A news article discussing the rise of electric scooters suggests that this figure was roughly 2-3%. For the impact of travel with scooters/mopeds, a share of 3% electric scooters is therefore assumed. The impact per kilometre travelled was calculated based on a composition of 97% *Transport, passenger, motor scooter (GLO)* and 3% *Transport, passenger, electric scooter (GLO)*. No data were found regarding the percentage of electric bicycles in 2016. Accordingly, only the impact of *Transport, passenger, bicycle (GLO)* is considered.

Table 6 The selected Ecoinvent activities to represent the means of transport. Table adapted from Steenmeijer et al. (2022) (link).

Means of transport	Corresponding Ecoinvent activities
Car (driver)	*Transport, passenger car, medium size, petrol, EURO 5 (RER)| Cut-off, U*
Car (passenger)	No effect
Train	*Transport, passenger train (BE)| processing | Cut-off, U*, adjusted for NL
Bus/tram/metro	50% *Transport, tram (GLO)| market for | Cut-off, U* and 50% *Transport, regular bus (GLO)| market for | Cut-off, U*
Moped/scooter	97% *Transport, passenger, motor scooter (GLO)| market for | Cut-off, U* and 3% *Transport, passenger, electric scooter (GLO)| market for | Cut-off, U*
Bicycle	*Transport, passenger, bicycle (GLO)| market for | Cut-off, U*
Walking	No effect
Other means of transport	-

2.2.2.5 Emissions due to administration of anaesthetic gases

Venema et al.[50] recently made a bottom-up inventory of the use of anaesthetic gases in Dutch hospitals. They estimate that the use of anaesthetic gases accounts for approximately 13.2 kt CO_2-eq (4,189 tonnes CO_2-eq due to sevoflurane and desflurane, and roughly 9,000 tonnes CO_2-eq due to nitrous oxide). Based on the footprint calculations of Gupta Strategists, this would amount to 0.1% of healthcare emissions.[50]

No other estimates for the Netherlands are available. Estimates have been made in studies for other regions, which typically use different scopes, definitions of care and years (see consolidated overview in Appendix D). Based on the study for England[24], which reports a time series of 1990-2019, a value for 2016 has been derived for the same scope and definition applied in this study. The footprint calculation for England reveals that, excluding emissions due to individual travel movements and the use of pMDI, 1.78% of the climate footprint for health and welfare is caused by anaesthetic gases. If this figure is adopted for the Dutch situation, it is much higher than the expected 0.1% reported in the study by Venema et al. According to the authors, this difference can be explained by lower use of nitrous oxide and/or isoflurane and desflurane. Because of the more intricate study that focuses specifically on the Netherlands, this study has opted to work with the bottom-up inventory of Venema et al., even though the reference year was 2019 and not 2016. For the other impact categories, there are no direct impacts related to the administration of anaesthetic gases.

2.2.3 *From environmental stressors to impact*

One of the final steps in the footprint calculation is the conversion of stressor quantities (emissions and raw material extractions) into impact using so-called characterisation factors. Because the EE-IOA is combined with LCA results, it is necessary to convert both results into the same impact categories. As a starting point, the midpoints of the lifecycle impact method ReCiPe 2016 (H)[43] were used for the LCA results, along with the characterisation table of project DESIRE FP7[51] for the EE-IOA. Below is a description of how the results were characterised for each impact category. The greenhouse gas emissions resulting from the use of PMDI have already been characterised using ReCiPe 2016 (H). Finally, for the sake of consistency, we converted the estimates of greenhouse gas emissions for anaesthetic gases according to ReCiPe 2016 (H), resulting in 14.6 kt CO_2-eq.

Climate change in kg CO_2-eq (the climate footprint)

Based on the characterised stressors for climate change in DESIRE FP7, this differs from ReCiPe 2016 (H) regarding the characterisation of NMVOC and SF_6. NMVOC is characterised in DESIRE FP7 (0.04521 kg CO_2-eq per kg), but not in ReCiPe 2016 (H). In addition, SF_6 has a characterisation factor of 22,800 kg CO_2-eq per kg in DESIRE FP7, and 26,087 in ReCiPe 2016 (H). For the harmonisation of the results, the characterisation factors for NMVOC and SF_6 in DESIRE FP7 are adjusted to match ReCiPe 2016 (H). See Appendix F.1 for the climate change characterisation factors for the environmental stressors in Exiobase v3.

Abiotic raw materials use in kt (the raw materials footprint)

There is as yet no consensus on how the use of raw materials should be weighted[52,53]. DESIRE FP7 uses mass-based accounting and expresses metal extraction in ores. ReCiPe 2016 uses surplus ore potential, and expresses this in copper equivalents (Cu-eq). To calculate the footprint in this study, mass-based accounting was chosen because it is less complicated to convert the LCA midpoint results into mass than it is to set up a characterisation table to express the Exiobase stressors in Cu-eq.

For the conversion from copper (Cu) to copper ore equivalents, a conversion factor provided by Impact World+[52] was used (8,674 kg extracted copper/kt copper ore). This percentage (0.87% copper ore content) is in line with the average copper ore content in recent years, which is approximately 0.9%.[54] To convert the LCA results into copper ore equivalents, 1 kg Cu-eq is therefore converted into ~0.00012 kt copper ore equivalent.
The *Domestic Extraction* category (without the *Unused Domestic Extraction*) from DESIRE FP7 has been used, but this was adjusted by removing the characterisation factors for all biotic materials (fossil and non-fossil). See Appendix F.2 for the raw materials use characterisation factors for the environmental stressors in Exiobase v3.

Blue water consumption in Mm^3 (the blue water footprint)
Blue water consumption is expressed in the same way in ReCiPe 2016 (H) and DESIRE FP7: *Water consumption in m^3* in ReCiPe, and *Water Consumption Blue – Total in Mm^3* in DESIRE FP7. The results for the LCA were divided by 1,000,000 to express these values in Mm^3 as well. See Appendix F.3 for the blue water consumption characterisation factors for the environmental stressors in Exiobase v3.

Land use in km^2
In ReCiPe 2016 (H), land use is translated into m^2 annual crop equivalents (m^{2}a), while DESIRE FP7 only considers the land area (in km^2) regardless of its application. Land use can be expressed in both km^2 and m^{2}a. In this case it was decided to once again convert the LCA results into km^2 because this is a simpler conversion. According to Table 11.1 in the ReCiPe 2016 documentation,[43] 1 m^{2}a crop equivalent is equal to 1 m^{2}land use. See Appendix F.4 for the land use characterisation factors for the environmental stressors in Exiobase v3.

Waste production in kt
Because no LCA midpoint exists for waste production, all waste fractions from the extensions of Exiobase v3's hybrid MRSUT were added together without further characterisation.

The update of ReCiPe will begin in 2022, at which time a characterisation table will also be developed for IO tables, including for Exiobase. We expect the first version of this characterisation table to be available in 2023.

2.2.4 Uncertainty analysis

In contrast to datasets like Eora,[26] Exiobase and the data provided by Statistics Netherlands do not include uncertainty data, meaning that a statistical analysis (such as a Monte Carlo analysis) is not possible. It is outside the scope of this project to collect uncertainty data. Another study[55] that used estimated uncertainties for another EE-MRIO, GTAP, found a low uncertainty from the Monte Carlo analysis of the Dutch consumptive climate footprint. However, the uncertainty grew once the sectors were examined further. The uncertainty was especially high for agricultural sectors, but *Public Administration, Defence, Education and Health* had a relatively high uncertainty level for a non-agricultural sector. It is difficult to say what role the healthcare sector plays in this regard, since it is aggregated with public administration, education and defence.

There can be significant differences in the national consumptive climate footprint results between different EE-MRIOs[56,57]. According to Rodrigues et al.[57], the Dutch consumptive climate footprint shows the highest variation compared to the footprints of other countries when calculated using various MRIOs. The environmental extensions differ between the MRIOs, but even when these differences have been corrected, the results differ from each other due to the differences in economic data[56]. According to Giljum et al.[58], the Dutch consumption footprint for raw materials use also varies significantly among the different MRIOs and is again one of the highest compared to other countries. According to this study, the uncertainty mainly stems from the supply of raw materials extraction to the fossil and chemical sector and the public sector (including the healthcare sector). The role of the different MRIOs in the uncertainty for the healthcare sector results has not yet been specifically investigated. Nor are there any studies examining the uncertainties of the consumption footprint of blue water consumption and waste production.

For the additional impact estimates, not enough comparable data sources are available for the sector-wide contributions of anaesthetics and pMDIs. Furthermore, the rough estimates of the total distance travelled per means of transport for individual travel movements likely produce more uncertainty than the LCA data. The 159 km travelled per year for personal medical purposes was adopted from a study on England, for instance, and it is not certain whether this distance is also representative for the Netherlands.

2.3 Results of environmental footprint of Dutch healthcare sector

This section presents the results of the sectoral footprint, calculated using the method outlined in Section 2.2. Section 2.3.1 first explains how the healthcare expenditure vector was roughly constructed. Next, the overall impact of the healthcare sector for the selected impact categories is discussed, along with the extent to which it contributes to the national footprint (Section 2.3.2). Section 2.3.3 then examines the composition of the footprint.

2.3.1 The healthcare expenditure vector

Table 7 presents an aggregated overview of the healthcare expenditure vector developed. The actual healthcare expenditure vector is 7,987 rows (163 sectors x 49 regions). The complete results can be found in the repository on RIVM’s Github page (link). Part of the table includes the consumption expenditure on pharmaceuticals & consumables and therapeutic aids. The other expenditure types are production expenditure (purchase/intermediate use) from care services, which were adopted and scaled from Exiobase v3. The absolute numbers are provided, but it should be noted that these figures are based on processed IO data and can therefore differ from the actual expenditure for the year 2016. For the sake of completeness, the production factors from care services are also provided, but these are not included in the healthcare expenditure. Accordingly, no impact has been attributed to these factors.

The table shows that 72% of healthcare expenditure goes towards production factors, i.e. (mainly) wage costs, taxes, capital costs and potential profit. It is not surprising that a large part of healthcare expenditure is spent on wage costs. After all, approximately 1.2 million people – or 16% of the total labour force – worked in the Dutch healthcare sector in 2016[45]. Healthcare expenditure leads to the purchase of 19.9 billion goods and services from healthcare services, in addition to consumer expenditure on medicines & consumables and therapeutic aids. Services (11%) are the largest expenditure type. Furthermore, approximately 6% is spent on medicines and other chemical products, with two-thirds of this being consumer expenditure. Therapeutic aids are also a major cost item at 4%, with consumer expenditure again making up two-thirds of this.

Table 7 The rough breakdown of healthcare expenditure in the healthcare expenditure vector. The production factors are excluded in the actual healthcare expenditure vector.

Expenditure	**millions of euros**	**%**
Production factors	66,232	72
Services	10162	11
Pharmaceuticals and other chemical products	5,386	6
Of which consumptive expenditure for medicines & consumables	*3,778*	
Medical devices and equipment	4,065	4
Of which consumptive expenditure for therapeutic aids	*2,641*	
Food and catering	1,948	2
Other	5,128	6
Total	92,515	100

2.3.2 *Total footprint results*

Table 8 Total environmental footprint, broken down into the expenditure categories for the EE-IOA calculation and the additional impact estimates. Table adapted from Steenmeijer et al. (2022) (link).

	Healthcare expenditure (basic price, in millions of euros)	**Climate change (kt CO_2-eq)**	**Abiotic raw materials extraction (kt)**	**Blue water consumption (Mm^3)**	**Land use (km^2)**	**Waste production (kt)**
Total	92,515 (100%)	17,575 (100%)	33,801 (100%)	394 (100%)	23,845 (100%)	4,803 (100%)
EE-IOA calculation						
Care services	86,096 (93%)	10,779 (61%)	14,715 (44%)	218 (55%)	13,748 (58%)	2,811 (59%)
Medicines & consumables	3778 (4.1%)	4,909 (28%)	18,261 (54%)	169 (43%)	9,744 (41%)	1,780 (37%)
Therapeutic aids	2,641 (2.9%)	864 (4.9%)	783 (2.3%)	6.6 (1.7%)	351 (1.5%)	212 (4.4%)
Additional calculations						

	Healthcare expenditure (basic price, in millions of euros)	Climate change (kt CO_2-eq)	Abiotic raw materials extraction (kt)	Blue water consumption (Mm^3)	Land use (km^2)	Waste production (kt)
Emission of anaesthetic gases	n/a	15 (0.083%)	-	-	-	-
Emission of propellants from pressurised metered-dose inhalers	n/a	77 (0.44%)	-	-	-	-
Individual travel movements	n/a	932 (5.3%)	42 (0.12%)	0.29 (0.074%)	2.7 (0.011%)	-

Table 8 presents the results for the top-down EE-IOA calculation based on the three expenditure types and the additional impact categories. These results show that the expenditure for care services (93% of the total expenditure) causes around half of the impact (44-61%) of the different impact categories. Pharmaceuticals & consumables also make a large contribution to the different impact categories (28-54%), despite the small expenditure (4%). The percentage of therapeutic aids is low for all impact categories (1-5%), as is the percentage of expenditure (3%). Emissions from anaesthetic gases and propellants from pMDIs amount to 0.08% and 0.04%, respectively, of the total climate footprint. The impact of individual travel movements is significant for the climate footprint (5%) and small (<1%) for the other impact categories.

When the results are compared to the national consumer footprint (see Table 9), we see that the healthcare sector is responsible for 7.3% of the national footprint. The percentage is smaller for waste production (4.2%) and larger for raw materials extraction (13.0%), while blue water consumption and land use are fairly similar (7.5% and 7.2%, respectively).

Table 9 Total footprint of the Dutch healthcare sector in relation to the national consumption footprint. Table adapted from Steenmeijer et al. (2022) (link).

Impact category	Healthcare sector footprint	National consumption footprint	Healthcare sector share in national consumption footprint
Climate change (kt CO_2-eq)	17,575	241,358	7.3%
Abiotic raw materials use (kt)	33,801	259,060	13.0%
Blue water consumption (Mm^3)	394	5,226	7.5%
Land use (km^2)	23,845	329,537	7.2%
Waste production (kt)	4,803	113,826	4.2%

2.3.3 *Composition of the environmental footprint*

To better understand the footprint, the composition of the footprint is presented from two different perspectives (by means of the contribution and hotspot analyses). These results were calculated using the level of detail of Exiobase v3, for 163 sectors in 49 countries and regions. However, to communicate the results more easily via figures, they are presented at a high aggregation level. The results are presented at a lower aggregation level in the appendices (see Appendix G for the corresponding aggregation table). For the non-aggregated results, please refer to the repository on the RIVM's Github page (link).

Contribution analysis

The contribution analysis of the footprint reveals that the contribution to climate change is more spread across the different product groups, while the other impact categories are mainly determined by two groups: Pharmaceuticals and other chemical products and Food & catering (Figure 8; underlying data in Appendix H). Figure 9 additionally reveals that the impacts of Scopes 1 and 2 constitute a larger problem for climate change, and less of a problem for the other impact categories. The most important similarity between the impact categories in the contribution analysis is that Pharmaceuticals and other chemical products make the largest contribution.

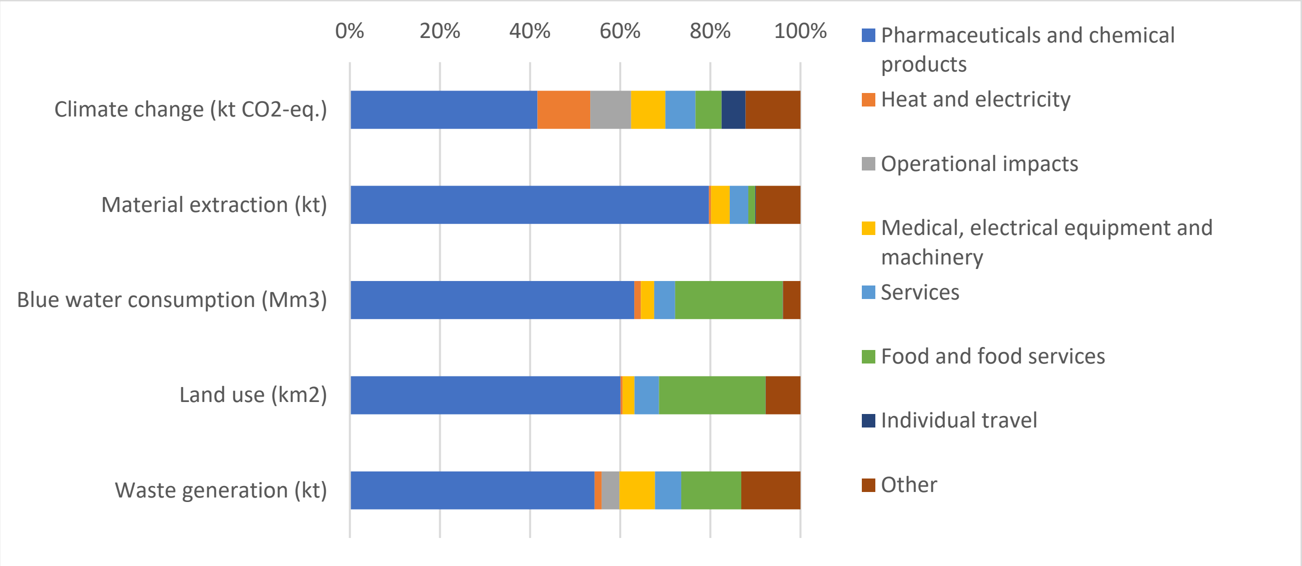

Figure 8 Contribution analysis of the environmental footprint of the healthcare sector for the selected impact categories. Results aggregated into seven groups, which cover at least 85% of all impact categories. The rest are combined in Other. The underlying data are included in Appendix H. Figure adapted from Steenmeijer et al. (2022) (link).

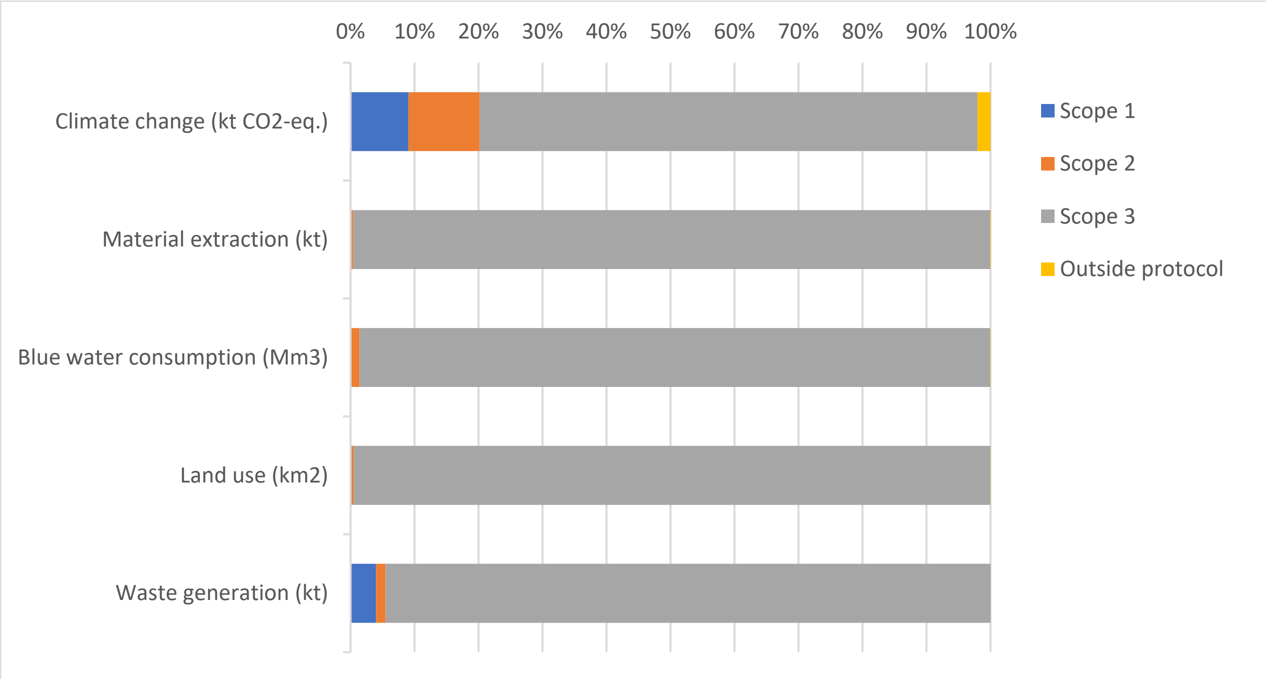

Figure 9 Contribution analysis of the environmental footprint of the healthcare sector, divided across the scopes according to the Greenhouse Gas Protocol[30]. The underlying data are included in Appendix H. Figure adapted from Steenmeijer et al. (2022) (link).

Hotspot analysis
The hotspot analysis of the footprint for the selected impact categories shows the sectors in which the impacts occur (Figure 10; underlying data in Appendix I). In this analysis, the spread is also the largest for climate change. As would be expected for the other impact categories, the mining sector mainly contributes to raw materials use, and agriculture largely contributes to blue water consumption and land use. In addition, both sectors are the largest contributors to waste production. While it is not surprising that mining and agriculture dominate the other impact categories, this is in contrast with the climate footprint, where the mining and agricultural sectors only account for 2.6% and 11.8%, respectively.

Figure 11 shows the hotspot analysis for the geographical spread of the footprint (underlying data in Appendix J). This reveals that greenhouse gas emissions mainly take place in the Netherlands (34%), while material extraction primarily occurs in Asia (75%). Land use and waste production primarily occur in North America, South America, Europe and Asia. Furthermore, both Asia and the Middle East play a major role in the healthcare sector’s blue water consumption.

When the different perspectives are combined, we see that medicines and other chemical products contribute the most to the selected environmental impact categories, although the category is less dominant in the climate footprint compared to the other impact categories. The greenhouse gas emissions in the climate footprint are more distributed across the different steps in the value chains and mainly take place in the Netherlands. This is in contrast to the other impact categories, where the impacts primarily occur in the mining and agricultural sectors and largely take place abroad.

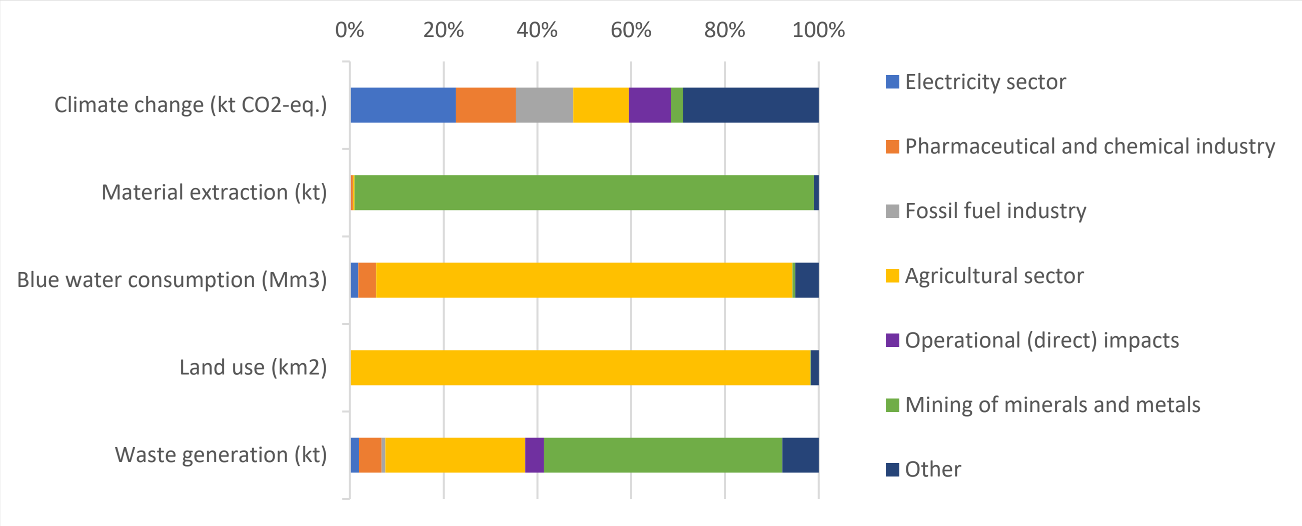

Figure 10 Sectoral hotspot analysis of the footprint of the healthcare sector for the selected impact categories. The results have been aggregated into six groups that contribute 9% or more to one of the impact categories. The rest are combined in Other. The indirect impact of individual travel movements is equally distributed across all groups. The underlying data are included in Appendix I. Figure adapted from Steenmeijer et al. (2022) (link).

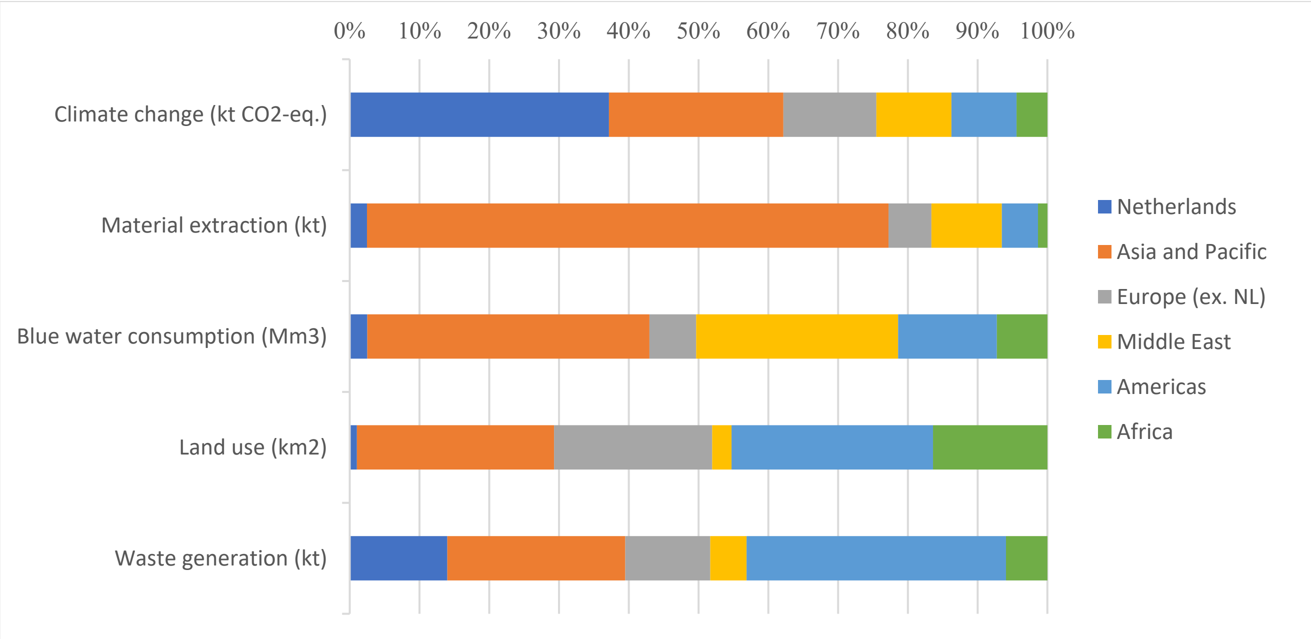

Figure 11 Geographical hotspot analysis of the footprint of the healthcare sector for the selected impact categories, aggregated into six regions worldwide. The indirect impact of individual travel movements is equally distributed across all groups. The underlying data are included in Appendix J. Figure adapted from Steenmeijer et al. (2022) (link).

2.4 Discussion of environmental footprint of Dutch healthcare sector

In Section 2.4.1, the results of this report are compared to similar footprint calculations for the Dutch healthcare sector and to international studies. Section 2.4.2 then outlines the current limitations of the data and the methods, and Section 2.4.3 explains how these can be addressed in future research. Section 2.4.4 concludes the chapter by discussing the relevance of this study.

2.4.1 Comparison of results

Footprint calculation for the Dutch healthcare sector

The results of this footprint calculation can only be compared to similar studies for the impact category of climate change. For the environmental impact of raw materials use, blue water consumption, land use and waste production, no other studies on the Dutch healthcare sector are available. The previously published studies that calculate the climate footprint for the Dutch healthcare sector differ in their use of MRIO, available environmental extensions, definitions of care, and/or reference year. Table 10 provides an overview of all these differences. While these differences make it difficult to compare the different healthcare sector footprint studies for the Netherlands, they make it even more difficult to compare the results to those for other countries.

Table 10 Overview of differences between the models that have been used to calculate the climate footprint of the Dutch healthcare sector. GHG = greenhouse gases. The SHA (System of Health Accounts) uses an internationally comparable definition of healthcare, proposed by the OECD, which takes into account healthcare provided to residents. For the results of the study by Lenzen at al. (2020), the derived national consumption footprint is fairly high compared to the other calculations. Therefore, the national consumption footprint as retrieved from the Eora 'footprint explorer' has been added as well. Table adapted from Steenmeijer et al. (2022) (link).

	RIVM, 2022 (this study)	**Gupta Strategists, 2019**	**HCWH & Arup, 2019**	**Pichler et al., 2019**	**Lenzen et al., 2020**
MRIO	Exiobase v3 (2018)	MRIO[a] for England (2004)	WIOD (2016)	Eora full version (2018)	Eora full version (2018)
Year	2016	2017	2014	2014	2015
Environmental stressors included	All GHG according to ReCiPe 2016	All GHG according to IPCC (2007)	CO_2, CH_4, N_2O	CO_2	All GHG according to IPCC (2007)
Environmental data	Exiobase environmental extensions	GHG emissions intensities (impact/euro) for England (2009)	CO_2: WIOD environmental extension; N_2O and CH_4: PRIMAP	Eora environmental extensions	Eora environmental extensions
Characterisation	ReCiPe 2016 (H)	IPCC (2007)	IPCC (2007)	-	IPCC (2007)
Definition used for the healthcare sector	Broad definition[b], health and welfare	Broad definition[b], healthcare	Internationally comparable[c], healthcare (SHA definition of care)	Internationally comparable[c], healthcare (SHA definition of care)	Internationally comparable[c], health and welfare (SHA definition of care)
Estimates added to footprint calculation	Individual travel movements of employees (Scope 3) and patients & visitors (outside scope), propellants from pMDIs (Scope 3), and anaesthetic gases (Scope 1)	Individual travel movements of employees (Scope 3) and patients & visitors (outside scope)	-	-	-
Calculation of Scope 1 (direct impact)	Direct CO_2-eq emissions of the healthcare sector (Health and welfare) as	Estimated total gas use from bottom-up approach based on	The study has linked all SHA expenditure categories to the related WIOD sector	No direct emissions; the footprint is approximated based	No direct emissions; the footprint is approximated based

	RIVM, 2022 (this study)	**Gupta Strategists, 2019**	**HCWH & Arup, 2019**	**Pichler et al., 2019**	**Lenzen et al., 2020**
	reported by Statistics Netherlands.	annual reports of Dutch Healthcare institutions, subsequently linked to CO_2 emissions intensities.	categories. These were then linked to the OECD healthcare statistics. The Scope 1 emissions were calculated by multiplying the direct emissions intensity for the related healthcare sectors by the healthcare expenditure.	on the consumption of care services and goods (assuming that consumption has no direct effects).	on the consumption of households (assuming that consumption has no direct impact).
Calculation of Scope 2 (indirect impact due to purchase of heating and electricity)	Indirect emissions based on purchase of energy and heating (under Exiobase i40.11, i40.12, i40.13, i40.3; see Appendix G) from *Health and social work* sector in Exiobase, scaled based on healthcare expenditure data from Statistics Netherlands.	Estimated total energy and heating purchase from bottom-up approach based on annual reports of Dutch Healthcare institutions, subsequently linked to CO_2 emissions intensities.	The study has linked all SHA expenditure categories to the related WIOD sector categories. These were then linked to the OECD healthcare statistics. Impact calculated for WIOD category *Electricity, gas, steam and air conditioning supply* based on the SPA.	The study has linked all SHA expenditure categories to the related EORA sector categories. These were then linked to the OECD healthcare statistics. No distinction is made between Scopes 2 and 3.	Footprint calculation for consumption of *Health and social work services* from the final demand in EORA (i.e. only the impact of care services). No distinction is made between Scopes 2 and 3 for the Netherlands specifically (only globally).
Calculation of Scope 3 (indirect impact due to purchasing other than heating and electricity)	Indirect emissions calculated for the total purchases (excl. Scope 2 categories, see cell above) from care services, and the consumption of Pharmaceuticals & consumables and	Purchase expenditure adopted from England, scaled according to the ratio of healthcare expenditure between the Netherlands and England – excluding the largest purchase	Scope 3 = total - Scope 1 - Scope 2. The study has linked all SHA expenditure categories to the related WIOD sector categories. The total impact was then calculated based on OECD healthcare statistics.		

	RIVM, 2022 (this study)	**Gupta Strategists, 2019**	**HCWH & Arup, 2019**	**Pichler et al., 2019**	**Lenzen et al., 2020**
	Therapeutic aids by linking the Statistics Netherlands healthcare expenditure to Exiobase.	categories (>5% of total), replaced by Dutch expenditure data.			
Perspective used for footprint composition	Contribution and hotspot analysis	Contribution analysis	SPA, but simplified into hotspot analysis per GHGP scope	Contribution analysis, global level only	SPA, global level only
Total healthcare sector footprint (Mt CO_2-eq)	17.6	11	13.3	15.8	13.4
Result for Scope 1 (Mt CO_2-eq)	1.6	4.2	1.6	-	-
Result for Scope 2 (Mt CO_2-eq)	2.0		0.7	-	-
Result for Scope 3 (Mt CO_2-eq)	13.7	6.2	11	-	-
Outside scope (Mt CO_2-eq)	0.4	0.6	n/a	n/a	n/a
Healthcare sector share in total Dutch consumption footprint	7.3%	7%	5.9%	8.1%	5.8%[e] /4.0%[d]
Dutch consumption footprint (Mt CO_2-eq)	241	163	225[f]	195[f]	231[e] /333[f]

a) National accounts (single region) of the British Office for National Statistics (ONS) for 2004, expanded into an MRIO with data from Eurostat, GTAP, OECD and IDE-JETRO
b) Excluding imports (care provided to Dutch residents abroad), including exports (care provided to non-residents in the Netherlands)
c) Including imports (care provided to Dutch residents abroad), excluding exports (care provided to non-residents in the Netherlands)
d) As reported by Lenzen et al. (2020)
e) Footprint based on percentage derived from 'Eora Explorer' on the Eora website.
f) Derived from the climate footprint and the percentage of the national consumption footprint as reported in the study by Lenzen et al.

The underlying differences between the models become more apparent when comparing the disaggregated footprint, in terms of both absolute values and the composition of the healthcare sector footprint (see last seven rows of Table 10). For example, the contribution analysis by Gupta Strategists reveals that energy (Scopes 1 and 2) is the largest contributor to the climate footprint at 38%, while that figure is 15% in this study (the impact of purchased fuels falls under Scope 3 in our study; see Appendix G). The hotspot analysis by HCWH and Arup shows that Food, catering and accommodation make the largest contribution to the climate footprint at 23%, while that figure is 6% in this study. As described in the uncertainty analysis (see Section 2.2.4), the use of different MRIOs can have a major effect on the results. To further explain the differences between the different footprint calculations, a thorough investigation into differences in the model choices, reported environmental stressors and design of the MRIOs would be required. However, this falls outside the scope of this study.

The MRIO, the reference year and the greenhouse gases included also affect the calculation of the national consumption footprint (see last row of Table 10). Due to the differences between the models, it is interesting to examine not only the absolute values, but also the contribution of the healthcare footprint to the total Dutch consumption footprint according to these models, calculated using their respective MRIO and for the respective greenhouse gases. The percentage of the national climate footprint calculated in this study (8%) falls within the range of previous calculations (6-8%). Viewed from a broader perspective, this suggests that current differences in system boundaries have little effect on the result of the healthcare sector's contribution to the national footprint.

Comparing national healthcare sector footprint calculations of other countries

The studies by Pichler et al.[4], Lenzen et al.[26] and HCWH and Arup[6] extensively discuss how the total footprint(s) of healthcare sectors differ from each other internationally. The studies show that so-called high-income countries (as defined by the World Bank[59]) have a relatively high per capita footprint. The per capita climate footprint is strongly correlated with healthcare expenditure, the national energy mix and the national energy intensity. According to the study by Pichler et al., the Dutch healthcare footprint contributes the most to the national consumption footprint compared to other OECD members, and the Netherlands has the highest per capita healthcare climate footprint after Luxembourg. However, according to the study by HCWH and Arup, the Dutch healthcare sector is not a top emitter (top 5), but a major emitter. The study by HCWH and Arup is not a specific national study like this RIVM study. The results for the disaggregated climate footprint are therefore compared to the more extensive national studies conducted for other countries in recent years.

This comparison shows that medicines and other chemical products also play a major role in the contribution analysis of the healthcare footprint for other countries. In the contribution analysis of the Japanese study[18], the purchase of medicines is the largest contributor to the climate footprint (18%), followed by electricity (17%). The contribution analysis in the study for Austria[22] indicates that pharmaceuticals as a product group also contribute the most to the total footprint (21%), followed by medical consumables (17%). In the study for the NHS in England[24], the product group *Pharmaceuticals and chemicals* likewise makes the largest contribution to the footprint (20%). The study for China[23] even shows that medicines contribute 55% to the total climate footprint for the Chinese healthcare sector. In the study for Australia[19] and Canada[21], only the consumption of pharmaceuticals is reported separately. The purchase of medicines is aggregated in the impact of care services. However, the study for Australia does indicate that the impact intensity of *Pharmaceuticals* and *Medication* is much higher than the other impact intensities used. Even then, direct consumption of medicines is the largest contributor to the climate footprint of the Canadian healthcare sector at 25%. Finally, Pichler et al.[4] show that, worldwide, *Pharmaceuticals/chemicals* are responsible for 20% of the climate footprint of the combined healthcare footprint of the OECD countries.

At 38%, the contribution of medicines and other chemical products to the total climate footprint of the Dutch healthcare sector turns out to be relatively high for a high-income country. Nevertheless, compared to other goods and services, this product group also contributes the most to the healthcare sector footprint in all these national studies in other countries.

2.4.2 Limitations

Interestingly, the calculations showed that healthcare makes a significantly larger contribution to the national abiotic materials extraction footprint (13%) than to the climate footprint (7%). Further research should focus on the question of whether this is caused by a 'disposables culture' in the healthcare sector, for instance, or by potential uncertainties in the model. Conversely, the contribution of waste production to the national footprint is smaller (4%) than the contribution of the climate footprint. This could be due to other sectors being more or less dominant in the national footprint, but there are many more uncertain factors. For waste production specifically, there is a mismatch in the time frame: the waste data are from 2011, while the footprint calculation is for 2016. However, the uncertainty could also be caused by classification mismatches, due to factors such as the level of aggregation or uncertainty in the MRIO data. Finally, it is not certain whether the footprint calculation is complete.

Aggregation level in EE-MRIO
EE-IOA is a method that can be used to quickly make a relatively complete footprint calculation for an economy (or a part thereof). However, because it is a macro-economic method and the data is aggregated at a high level (sectoral or combined sectors), EE-IOA is not sub-sector or product-specific. Aggregation problems are therefore inherent in EE-IOA calculations, and that is precisely why the results are most useful for calculating the footprint for a country and/or sector, rather than for one specific product or product group. The aggregation level of the sectors depends on the IO table. This discussion covers two Exiobase categories whose aggregation level has a major impact on the calculation and the interpretation thereof: *Health and social work* and *Chemicals n.e.c.*

Exiobase v3 combines and health and welfare services into one category (*Health and social work*). Consequently, the results only provide general insights for all types of care services, while costs and impacts may differ between hospitals and long-term care facilities, for instance. For some other countries, however, there is a distinction between different care functions in the input-output sector categories (see Table SI 2.1 and 2.2 in Lenzen et al.[26]). Similarly, expenditure on Pharmaceuticals & consumables is covered by Exiobase's *Chemicals n.e.c.* This is a heterogeneous product group that includes products with different prices and volumes (e.g. basic soap versus pharmaceutical products). As a result, it is unclear how representative the calculated impact – the largest contribution to the footprint for all impact categories – is for this product group. In addition to the so-called aggregation bias, which makes it unclear whether a specific product is correctly represented within a product group, there is also a classification mismatch because not all medicines can be regarded as chemical products.

For future analyses, it is recommended to disaggregate some of the sector data, starting with the categories *Health and social work* and *Chemicals n.e.c*.. *Health and social work* could be broken down into different types of care providers, based on the purchasing data collected. This kind of useful overview of purchasing data for the various types of care providers does not yet exist. It is currently being developed as part of the knowledge base development. For *Chemicals n.e.c.*, future studies should examine how this category could be broken down into more specific sub-categories, with at least one sub-category specifically for pharmaceuticals. *Chemicals n.e.c.* is a heterogeneous group that includes products with different prices and volumes (e.g. basic soap versus pharmaceutical products). As a result, it is unclear how representative the calculated impact is for the expenditure category. A study[60] supervised by RIVM shows that the impact per euro of *Basic pharmaceuticals and pharmaceutical preparations* produced in the Netherlands on the climate footprint and abiotic raw materials footprint is three and seven times smaller, respectively, than that of *Chemicals and chemical products* produced in the Netherlands. This was calculated using the SNAC-Exiobase, where a distinction is made between the two types of products for the Dutch section of the MRIO table only. However, it is expected that the majority of pharmaceuticals are imported. According to Exiobase, 2.4% of *Chemicals n.e.c.* consumed in 2016 were imported (see appendix C). The values for the Netherlands probably have little effect on the average weighted environmental impact per euro for *Chemicals n.e.c..* Once these figures are also available for other producing countries, a more accurate analysis can be performed: not only of the impact of pharmaceuticals, but also of the total footprint, since pharmaceuticals make up a large part of that. In the MRIO WIOD,[61] for example, there is a category for *Basic pharmaceuticals and pharmaceutical preparations* that is available for all regions, but WIOD has trade-offs such as a lower sector resolution and fewer available environmental stressors (see Section 2.2.1.3). For an even more accurate result, and to gain insight into how different pharmaceuticals and/or chemical products contribute to this impact, a product-specific analysis is needed, such as a lifecycle analysis (see Chapter 3).

Disaggregation of the two Exiobase categories mentioned helps to produce more specific insight into potential actions for different sub-sectors of the healthcare sector, and would increase the accuracy of the results for products under the heading 'chemical products'. As for the expenditure on consumptive care products, (Pharmaceuticals & consumables and Therapeutic aids), it would also be helpful to make more of a distinction between the different products in these expenditure categories. After all, these two categories cover a wide variety of products. If Pharmaceuticals and consumables are further broken down into items such as paper, textiles, plastic and other chemical consumables, the footprint for Pharmaceuticals & consumables can be more accurately determined.

Uncertainties in EE-MRIO
In future studies, it is also recommended to investigate the uncertainty of the results using a statistical analysis, especially for the less analysed impact categories. The variation in results due to the use of different EE-MRIOs could be countered in the future by applying a more structurally updated and internationally recommended MRIO made available by a large international organisation, such as the OECD's ICIO database or Eurostat's Figaro[62]. This study did not select such an MRIO due to the low current sectoral resolution and the limited number of environmental stressors. Finally, it is also possible within Exiobase to replace the IO data for the Netherlands with a Statistics Netherlands database designed specifically for that purpose[63]. This is called a Single-country National Accounts Consistent MRIO (SNAC-MRIO). The SNAC Exiobase was not used in this study because it offers fewer environmental extensions (only greenhouse gas emissions and raw materials extraction) than the original Exiobase. In addition, the public SNAC-MRIO has been aggregated at a higher sectoral level due to potentially traceable sensitive information for certain industries.

Completeness of the footprint calculation
The use of EE-IOA to calculate the sectoral footprint is accompanied by a limitation of the system boundaries. In calculating the sectoral footprint, the impact of home consumption of care products and services is not taken into account. Because all environmental stressors caused by households (such as emissions from gas heating, driving a car, etc.) are combined into one account in the MRIO, the exact source of the stressor cannot be determined. One source of environmental impact of home consumption has been added, namely the release of propellants when using pMDIs. It would be valuable to conduct further research into other environmental impacts that have not yet been included, such as those resulting from home treatments. The environmental impact of capital investments by the healthcare sector is also excluded in the current approach, since Exiobase combines the gross fixed capital formation of all sectors in one account, as part of the final demand. Because sustainability strategies also include investments in long-term impact, for the sake of completeness, future studies should examine whether impact relating to investments in the healthcare sector (e.g. construction of healthcare facilities) could be added to the footprint results. Estimates could be made for this, for example based on spending data and/or a bottom-up analysis such as LCA.

2.4.3 Use of the method and recommendations

Supplementing EE-IOA results with LCA data
In this study, product-specific data (including LCA results) were used to supplement and thus improve the EE-IOA environmental footprint results. When integrating such data into the EE-IOA results, a few points should be considered. The available bottom-up impact data do not always include the same phases of the lifecycle as the EE-IOA, nor are results reported for the same impact categories or the same characterisation factors used. Impact categories that are less standardised, such as abiotic raw materials use, require attention to ensure that the data match the EE-IOA impact categories, while waste streams are excluded from an LCA entirely. To integrate the current data into future work more easily, the EE-IOA results could be converted into impacts with a commonly used LCA characterisation. A top-down study like this could serve as a guide for future bottom-up estimates. If the same impact categories, characterisation and lifecycle phases are chosen, bottom-up estimates can be more easily incorporated into the top-down footprint. Furthermore, new bottom-up estimates can be put into perspective more easily by measuring approximately how much these contribute to the national healthcare sector footprint.

Monitoring
In this study, a 'snapshot' calculation was made of the environmental footprint of the healthcare sector in 2016, but this method is in principle applicable to all years for which MRIO data is available. At the time this report was written, data also became available that can be used to calculate the footprint for the years between 2016 and 2022. In these calculations, the annual impact-per-euro figures (i.e. impact intensities) would then be re-calculated based on the macro-economic trade data in the MRIO, which would subsequently be used for the footprint calculation for that year. It should be noted that the impact of sustainability is not always reflected in the results for the new years, if such impact has actually taken place. With EE-IOA alone, no distinction can be made between sustainable purchases within a single product group, e.g. within *(Manufacturing of) office machinery and equipment.* The same average impact intensity will be calculated in all cases, regardless of whether or not the item is, for example, a 'greener' printer. EE-IOA assumes that the impact is linear with respect to expenditure. A more expensive, more sustainable alternative can therefore have an even greater impact. To determine the impact of a sustainability strategy – in which the more sustainable alternative falls under the same MRIO product group as the standard product – on the footprint, a bottom-up study is needed.

Scenario analysis
Lastly, this EE-IOA footprint calculation serves as a basis for scenario analysis. EE-IOA is a suitable method for calculating rough 'what-if' scenarios for sustainable[64] and circular[65] transitions. Compared to LCA, EE-IOA can more easily calculate the impact of changes (deep) in the chain. In addition to calculating the impact of 'more direct' strategies (such as reducing food waste), it can also calculate the impact of the global energy transition on the healthcare sector footprint predicted by the International Energy Agency[66]. as was done by HCWH and Arup[67].

2.4.4 *Conclusion on environmental footprint of Dutch healthcare sector*

This report presents the first sector-wide footprint study for the Dutch healthcare sector in which multiple environmental impact categories are analysed, and that is intended to help formulate sustainability strategies and objectives. We have demonstrated that a set of environmental impact categories broader than climate change (including abiotic raw materials extraction, blue water consumption, land use and waste production) provides more comprehensive insight into the healthcare sector's impact on the environment. EE-IOA, the primary method used in this study, has proved to be a suitable method for calculating the total environmental footprint, identifying sectoral hotspots and allowing consistent comparison between different environmental impact categories. The results are also presented from two perspectives: a contribution analysis and a hotspot analysis. This provides insight for the first time into which products and activities contribute to different environmental impact categories, and where these impacts arise. The results also show that, compared to other environmental impact categories, greenhouse gas emissions and waste production occur more operationally and within the Netherlands, and therefore offer direct potential avenues for action to work in a more climate-neutral manner and reduce waste. For the other impact categories, the impact mainly seem to occur in the chain of purchased goods and services. This requires different sustainability strategies, such as green purchasing and cooperation within the value chain.

The present study has used the most recent national statistics in combination with the MRIO Exiobase, adopted the broad definition of healthcare (health and welfare) to align with the healthcare sector in the MRIO, and added the healthcare sector-specific impacts to the footprint. Our approach therefore differs from that of other studies on the Dutch healthcare sectors, which partly explains the observed difference between the results for the climate footprint. Nevertheless, the aggregated result for the climate footprint is comparable to the other studies when considering the healthcare sector's contribution to the national consumptive footprint (6-8%). As in other studies (for the Netherlands and other countries), the contribution analysis shows that the impact of medicines and other chemical products as a product group makes the largest contribution to the climate footprint. It is also evident that this product group accounts for a larger share in the other impact categories. Due to the high aggregation level in the MRIO data and the healthcare expenditure, the effect of medicines and other chemical products using a bottom-up analysis is examined in Chapter 3.

In short, the state-of-the-art environmental footprint presented in this study provides a clearer picture of the environmental impact of the Dutch healthcare sector, including which product groups contribute, where the impact take place and how this differs for each environmental impact category. The model serves as a starting point to further improve insights with steps of disaggregation and additional bottom-up data, and can be used for scenario modelling to estimate the impact of sustainability strategies. This study is relevant for both policymakers and healthcare organisations that wish to work on climate mitigation, along with other societal challenges such as the transition to a circular economy (material extraction and waste production), feeding the growing world population (blue water consumption and land use) and biodiversity (same as above), to create a healthy future for all. A general reflection, discussion and further recommendations are presented in Chapter 5.

3 In-depth analysis of chemical products, including pharmaceuticals

Chapter 2 shows that the Dutch healthcare sector has a significant environmental footprint that goes beyond climate change alone. Three quarters of the climate footprint comes from goods and services purchased by the Dutch healthcare sector. Out of all the products and services that are purchased, chemical products – with the largest share of expenditure spent on pharmaceuticals – contribute the most to climate change, extraction of resources, water consumption, land use and waste production (see Figure 8 in Chapter 2).

In order to take a step towards sustainability, a better understanding of the environmental impact of chemical products is required. This requires ascertaining which individual chemicals or pharmaceuticals have the greatest impact and in which part of the life cycle this environmental burden takes place. This chapter outlines the two ways in which greater insight has been gained into the environmental impact of chemical products and into what else is needed to increase this insight or to be able to predict impact. The first approach consists of a bottom-up approach, involving the acquisition and assessment of data on life cycle assessments (LCAs) of pharmaceutical products from existing literature (see section 3.1). The second approach involved carrying out a review into predicting and estimating life cycle impact using artificial intelligence (see section 3.2).

3.1 Literature review regarding the environmental footprint of chemical products

3.1.1 Introduction

As outlined in Chapter 2, medicines and other chemical products contribute to the environmental footprint of the Dutch healthcare sector to a significant degree. The reported climate footprint of this group of products is similarly high in other countries. Procurement of pharmaceuticals and other chemical products contributes 20% of the climate footprint of the healthcare sectors of all OECD countries [4]. However, studies on the healthcare sectors of individual countries, such as Japan (18%)[18], Austria (21%)[22], the UK (20%)[24] and China (55%)[23], also report a significant contribution of chemical products, including pharmaceuticals. An in-depth analysis of the environmental footprint of chemical products, including pharmaceuticals, is therefore not just relevant to reducing the footprint of the Dutch healthcare sector. Gaining more insight into this footprint likewise provides other countries with prospects for reducing the environmental impact of their healthcare sector.

Adding detail about chemical products to the national environmental footprint of the healthcare sector creates a hybrid footprint analysis, which refers to the combination of generic national data (calculated using input-output analysis, IOA) and specific data (calculated using LCA), as has been done in this report. A national environmental footprint of pharmaceuticals will ideally combine statistics on medication dispensing and LCA data. Within this LCA data, a distinction is made between inventory data, such as emissions, raw material use and energy consumption, and impact, i.e. the quantified effect caused by the emissions and extraction of resources.

A review into the available LCA data on pharmaceuticals shows whether combining the footprint calculations from the literature with national statistics on medication is a viable route. In addition, it was examined whether the literature revealed any sustainable alternatives. Finally, communication on this issue contributes to a greater awareness of the sustainable use of pharmaceuticals and chemical products in healthcare.

The purpose of the chapter is to explore how LCA studies can contribute to a more detailed national environmental footprint of chemical products in healthcare. This information can ultimately be used to provide a better understanding of the environmental impact of (groups of) pharmaceuticals as part of the overall, national environmental footprint of the healthcare sector. The information serves to provide an overview of where and how the environmental impact of pharmaceuticals takes place (hotspots), what the opportunities could be to reduce environmental impact or which issues out to be prioritised to achieve a greater degree of sustainability.

3.1.2 Method

Searches were carried out into LCAs for pharmaceuticals and chemicals used in healthcare using the PubMed Scopus and Google Scholar search engines. The searches used combinations of search terms, such as ‘Life Cycle Assessment/Analysis’, ‘LCA’, ‘medicines’, ‘chemicals’, ‘pharmaceuticals’, ‘API’, ‘health care’, ‘hospitals’, ‘footprint’, ‘green deal’ and ‘production’. The focus was on the production process and the use phase of pharmaceuticals and chemicals in healthcare. However, the end-of-life phase likewise falls within the scope.

In addition, we reached out to various stakeholders within the sector. In order to refine the search and to retrieve more (primary) LCAs, discussions were held with employees of pharmaceutical companies (AstraZeneca and Johnson & Johnson), with scientists from Ghent University in Belgium and with experts in the field of sustainability or pharmaceuticals (National Institute for Public Health and the Environment, RIVM).

National statistics on the use of pharmaceutical products were obtained from GIPdatabank. The National Health Care Institute (Zorginstituut Nederland) collects dispensing figures per type of medication in the GIPdatabank, to which health insurance companies provide statistics each year. Over-the-counter medicines are not included in these statistics.

3.1.3 Results

The collected literature shows that most research has been carried out on pharmaceutical products used for anaesthesia[68-71], inhalers for asthma and COPD[72-74] and analgesics[22,75,76]. Research has likewise been carried out into the climate footprint of antibiotics[22]. These studies have therefore been used for the further interpretation of the suitability of a footprint calculation of Dutch pharmaceutical use.

In a number of studies, the scope of the LCAs examined is solely on the production component of the life cycle (cradle-to-gate, often from extraction of resources to the factory/gate). In other studies, the focus is on the life cycle as a whole, i.e. cradle-to-grave. In addition to the environmental impact of the production process, cradle-to-grave studies also take into account the use phase and the end-of-life phase (waste) of the product. Demarcations such as gate-to-gate (confined to a factory, for example) or cradle-to-cradle (second life cycle or beyond) are also used, however, the latter is less appropriate in this case. Little data was found on waste treatment methods other than wastewater treatment. Finally, studies frequently only reported on the climate footprint (in CO2 equivalents, CO2-eq), and not on other environmental impact categories.

3.1.3.1 Anaesthetics

A cradle-to-grave LCA carried out by Sherman et al.[71] into four anaesthetic gases intended for inhalation (desflurane, sevoflurane, isoflurane and nitrous oxide) and one intended for intravenous (IV) administration (propofol) shows that more sustainable choices can be made in methods of anaesthesia. Desflurane is the most harmful to the climate in terms of greenhouse gas emissions, followed by sevoflurane and isoflurane. Propofol is the most climate-friendly alternative. There are also other non-inhalation anaesthesia techniques that are less harmful to the environment, such as intravenous anaesthesia and neuraxial of peripheral nerve blocks.[71] Greenhouse gas emissions increased significantly for all vaporous anaesthetics when administered with a combination of oxygen and nitrous oxide (N_2O, or laughing gas). N_2O is a standard carrier gas for inhalation anaesthetics in clinical applications. The gas has a very strong global warming potential over a period of 100 years (usual period). With a GWP100 of 298, 1 kg of nitrous oxide (N_2O) is just as harmful to the climate as 298 kg of carbon dioxide (CO_2).[70]

A combination of oxygen and air would provide a more sustainable form of administration[71]. The researchers recommend that desflurane and nitrous oxide should only be used if they were to reduce morbidity (disease rate) and mortality (death rate) in respect of the alternatives. In addition, it is recommended that the use of unnecessarily high gas flow rates for all inhalation anaesthetics should be avoided.
A UK cradle-to-grave study from 2021 on inhalation anaesthetics and intravenous anaesthetics indeed shows that the inhalation gas sevoflurane can have a similar climate footprint to propofol when administered at the slowest possible gas flow rate, with oxygen and air acting as carrier gases instead of nitrous oxide and if vapour capture technology (VCT) is used for administration[69].

Alternative administration by anaesthetists can therefore reduce the climate footprint of inhalation anaesthetics. However, the researchers also highlight the fact that VCT is as yet a type of technology that is used infrequently. In addition, they highlight the fact that propofol would, in turn, entail significantly lower greenhouse gas emissions than inhalation anaesthetics used with VCT if the medication were to be produced using renewable energy.

The fact that there are more climate-friendly alternative anaesthetic drugs also becomes apparent from a study by Parvatker et al.[68]. In this study, a cradle-to-gate LCA was carried out on twenty different injectable anaesthetic agents in bulk packaging, examining the various associated greenhouse gas emissions. The impact of the drugs on the climate vary significantly, falling within a range of 11 kg of CO_2 equivalent (succinylcholine) to approximately 3,000 kg of CO_2-eq (dexmedetomidine) per kg of active pharmaceutical ingredient (API). The scientists suggest that these differences may be related to the number of steps associated in the synthesis of each individual substance. This is based on a weak positive trend (R^2=0.39) between the greenhouse gas emissions of the anaesthetics and the number of synthesis steps of each substance.

A literature review carried out by McGain et al.[70] on sustainability aspects of anaesthetics in critical care (no further definition) recommends avoiding the use of anaesthetic gases with a high global warming potential, expressed in GWP, and to reduce the overall use of anaesthetic gases.

3.1.3.2 Inhalation medication for asthma and COPD

Symptoms associated with asthma and COPD (chronic obstructive pulmonary disease) can be alleviated with the use of pressurised metered dose inhalers. Pressurised metered dose inhalers (pMDI) are also known as ‘metered dose inhalers’ or ‘inhalers’.

Table 11 provides an overview of the various studies conducted on climate impact in the life cycle of inhalers. The table shows that the types of pMDI on the market have different climate footprints over the course of their life cycle. The Proventil® pMDI in Goulet et al.[73], for example, uses 60% less norflurane (HFC134a) than the market standard. According to Jeswani & Azapagic[74], the impact of this inhaler is comparable to another type of pMDI that uses less propellant, Airomir®. Another explanation that can account for the differences is the calculations used to determine the global warming potential. Wilkinson et al.[77] use a global warming potential (GWP) of 1,300 for HFC134a, whereas Jeswani & Azapagic[74] uses a GWP of 1,550 (including climate-carbon feedback, the assumption that carbon reservoirs weaken significantly due to global warming). A single dose is defined as two inhalations/actuations with a pMDI and only one inhalation using a dry powder inhaler.[78] Jeswani & Azapagic[74] indicate that the recommended dose for metered dose inhalers varies from one puff (for mild symptoms) to 4 puffs (for severe symptoms) per dose.

Table 11 Overview of the results from the literature on the climate impact for pressurised metered- dose inhalers and dry powder inhalers.

Source	**g CO_2-eq /dose HFC-134a pMDI**	**g CO_2-eq /dose HFC-227ea pMDI**	**g CO_2-eq /dose DPI**	**Product name**	**Remarks**
Jeswani & Azapagic[74]	263	697	9	DPI: Diskus inhaler	Spacers not included for pMDI. Cradle-to-grave.
Wilkinson et al.[77]	260-394	590	-	HFC134a: ICS/LABA such as Fostair® HFC227ea: ICS/LABA such as Flutiform®	Including through FDA report, patents. Scope unclear.
Goulet et al.[73]	97	-	-	HFC134a: Proventil®	Proventil® inhaler that already uses 60% less propellant than comparable products. Cradle-to-use phase, without packaging and transport.
UNEP[78]	200-300	600-800	8-60	Not specified	Emissions from production and use
Orion Pharma[79]	-	-	3.05 – 9.53	DPI: Easyhaler®	6 types of Easyhaler powder inhalers, cradle-to-grave. Industry data.
Fulford et al.[72]	-	-	1.54 – 15.77	DPI: Breezhaler®	Breezhaler® 90 day & 30 day dry powder inhalers delivering IND/MF or IND/GLY/MF. 1 capsule per day = 1 dose. Cradle-to-grave, with capsule production, but without API.

* HFC: Hydrofluorocarbon; HFC134a: 1,1,1,2-Tetrafluoroethane; HFC227ea: 1,1,1,2,3,3,3-Heptafluoropropane. One dose = 2 inhalations (puffs) from the metered-dose inhaler or 1 inhalation from a dry powder inhaler. DPI: dry powder inhaler. ICS: Inhaled Corticosteroids; LABA: Long-Acting Beta-Antagonists. Indacaterol acetate (IND), glycopyrronium bromide (GLY) and mometasone furoate (MF) are substitutes for cases where inhaled steroids and beta-antagonists do no work properly.

The propellants in these inhalers have a significant global warming potential[74]. As the footprint calculation in Chapter 2 shows, the use of pMDIs leads to a contribution of almost 0.4% to the climate footprint of the Dutch healthcare system. Dry powder inhalers[74] and electric nebulisers[73] are alternatives with a lower climate impact. The production of one particular type of dry powder inhaler - the Diskus -, however, requires more raw materials than for pMDI.[74] A caveat made to this study by Wichers & Pieters[80] is that the production of spacers has not been included for pMDI. Spacers are needed when using pMDI in order to be able to inhale properly. Patients of any age have to use a spacer to be able to inhale a sufficient amount of inhaled corticosteroids. According to Jeswani & Azapagic[74], the higher consumption of resources of the Diskus dry powder inhaler compared to the pMDI leads to an increase in the environmental impact of the production of the Diskus, including toxicity to humans, marine eutrophication and depletion of fossil resources. The environmental impact of the two are not subsequently weighed against one another by Jeswani & Azapagic[74].

3.1.3.3 Painkillers

LCA studies are available for five types of active ingredients in painkillers: morphine, ibuprofen, naproxen, paracetamol and acetylsalicylic acid (aspirin). A number of these substances are not only used for pain relief but are used for other indications, one example being the use of acetylsalicylic acid as a thrombosis inhibitor. The application and possible footprint for these indications will likewise be discussed here.

A cradle-to-gate LCA into the production of IV morphine (100 mg/100 ml) shows that the production of 100 mg of final packaged morphine contributes 204 g of CO_2-eq to climate change[76]. The majority of which (90%) is caused by the final production steps: sterilisation and packaging. The scientists indicate that there may also be opportunities to increase sustainability, given that the sterilisation and packaging of pharmaceuticals is a universal process and is not limited to morphine alone. In terms of CO_2 emissions, the study compares the production of a single dose of morphine to driving one kilometre in an average Australian car or to the one-off use of a plastic anaesthesia drug tray.

The researchers recommend that the pharmaceutical industry reduce their climate footprint through more efficient use of energy and by using renewable energy, by focusing on recycling of inter alia PVC plastic and by making improvements to the packaging of substances (making them more sustainable).

A study by Parvatker et al.[68] referred to previously into various anaesthetics also looked at morphine. With a climate impact of 1,506 kg or CO_2 equivalent per kg of morphine for the synthetic production of morphine, this differs from the 240 kg of CO_2 equivalent for 1 kg of morphine in bulk form, as argued by McAlister et al.[76] Parvatker et al.[68] account for the difference between these findings in terms of a difference in the synthesis process. It appears that the synthetic production of morphine has a greater effect on the climate than when the main component of morphine is produced using natural opium from poppies[68].

Siegert et al. [75] carried out a full cradle-to-grave LCA into the following environmental impact categories of ibuprofen tablets: climate change, toxicity to humans (both carcinogenic and non-carcinogenic), ecotoxicity and consumption of abiotic resources. The geographical scope was Germany and included packaging and distribution of the tablets. The researchers concluded that the production step (manufacturing of the active pharmaceutical ingredient, galenic formulation and packaging) of this medicine makes the largest contribution to all types of environmental impact in the life cycle, whereas the types of environmental impact of the use phase and end-of-life phase are negligible. Distribution contributes to the overall climate footprint to the amount of slightly over 25%[75]. The scientists do, however, note that little is known about the environmental impact of ibuprofen metabolites. Ibuprofen is likely to be placed on the priority list of substances of the Water Framework Directive, in which case European standards will apply, which may lead to need for sewage treatment plants to be adapted[81]. This will likewise use up energy and materials.

A study conducted by Weisz et al.[22] examined the impact of the Austrian healthcare sector on the climate and inter alia involved a review of the climate impact of four different analgesics. Emissions for analgesics were calculated using a stoichiometric approach, based on the chemical reactions of the API synthesis process, where emission factors (derived from the Ecoinvent database v3.2) were established for individual API components of each analgesic. Other components (excipients) and production steps (such as sterilisation, packaging and transport) have not been taken into account in this calculation. Naproxen, ibuprofen, aspirin and paracetamol contribute to climate changes to the amount of 2.3, 3.1, 4.9 and 7.8 grams of CO_2 equivalent per gram of active ingredient respectively. The scientists also highlight the fact that despite their low emissions intensity (in grams of CO_2 equivalent per gram of API), for example, compared to antibiotics, the analgesics do make a significant annual contribution to overall emissions due to medication use and due to the large volumes in which these drugs are used. In 2014, the four types of painkillers produced 0.69 kilotonnes of CO2-q worth of emissions in Austria. The following sections will calculate the emissions of analgesics in the Netherlands based on the emissions factors of Weisz et al.[22].

Acetylsalicylic acid (aspirin) sits at number 8 of the Top 500 of pharmaceuticals based on the number defined daily doses (DDDs) in the Netherlands, when it is prescribed as a platelet aggregation inhibitor (ATC code B01AC06)[82]. A DDD is intended as a unit of calculation for the comparison of pharmaceuticals based on dose-equivalent amounts. The World Health Organization (WHO) has established DDDs for drugs for certain (key) indications. The weight of a DDD of a drug is available via the WHO database and the Pharmacotherapeutic Compass (Farmacotherapeutisch Kompas, FK)[83]. The annual number of DDDs in the Netherlands of the analgesics described by Weisz et al.[22] is outlined in Table 12 and Appendix K. The table also includes combination preparations administered using the analgesics.

The information in Table 12 only relates to products that have been declared to health insurance companies. Acetylsalicylic acid as an analgesic (ATC code N02BA01) only appears on the list in small volumes given that only a small number of parenterally administered doses have been declared. The amounts of oral administration are not included in the list, given that aspirin is also sold at drugstores and is subsequently not included in the data held by health insurers. If a drug is not reimbursed under the Health Insurance Act, it is not reported in the GIPdatabank. Given that the annual DDDs of over-the-counter (OTC) pharmaceuticals are not shown in the statistics of GIPdatabank, the environmental pressure of a large portion of the analgesics cannot be calculated at this stage.

It is striking that the composition of paracetamol should lead to relatively high emissions of 23.4 g of CO_2-eq per DDD. Paracetamol is obtained by means of a reaction of 4-aminophenol with acetic anhydride, which forms an amide bond and yields acetic acid as a by-product.
The production of acetic anhydride has a relatively high climate footprint[22].

Table 12 only shows the climate footprint of resources used for the active pharmaceutical ingredient (API), which is only part of the impact of the overall chain of these drugs. By comparison, the climate impact across the entire life cycle of ibuprofen in Siegert et al.[75], at 36.25 grams of CO_2-eq per gram of API is more than ten times greater than the calculation of Weisz et al. in Table 12. Also, the formulation of ibuprofen tablets with excipients has a significant environmental pressure[84]. It can therefore be expected that the greatest climate impact of these drugs should take place in the formulation and distribution stages. In addition, Weisz et al.[22] have not taken into account other types of environmental impact, such as toxicity and water consumption. It is therefore not yet possible to weigh these drugs up against one another based on this table. The table does, however, show how the dosage and administration can have an effect on the climate footprint of the resources used for the API. It allows for an assessment of which APIs should be examined further to ascertain how and where in the chain sustainability improvements can be achieved. This data can also be used in follow-up studies in relation to the overall life cycle, with multiple types of (environmental) impact categories.

Table 12 The number of daily doses (DDDs) in 2020 from the GIPdatabank and emission factors of resources for the active ingredient of acetylsalicylic acid, ibuprofen, naproxen and paracetamol and combination preparations from Weisz et al.[22] (2020). Please note that this table is restricted to the climate footprint of a section of the life cycle and that no other types of environmental impact categories, such as land use, waste or ecotoxicity, have been taken into account. As such, on the basis of this table, no statement can be made as to whether the use of a particular drug is more sustainable than the other. Over-the-counter pharmaceuticals have not been taken into account.

ATC code, active pharmaceutical ingredients (product name)	DDD in 2020	g of API /DDD	Administration	g of CO_2-eq g of API	g of CO_2-eq /DDD
B01AC06 Acetylsalicylic acid (Aspirin protect ®)	211,497,137	0.1	O	4.9	0.49
B01AC30 Clopidogrel/acetylsalicylic acid	44,536	0.075	O	4.9	0.37
N02BA01 Acetylsalicylic acid	1,151	1	P	4.9	4.9
N02BA51 Acetylsalicylic combination preparations	44,181	2.7	O	4.9	13.23
M01AE01 Ibuprofen	10,211,585	1.2	O,P,R	3.1	3.72
M01AE02 Naproxen	36,748,218	0.5	O,R	2.3	1.15
M01AE52 Naproxen with esomeprazole	100,870	0.5	O	2.3	1.15
N02BE01 Paracetamol	.	3	O,P,R	7.8	23.4
N02AJ13 Tramadol with paracetamol	7,275,684	3	O	7.8	23.4

Administration: O = oral, P = parenteral, R = rectal

One DDD of acetylsalicylic acid as a platelet aggregation inhibitor (ATC code B01AC06)[83] has been established at one tablet. Because the WHO does not specify the DDD any further, we have assumed an amount of 100 mg if the brand Aspirin Protect ® is used[85]. In 2020, the number of DDDs for this drug was 211,497,137. The emissions in CO_2-eq in the Netherlands for 2020 is therefore estimated at 211,497,137 DDDs x 0.1 g x 4.9 g of CO_2-eq = 0.1 kilotonnes of CO2-eq (please also see Table 13). The weight per DDD is higher if acetylsalicylic acid is used as an analgesic. The daily dose is consequently 3 grams for oral and rectal use and 1 gram for parenteral administration (expressed as lysine acetylsalicylate in such cases; ATC code N02BA01)[83].

Table 13 provides an overview of the climate footprint of the resources used for the APIs of aspirin, ibuprofen, naproxen and paracetamol (combinations). Between 2016 and 2018, the climate footprint calculated for these drugs had stabilised between 1.1 and 1.4 kilotonnes of CO_2-eq per year. The figures for 2019 and 2020 show a lower trend for the total emissions of these four types of analgesics, given that DDDs of paracetamol as a single API were not reported at the time. It should also be noted that Weisz et al.[22] only calculated the emissions factor for the production of the components of the API. The formulation into a pharmaceutical product, the use of excipients, transport, packaging, the use phase and the end-of-life phase are not covered by this emissions factor. This leads to an underestimation of the overall climate footprint of the end products. The emissions of the full life cycle of analgesics will therefore be higher.

Table 13 Dutch climate footprint of resources used for the active pharmaceutical ingredients of acetylsalicylic acid, ibuprofen, naproxen and paracetamol in kilotonnes of CO2-eq based on the figure provided by GIPdatabank and emissions factors from Weisz et al. [22]. Please note that the table only relates to the climate footprint of part of the life cycle and that over-the-counter drugs have not been taken into account.

Active pharmaceutical ingredients (ATC codes)	kt of CO_2-eq in 2016	kt of CO_2-eq in 2017	kt of CO_2-eq in 2018	kt of CO_2-eq in 2019	kt of CO_2-eq in 2020
Acetylsalicylic acid, all combinations (BA01AC06, BA01AC30, N02BA01, N02BA51)	0.11	0.11	0.11	0.11	0.10
Ibuprofen (M01AE01)	0.05	0.05	0.05	0.04	0.04
Naproxen, all combinations (M01AE02, M01AE52)	0.04	0.04	0.04	0.04	0.04
Paracetamol, all combinations (N02BE01, N02AJ13)	0.93	1.02	1.15	0.18	0.17
Total	1.13	1.23	1.35	0.37	0.35

These calculations are an example of how bottom-up data can contribute to calculating the overall national environmental footprint of the healthcare sector. One disadvantage of this calculation is that the emission factors have only been calculated stoichiometrically and that the data of the GIPdatabank only relates to medication that is reimbursed by health insurers. The climate footprint of analgesics sold at chemists or supermarkets are not included in this data, which means that the climate footprint of these drugs is most likely underestimated.

3.1.3.4 Antibiotics

Weisz et al.[22] have also provided a rough estimate for an emission factor for the antibiotic amoxicillin, based on direct energy consumption during the production process. The estimate relates to amoxicillin produced in Austria by Sandoz using the Austrian energy mix. The estimated emissions factor at 14.3 g of CO_2-eq per gram of API is considerably higher than for analgesics. Weisz et al.[22] do not provide an explanation to account for this major discrepancy. In 2014, the use of amoxicillin in

Austria resulted in a climate footprint of 0.3 kilotonnes of CO_2 equivalent.

In the Netherlands, amoxicillin is used in a variety of pharmaceuticals. As a stand-alone drug, the daily dose of amoxicillin (ATC code J01CA04) is 1.5 g for oral use and 3 g for parenteral administration[83]. The daily dose is the same in combination with a beta-lactamase inhibitor (amoxicillin/clavulanic acid). The DDDs broken down by form of administration are shown in Table 14 and Appendix K. In combination with proton pump inhibitors (pantoprazole/clarithromycin/amoxicillin), the defined daily dose has been established at 5.99 tablets of 40 mg, meaning 0.2396 grams per day for all forms of administration[85]. It is essential to keep in mind that Table 14 only relates to the climate footprint of part of the life cycle and that no other types of environmental impact, such as land use, waste or ecotoxicity, have been taken into account. As such, on the basis of this table, no statement can be made as to whether the use of a particular drug is more sustainable than the other. However, it is possible to determine which active ingredient warrants further examination as to how and where in the chain sustainability improvements can be made. This data can also be used in follow-up studies in relation to the overall life cycle, with multiple types of (environmental) impact.

Table 14 The number of daily doses (DDDs) in 2020 from the GIPdatabank and estimated emissions factors for the production of amoxicillin from Weisz et al.[22]. Please note that this table only relates to the climate footprint of part of the life cycle and that no other types of environmental impact categories, such as land use, waste or ecotoxicity, have been taken into account. As such, on the basis of this table, no statement can be made as to whether the use of a particular drug is more sustainable than the other.

ATC code, active pharmaceutical ingredient (product name)	DDDs (2020)	g of API /DDD	Administration	g of CO_2-eq g of API	g of CO_2-eq /DDD
J01CA04 Amoxicillin	5,858,768	1.5	O	14.3	21.45
J01CA04 Amoxicillin	11,357	3	P	14.3	42.9
A02BD04 Pantoprazole Amoxicillin and Clarithromycin	129,893	0.2396	O	14.3	3.43
J01CR02 Amoxicillin with beta-lactamase inhibitor	4,862,614	1.5	O	14.3	21.45
J01CR02 Amoxicillin with beta-lactamase inhibitor	2,185	3	P	14.3	42.9

Form of administration: O = oral, P = parenteral, R = rectal

The emissions from the production of amoxicillin in combination with proton pump inhibitors are the lowest out of all the amoxicillin combinations, both because the number of DDDs per year as well as the established weight of 40 mg per DDD are relatively low. As regards

combination preparations, the emissions of the active ingredients of the drugs that are administered in conjunction with amoxicillin cannot yet be included.
In Table 15, our calculations show that the climate footprint of amoxicillin production for the Dutch market results in approximately 0.2-0.5 kilotonnes of CO_2 equivalent emissions each year. Amoxicillin use fell between 2018 and 2020, resulting in a decrease in the estimated annual emissions.

Table 15 Dutch climate footprint for the production of the antibiotic amoxicillin in various combinations in kilotonnes of CO_2-eq, based on the figures issued by the GIPdatabank and the emissions factors from Weisz et al.[22] Please note that this table only relates to the climate footprint of part of the life cycle (production).

ATC code, active ingredient (product name)	kt of CO_2-eq in 2016	kt of CO_2-eq in 2017	kt of CO_2-eq in 2018	kt of CO_2-eq in 2019	kt of CO_2-eq in 2020
J01CA04 Amoxicillin	0.26	0.24	0.26	0.16	0.13
A02BD04 Pantoprazole Amoxicillin and Clarithromycin	<0.01	<0.01	<0.01	<0.01	<0.01
J01CR02 Amoxicillin with beta-lactamase inhibitor	0.19	0.18	0.18	0.12	0.10
Total	0.45	0.42	0.44	0.28	0.23

3.1.3.5 Environmental impact of synthesis: complexity of chemicals

The notion put forward by Parvatker et al.[68] that environmental profiles may be linked to the number of synthesis steps of an API had been previously cited by Wernet et al.[86]. Wernet et al. carried out a cradle-to-gate LCA study into the environmental footprint of the production of more complex pharmaceutical chemicals and compared it with the environmental footprint of basic chemicals. The study showed that the production of pharmaceutical chemicals had a greater impact on the environment than the production of basic chemicals, with a cumulative energy demand that was 20 times greater and a global warming potential (GWP) that was 25 times greater[86]. The researchers suggested that the higher environmental footprint of pharmaceutical products is caused by the higher degree of complexity of these substances and by the additional transformation and purification steps in the production process. In addition, according to the scientists, the production method of APIs is often newer and therefore less refined or optimised than with simple chemicals. Furthermore, APIs are also produced in smaller volumes. Energy production and consumption contributed most to the environmental impact during the production of APIs[86].

3.1.3.6 Environmental impact of synthesis: excipients used for formulation

Wang et al.[84] point to the fact that drug manufacturing should also take into account the sustainability aspects of the excipients in order to make APIs suitable for administration (the formulation of the pharmaceutical product). According to their research results, these excipients contribute as much to the environmental profile of drugs as the API itself. In this cradle-to-gate LCA study, Wang et al.[84] used ibuprofen as the model API and examined various formulations of ibuprofen (F1 and F2), each using different excipients. In F1, for example, more frequent use was made of lactose and pregelatinised starch, whereas F2 contained more raw starch. This difference, for example, manifested itself in the electricity consumption for the drying process, which was almost 20% higher for F2 than for F1. According to the researchers, more water was needed when mixing the powder as a result of a higher amount of raw starch, extending the duration of the drying process.

3.1.3.7 Environmental impact of synthesis: solvents

Solvents are chemicals that can dissolve, absorb or extract other materials to facilitate synthesis. The solvent or the treated substance does not usually change in chemical terms. The solvent does not participate in the synthesis process, which means it remains after production. Solvents have various functions in the synthesis of drugs, occasionally supplying molecules to make drugs with or acting as reagents. In other drugs, solvents are used to carry out extraction and purification steps.

In the production of an active pharmaceutical ingredient (API), on average 80 to 90% of the required weight of resources used consists of solvents[87,88]. There are ten commonly used organic solvents used in the pharmaceutical industry specifically: Acetone, Acetonitrile, Diethyl ether, Ethanol, Hexane, IPA, MeOH, THF, Toluene and a generic solvent. In the United States, these were compared with data from Pfizer, Bristol-Myers Squibb and Novartis in an LCA[87]. Due to the large relative mass of the solvents, their reuse is seen as an important contribution to limiting the environmental impact of pharmaceuticals[87]. In addition, the reuse of solvents is cheaper if the system can be used for various flows of solvents. Although purification and reuse of solvent waste flows in a small volume proved not to be economically feasible, Savelski et al.[88] showed that solvent recovery in a larger system in a single production facility could be both affordable and environmentally friendly.

3.1.3.8 Environmental impact of synthesis: the process

On the one hand, the literature results above show that sustainability improvements can be achieved within the healthcare sector by selecting more sustainable alternative (excipients for) APIs. On the other hand, Henderson et al.[89] showed that the synthesis process itself could also be made more sustainable by using biocatalytic synthesis with enzymes instead of chemical synthesis. In this study, a comparison was made between the different ways of synthesis for 7-aminocephalosporic acid (7-ACA), which is a basic substance used for various antibiotics. The chemical method of 7-ACA synthesis involves more harmful substances and requires 25% more energy compared to the enzymatic process. Subsequently, looking at the cradle-to-gate LCA, and comparing the chemical method to the enzymatic approach, the chemical approach requires 60% more energy as well as 16% more mass (excluding water). In addition, the climate footprint is twice as great and the effects of ozone-forming substances and acidification are 30% higher than with the enzymatic method[89]. Moreover, fewer steps are required for the synthesis of 7-ACA if the biocatalytic method were used.

3.1.3.9 Environmental impact of various production processes

The fact that there may be different in environmental profiles of the same substance produced in different ways, as outlined above, is emphasised by a study conducted by Muñoz et al.[90] This study compares two production processes of chitosan in India and in Europe. Chitosan is made from chitin, which is found in the shells of shrimp and crab, among other animals. The production of chitosan in India takes place for agricultural purposes, whereas production in Europe is fully focused on applications in the medical sector. It is not possible to determine from the study whether the type of market that is targeted determines the quality and safety steps in the production process. The LCA analyses show that the production process in India has less of an impact on climate change, water consumption and the estimated ecotoxicity than the European production process. It is vital to keep in mind in this regard that ecotoxicity is taken into account in a different way in an LCA than in a risk assessment for the ecosystem at the local level and that this therefore is not done according to regulatory guidelines that determine environmental risks as a result of ecotoxicity. The European production process, on the other hand, has a small impact on soil acidification, because chitosan is not composted in Europe. The scientists concluded that the reason for the greater impact of the European production process of chitosan is related to the cumulative energy demand (CED), with high fossil fuel consumption[90]. Four times as much primary renewable and fossil energy is needed for the European production process as for the process in India.

3.1.4 Discussion, conclusion and recommendations

3.1.4.1 Discussion

Noting that chemical products (including pharmaceuticals) make the largest contribution to environmental impact such as climate change compared to other groups of products and services studied, this literature review emphasises the importance of carrying out research into the environmental footprint of chemicals and pharmaceuticals in healthcare. This will help identify how and why effects take place and what potential solutions can reduce the environmental impact of these products.

Section 3.1 discussed the use of LCAs for bottom-up footprint calculations, which provide a good starting point. However, as described in the chapter, there can still be a great deal of variation between LCAs of the same products. These variations will depend on methodological choices, assumptions and the structure of inventory data, such as emissions, resource and energy consumption in the life cycle inventory (LCI). The emission factors adopted from Weisz et al.[22] are based on various system boundaries. Consequently, results on the estimated climate footprint of drugs cannot be weighed up against one another, but rather provide an indication of the magnitude of that climate footprint. Using LCAs in a bottom-up manner, with extrapolation to the national level, can magnify the uncertainty and incompleteness of LCAs. A greater degree of caution should therefore be adopted with regard to the use of LCAs in hybrid footprint analyses than with regard to LCAs that only consider two alternatives at the product level.

It is important to keep in mind that sustainability is an issue that entails multiple aspects and issues that are often interrelated and that circumstances and impact over time can likewise change over time (please also see Chapter 5). In addition to the environment, other issues, such as individual patient-related issues (such as medication compliance or side-effects), as well as socio-economic aspects (e.g. culture or security of supply) may likewise play a key role. It is therefore often difficult to compare individual drugs with one another. Certain aspects may equally be contradictory. There are already many uncertainties from an environmental point of view alone. For example, a drug that is more biodegradable may reduce drug residue, however, it may have to be transported and stored in refrigerated conditions to maintain its stability – which results in a higher climate footprint. However, the results of this study can be applied directly in order to identify key areas of focus, such as lack of data on the start of the production chain. The results also indicate that any follow-up research – involving manufacturer and other parties within the chain – is needed to ascertain what the possibilities are to manufacture or supply certain (active) ingredients more sustainably.

The literature review shows that no harmonised method is used to carry out LCAs in most studies. Standardisation, however, can be achieved and would likewise increase the comparability of studies. One example of standardisation for drug LCAs is described by Siegert et al.[90] Siegert et al.[90] drew up a set of draft product category rules (PCR) for footprint research into drugs. These rules include established methodological requirements, agreements on the level of detail and content of an LCA. The proposed PCR are based on the ISO 14044 standard for life cycle assessments, however, the rules are more focused on the drug product category. One example is a mandatory cradle-to-grave scope for LCAs on pharmaceutical products (meaning final, packaged products) and cradle-to-gate system boundaries for LCAs on pharmaceutical processes (such as the manufacturing of an API, including waste streams that are released during production).

The draft PCR recommend an effect-based functional unit (FU) for pharmaceutical products, with a specified patient type, medical indication, geography and duration of treatment, such as 'the treatment of one adult with asthma in the Netherlands for the period of 1 year'. According to the PCR, an FU of this kind should be applied when identifying hotspots or for product optimisation[90]. This type of FU would most likely also be able to be used in the event treatments would have to be weighed up against one another, given that the function has a therapeutic impact in this case. This must be investigated further, such as, in a review into the opportunities for an assessment framework on health, the environment and socio-economic effects associated with the life cycle of medicines.

Furthermore, pharmaceutical processes can be organised based on volume of use in order to gain a better understanding of the environmental footprint. In their PCR, Siegert et al.[90] write that the functional unit in LCAs for pharmaceutical processes must be expressed in mass (a so-called mass-based FU), which, according to the PCR, can take place both in kg of API or in DDDs. A mass-based FU can have same applications as an impact-based FU (compare processes, optimisation), however, could, in principle, also be used to identify and map out a sectoral or national environmental footprint.

With regard to Dutch LCAs into pharmaceuticals, this report has demonstrated that it is possible to start with the most commonly used drugs based on defined daily doses (DDD) using the GIPdatabank. The DDD can be converted into mass units using the DDD index tool of the WHO or the Pharmacotherapeutic Compass (Farmacotherapeutisch Kompas). Once the emissions factor per kg of API of the end product is known, it can then immediately be calculated into national environmental impact in this way using the available DDDs. One key condition is that there should be possible to distinguish between DDDs per delivery form, given that the active ingredient, for example, will have a higher daily dose in the case of intravenous administration than for oral delivery.

A large number of the studies discussed only show cradle-to-gate analyses, which provides a distorted picture of the actual impact, given that more and possibly harmful emissions may take place in the use phase and the end-of-life phase (waste processing)[90]. This has been highlighted on several occasions as a subject for further research[90].

Drugs such as hormones and antibiotics, such as endocrine disruptors, can likewise cause ecotoxicity. Antibiotic resistance also plays a key role in respect of antibiotics. Neither group of substances have as yet been included in LCA methods used to determine environmental impact (such as ReCiPe) and, as such, these results are not yet reflected in the LCA studies in this literature review. However, characterisation models are available for drugs containing endocrine disrupting substances[91]. Midpoint indicators for characterisation are likewise available for drugs in respect of antibiotic resistance[92].

In addition, toxicity and ecotoxicity are types of impacts that are more often included in LCA studies. However, it is vital to realise that these are not the same as risk assessments. Ecological (ecotoxicological) or human (toxicological) risk assessments examine exposure, impact and subsequently the risks, for example, to aquatic life or a particular demographic. For example, take the impact that may occur on aquatic life as a result of residues of medicines that end up in surface water after use by patients. Risk assessments of that kind will use specific, local data, such as local pollution, degree of exposure and the degree of sensitivity of the various organisms. This provides crucial additional information for an LCA. Risk assessments are often based on national or international statutory assessment frameworks, in which agreements have been made with regard to what exactly is required to make an assessment of environmental and health risk that is as reliable as possible as well as with regard to maximum values. Certain (eco)toxicity impacts can therefore form part of an LCA, however, an LCA is not sufficient in being able to carry out an environmental or health risk assessment – additional information is required to be able to do so, in addition to a separate methodology[91].

3.1.4.2 Conclusion

This chapter carried out a review of the literature with regard to how calculations of the environmental footprint of chemicals and drugs at product level may contribute to the national environmental footprint of the healthcare sector with a greater degree of detail.
The literature review sets out that LCAs appear to be available for a limited group of active ingredients in pharmaceuticals. Initial calculations using emission factors for the production of (raw materials for) active pharmaceutical ingredients of analgesics and antibiotics show how bottom-up data can contribute to refining the overall national environmental footprint of the healthcare sector. The calculations show that a national footprint calculation can be achieved for certain products, but that implementation is still associated with certain limitations. For example, more data is needed to specify the total of daily doses per administration route and the emission factor must take into account the full life cycle from resource extraction to waste (cradle-to-grave) in order to be able to contribute to a more accurate picture of the national environmental footprint of the healthcare sector. The uncertainties of the LCAs must likewise be properly examined and communicated when extrapolating to the national level. The literature indicates that when calculating the environmental footprint at product level, attention should in any case be devoted to energy consumption during production and for the synthesis process, including the use of solvents and excipients in the formulation.

The studies discussed occasionally refer to opportunities to make sustainability improvements in healthcare and identify prospects for action. For example, more sustainable alternative (excipients for) APIs may be investigated: examples of which are intravenous anaesthesia instead of vaporous anaesthetics or the use of oxygen and air instead of nitrous oxide and as an adjuvant for vaporous anaesthetics. In addition, more sustainable ways of synthesis (biocatalytic using enzymes instead of chemical) can be examined. This has not yet been extensively examined in this literature reviews. Additional research is required.

The studies that are available differ from one another in terms of their delineation, approach and the quality of the date, which likewise hinders the comparability and application of these studies. Due to the limited scope of the literature review, it is therefore too early to draw any general conclusions from the selection presented in this report. Any follow-up research conducted by RIVM will entail a further examination of life cycle analyses of pharmaceutical products.

The lack of sufficient and reliable information shows that it is currently very difficult either to determine exactly how production chains can become more sustainable (supplier, industry) or to be able to choose between the various environmental profiles of drugs (customer, healthcare sector). Further research into these aspects is currently underway in the EU project TransPharm (2022-2026). Additional knowledge about the environmental footprint of individual steps in the production process can also create more options to achieve additional strides in sustainability, focused on specific medication.

3.1.4.3 Recommendations

At present, it does not yet appear to be possible to carry out a hotspot analysis into pharmaceutical products with the largest environmental footprint based on the data currently available. With regard to follow-up research, we make the following recommendations to any future parties carrying out drug LCAs:

1. Develop a life cycle inventory dataset with data on resource use, energy consumption, water consumption, transport distances and waste from drug production. Key resources to focus on include solvents, excipients and active pharmaceutical ingredients;
2. Make use of the harmonised LCA rules for chemicals developed by Siegert et al. (2019) in order to standardise the comparability and study structure based on product category rules (PCR);

Effective execution of LCAs also requires the following scientific depth for LCAs relating to chemical products, including drugs:

3. Improved detailing of the environmental impact, and toxicity in particular, of the end-of-life phase of drugs;
4. Additional research into the implementation of impact categories that are related to the toxicity of drugs, such as endocrine disruption. In addition, antibiotic resistance should also be included in the environmental impact of antibiotics.

A large amount of data and time-consuming analyses are required in order to carry out a full LCA. A potential alternative approach to carrying out a full cradle-to-grave LCA is to carry out a hotspot analysis using artificial intelligence (AI), which may be accomplished by processing information in a computer model. Training data for the model should, however, be made available to do so. Section 3.4 will explore the opportunities relating to predicting and estimating life cycle impact using artificial intelligence.

3.2 Machine learning: methods to predict the environmental impact of chemical products, including pharmaceuticals

3.2.1 Introduction

The aim of the RIVM Green Deal for Sustainable Healthcare Knowledge Base (RIVM Kennisbasis Green Deal Duurzame Zorg), among other things, is to support the healthcare sector in making decisions or in prioritising[11,12] and to support the healthcare sector in approaching and understanding its own environmental footprint. Prioritisation requires a better understanding of the footprint of chemical products, including pharmaceuticals, given that these account for the largest share of the environmental footprint of the Dutch healthcare sector (Chapter 2). At the same time, the literature review into drug LCAs shows that there are currently too few (detailed and comprehensive) studies into individual pharmaceutical products, APIs and excipients to better identify and interpret the national environmental impact.

How can insights into the environmental footprint of drugs nevertheless be gained if insufficient data is available to carry out a detailed LCA? Artificial intelligence may be able to assist in this regard by making estimates of environmental burden. Earlier in this report (section 3.2), it was discussed that determining the environmental footprint based on the number of synthesis steps may be an option[86]. Once the synthesis steps are known, these may provide information on (part of) the environmental footprint of chemicals.

By training a computer model with LCA data of pharmaceutical products, it is possible to estimate the environmental impact of pharmaceuticals with the help of predictor variables. This section (3.2) explores what information is available in the literature on estimating and predicting the environmental impact of chemicals using various models that rely on artificial intelligence.

3.2.2 *Review of machine learning methods for chemical products*

One way to predict environmental impact is with quantitative structure-activity relationship (QSAR) models. Traditional QSARs are often based on linear models, which work with predictor and response variables. The relationship between these variables can be used to predict the effects of new or untested chemicals. Recently, the focus in respect of impact predictions has shifted to more complex, non-linear models, such as many machine learning models. Machine learning models (also referred to as machine learning or automatic learning) are a specific form of artificial intelligence that use algorithms that allow computers to learn autonomously. The reason underlying the shift toward non-linear models is that more and more (complex) data is becoming available and that there are also increasingly better computers available that can work with non-linear models. Provided there is enough data to train with, these types of models can make more accurate predictions than linear regression models, such as QSARs[92]. Furthermore, QSARs sometimes prove difficult to perform for drugs, given that they will often consist of polar substances and have very specific mechanisms of action.

There are several machine learning models that are used to predict the environmental footprint of chemicals. One of the examples of a screening method used to predict the impact over the entire life cycle of chemicals that is frequently cited in the literature is that which uses artificial neural networks (ANN)[92-96]. Neural networks are regression-based machine learning models. An ANN resembles the biological nervous system (such as the brain) in the way it processes information. The ANN consists of several layers: the predictor variables (inputs) form the first layer, with the responses (outputs) forming the final layer. The hidden layers, which are connected to one another by ‘neurons’, are situated in between the input and output layers.

An ANN model will look for (‘learns’) patterns between the input variables and the output variables in a database. Once these patterns have been found, the ANN model can be used to search for patterns in new data and make relevant predictions on that basis. ANN models can be applied to large-scale datasets, such as for drugs and other chemicals, and they provide a relatively rapid method for assessing various substances[94].

Wernet et al.[93,97] previously developed FineChem, a software tool that runs in the programming language R, which is able to estimate resource use and the environmental impact of petrochemical production based on molecular structure. The tool has also been used for pharmaceuticals, including to estimate the cumulative energy demand (CED) of an expensive cancer drug manufactured by Sanofi[98] and to determine the CED of four active components of Viagra™.[99] FineChem is a molecular structure based model (MSM) that contains one hidden layer based on neural networks (ANN) and which is capable of estimating the direct correlation between molecular structures and a number of key production and emissions parameters. According to the developers, an MSM cannot replace the usual inventory analysis in an LCA, but acts as a screening tool to support parties carrying out an LCA[93]. In FineChem, the life cycle inventory (LCI) can be derived by using ten chemical properties (so-called molecular descriptors)[97]:

1. Molecular weight [g/mol]
2. Number of nitrogen atoms [N]
3. Number of halogen atoms (Fluorine [F], Chlorine [Cl], Bromine [Br])
4. Number of rings (both aromatic and aliphatic rings)
5. Number of tertiary and quaternary carbon atoms
6. Number of heteroatoms in the rings
7. Number of unique substituents on aromatic rings
8. Number of functional groups
9. Number of oxygen atoms in carbonyl groups (keto and aldehyde)
10. Number of oxygen atoms, except those in carbonyl groups

FineChem is able to analyse the cumulative energy demand (CED) and the global warming potential (expressed in GWP) per kg of the analysed substance. The tool was trained with mass and energy flow data from the petrochemical production of 338 chemicals, ranging from basic chemicals to more complex chemicals. By randomly separating the input data into training and test sets 30 times, each test set contained 51 random chemicals (15% of the data). Thereafter, 30 neural networks were built using the 30 test sets[97]. Wernet et al.[97] then assessed the quality of their tool using the coefficient of determination (q^2), which determines the extent to which the test data influences the predictions of the model. The coefficient of determination was lower (q^2=0.41) for the GWP model (n=338) than for CED (n=338, q^2=0.58) due to the more heterogeneous input data for greenhouse gas emissions than for energy consumption. The 30 networks that performed best for the 30 test sets were then selected for the final model.

Although the predictions of the CED were fairly accurate, the GWP model performed less well. The CED model had an average relative error of 29.1%. Given the degree of uncertainty of roughly 20% in the original training data, this represents a convincing result. The GWP model had an average relative error of 58.2% over a mean standard deviation of 40% – to be expected due to the lower coefficients of determination and a higher degree of variation in the original data[97]. Because in most cases the prediction errors are significantly smaller than the uncertainty range of the models, Wernet et al.[97] concluded that their tool was particularly suitable for prediction properties of more complex chemicals. The tool was therefore used for subsequent research into drugs[98,99]. Based on the molecular structure, it appears that a reasonable estimate can be made of the direct energy consumption used for the production of the analysed substance using a molecular structure model. This, however, does require the molecular properties of all chemicals used.

Cespi et al.[99] used the FineChem tool developed by Wernet to arrive at more complete life cycle inventories (LCI) for catalyst substances used in the synthesis of sildenafil, also known as Pfizer's Viagra^{TM}. This particular instance did not relate to the active pharmaceutical ingredient (API) itself. In doing so, they presented a practical approach to building an LCI based on patents and data from the literature. Where Wernet et al.[97] showed a direct correlation between molecular structure and production and emissions characteristics, such as CED, Cespi et al.[99] found a direct correlation between molecular complexity (expressed in various synthesis steps) and the process mass intensity (PMI, expressed in kg of raw material inputs/kg of API). By means of this rapid impact screening of excipients in the synthesis of an API, the researchers were able to show that it is vital to take into account downstream outsourced processes, such as the production of reagents, in the LCA for the drug[99].

According to Song et al.[94] the predictive performance of the single-layer FineChem MSM is limited due to the fact that there are no well-defined model training procedures. In addition, uncertainty characterisation of the output for new chemicals is missing. For that reason, Song et al.[94] used a more comprehensive, multi-layered ANN to determine a number of environmental impact categories (3 midpoints: cumulative energy demand (CED), climate change, calculated using global warming potential (GWP100), acidification; 2 endpoints: human health, ecosystem quality and the Eco-indicator 99 method) for chemicals based on information on their molecular structure. To set up the ANN, the researchers collected training data from 166 unit process datasets for organic chemicals from the Ecoinvent v3.01 LCI database. They then divided the chemical data into three groups to further develop the model: for training, validation and testing. Molecular descriptors, such as molecular mass or the percentage of N atoms) calculated using the Dragon 7 software programme acted as the input for the ANN model. The output of the ANN consists of characterised environmental impacts, which have been checked with validation data. Dragon 7 yielded some 4,000 molecular descriptors for each chemical, including topological descriptors and structure and ring descriptors. In order to avoid overfitting, the number of dimensions was limited and an informative subset of descriptors was reduced to a smaller dataset using a Principal Component Analysis (PCA). Song et al.[94] subsequently study three model options: (1) all molecular descriptors from Dragon 7 (3,839 characteristics); (2) descriptors selected using filter-based methods (58 descriptors); and (3) descriptors selected using PCA, retaining 95% of the variance in the original descriptor sets (60 descriptors). Song et al.[94] concluded that out of the three options, a PCA with 95% variance retention of the original dataset made the most accurate predictions. The predictive performance is expressed in R^2: the percentage of correctly predicted values based on actual values. The ANN had a greater predictive performance for acidification (R^2 of 0.73), human health (R^2 of 0.71) and Eco-indicator 99 (R^2 of 0.87) than for climate change impact over a period of 100 years (GWP100 with an R^2 of 0.48).

The results of the ANN model suggest that the chemicals with higher impact values also present with greater prediction errors, given that less training data with impact values of complex chemicals as pharmaceuticals is available[94]. The same researchers subsequently characterised the degree of reliability of the results of the ANN model based on the Applicability Domain (AD) concept – after all, a model cannot predict things for which it has not been trained. They applied this in the context of predictive LCA for the first time.

Song et al.[94] specifically go further with regard to the pharmaceuticals component. For example, according to Song et al.[94], chemicals with a very high characterised impact (such as CED in particular) usually fall into the pharmaceuticals category (e.g. pyrazole). This group therefore presents with greater prediction errors. Furthermore, they highlight the fact that in the case of pharmaceuticals, it is not only the molecular structure that has an impact, but that the production process similarly contributes to the environmental burden (such as energy intensity) to a significant extent, particularly due to the strict selectivity and purity requirements for pharmaceuticals.

Additional predictions on the production process of pharmaceuticals can be made by means of so-called synthesis pathway descriptors. Song et al.[94] cite this type of property as a valuable addition to an ANN model in addition to molecular descriptors, in order to gain more insight into the chemical production process. De Soete et al.[100] examined fifteen of these possible predictor variables to determine which data from the synthesis of drugs are key to estimating their environmental impact. The three main predictor variables for the impact of drugs are:

1. the amount of organic solvents used (in L/mol);
2. molar efficiency (in mol/mol);
3. the duration of the synthesis steps (Δt, in s/mol).

Process-based material indicators (numbers 1 & 2) and the process operational parameter (number 3) had the most significant contribution to the prediction. Equipment parameters, such as the number of dryers in the process, and chemical parameters, such as the addition per mole in a synthesis step, did not contribute to the prediction of the selected environmental pressure indicator *cumulative exergy extracted from the natural environment* (CEENE). CEENE is a comprehensive method for lifecycle impact assessment (LCIA) for the calculation of resource reserves. Wernet et al.[86] suggest that the use of resources and the associated emissions in a cradle-to-gate synthesis process of an API make the largest contribution to the environmental impact of pharmaceutical production. De Soete et al.[100] indicate that a similar correlation with synthesis pathway descriptors can be made for other impact categories than CEENE in the life cycle, such as climate change or ozone depletion.

Another approach to estimate the environmental impact of chemicals with missing data is to use alternatives with a similar molecular structure. Following Song et al., Zhu et al.[95] used molecular descriptors and PCA to examine how sustainable chemical alternatives could be screened using an ANN model. The researchers used Eco-indicator 99 (EI99) and ReCiPe endpoints as LCIA methods to determine the impact on the ecosystem, human health and resources. The predictive power of the neural network developed by Zhu et al.[95] appears to be high. The combined EI99 endpoints (R^2 = 0.8356) and the total of ReCiPe endpoints (R^2 = 0.883) show the most accurate prediction values compared to the individual endpoints determined for the impact. Of these individual impact categories, EI99 for resources (R^2 = 0.622) had the lowest predictive power. Figure 12 shows a roadmap from data collection to LCIA predictions.

The method put forward by Zhu et al.[95] highlights the problem for pharmaceuticals that Ecoinvent contains almost no data on the environmental impact of pharmaceuticals that can serve as training data. However, this method may provide a possibility for inverse screening: similar pharmaceuticals can be determined on the basis of their comparability in molecular structure based on the data available in Ecoinvent and published drug LCAs. The comparability of the molecules could, for example, be determined by the Euclidean distance. This measures the distance in the descriptor space of the molecule of the desired chemical to the average of the training data set, in order to determine the most similar substance.

Calvo-Serrano et al.[101] also take into account molecular descriptors to determine the cradle-to-gate environmental impact of chemicals – in this case, mainly organic solvents. They based their study on the molecular descriptors from the model developed by Wernet et al.[93], but in addition added thermodynamic properties (boiling point of the substance) in order to be able to make a prediction on the impact during the life cycle of chemicals using mixed-integer programming (MIP). An MIP is an optimisation framework that systematically constructs accelerated predictive models of life cycle impacts. The thermodynamic properties were estimated using the Peng-Robinson thermodynamic package in the software Aspen Plus v8.2. Some 83 chemicals were selected from the original Wernet et al.[93] dataset (a small dataset containing mainly organic solvents and other organic compounds commonly used in the industry). The same 17 molecular descriptors as used by Wernet et al.[93] and 15 additional thermodynamic properties were used to predict the cradle-to-gate environmental pressures of organic chemicals with nine impact categories, including climate change (expressed in GWP). According to the authors, the impact categories could be determined with sufficient accuracy with this dataset to be able to perform a standard LCA. Although not specifically aimed at pharmaceutical chemicals, the Calvo-Serrano et al.[101] approach was cited by Parvatker et al.[68] with regard to estimating the environmental impact of medicines.

Zhao et al.[96] likewise built a machine learning model to be able to estimate the missing life cycle inventory (LCI) data. They focused on estimating data in cases where individual process units are missing (so-called unit process data) and used Ecoinvent v3.1 unit process data sets (UPR) as a training set. They applied this model to the entire Ecoinvent database rather than merely on chemicals. The study compares four distinct machine learning methods: ANN, Random Forests (RF), Support Vector Machine (SVM) & Extreme Gradient Boosting (XGBoost). The final method classifies decision trees based on training data and makes predictions by calculating weighted means. This study found that out of the four methods, XGBoost was the fastest and most powerful with regard to predicting unit process data for LCAs. Zhao et al.[92] indicate that their method may be useful in providing an initial insight into the environmental impact of new materials and technologies for which only part of the LCI data is available. A method of this type can therefore equally contribute to gaining an initial insight into the environmental impact of pharmaceuticals that do not feature in LCIs.

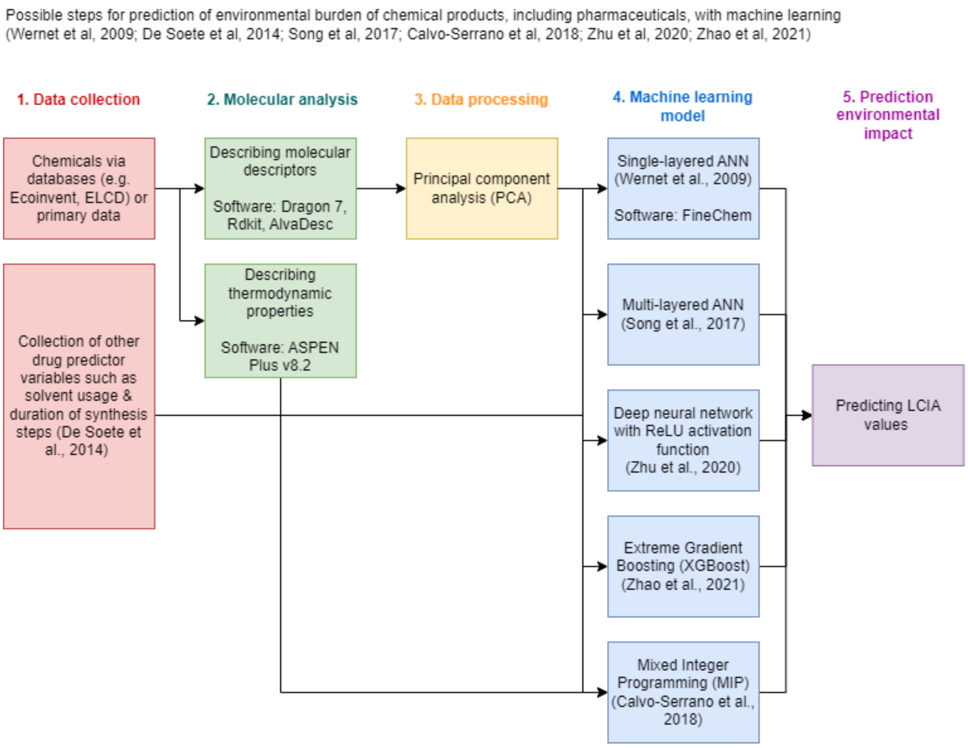

Figure 12 Visual summary of potential approaches and steps in using machine learning models to predict the environmental pressures of pharmaceuticals.

3.2.3 Discussion

Although machine learning models are widely used for predictions on the environmental impact of chemicals, the method has a number of weaknesses. First and foremost, machine learning can lead to problems of interpretation. Many models, such as ANN, are a black box, given that there is no insight into the connections and relationships within the model. As such, the model is not transparent, which complicates the accessibility and interpretability of the data. The lack of an underlying inventory makes it difficult to interpret the environmental impact[102]. On the other hand, using a black box model makes it easier to use confidential manufacturing data[97].

Secondly, the weighting and handling of overlapping data is a key areas of focus when working with machine learning models. In ANN models, for example, the invisible layers are connected to one another based on weights, however, these must be properly calibrated by means of training.

Thirdly, any such training of the model requires close supervision. The training process needs enough predictor variables and training goals. For pharmaceuticals, that data is most likely not readily available in a database or in the literature. The question is therefore whether a sufficient amount of data is available to be able to train and validate the models. Moreover, it is generally the case that each uncertainty will build upon another in the model if predicted (or other inaccurate) data is used as an input for a machine learning model, which increases the probability of incorrect predictions.

Finally, an ANN model cannot be used as a substitute for a risk assessment. Like an LCA, an ANN model does not contain a sufficient amount of information to determine the risk of chemical substances. This means that although ecotoxicity characteristics as described by Hou et al.[92] can support an LCA, they are insufficient to be able to assess health and environmental risks.

3.2.4 *Conclusion*

There are ways to estimate the sustainability of medication based on predictors and artificial intelligence. Once again, a sufficient volume of qualitative and reliable information about a portion of the pharmaceuticals must be available in order to train and validate the models for this purpose. This is a fascinating direction that warrants further investigation, given that artificial intelligence can allow the initial environmental impact of pharmaceuticals to be estimated without all data having to be available.

In short, machine learning can provide a way to screen the environmental impact of pharmaceuticals and medicines more rapidly as more and more data become available. However, it is currently unclear whether sufficient training and validation data is available. In addition to molecular descriptions, data on the synthesis of chemicals is needed to provide the most complete estimate of the environmental impact of pharmaceuticals. This requires molecular information of all chemicals involved in the synthesis of an API, as well as the formulation. The industry will be able to assist in this regard. There may also be the option of inverse screening for chemicals with a comparable molecular structure, using pharmaceuticals from Ecoinvent as the LCI database, in order to achieve a rough impact estimate more rapidly.

If the inventory of the raw data and LCA studies for training and validation should show that enough data were available, then machine learning could be used to make quicker estimates of the environmental footprint of pharmaceuticals. The opportunities with regard to estimating the environmental impact of medicines are currently being fleshed out further inter alia in the EU Horizon project TransPharm 2022-2026.

4 A health-promoting healthcare environment: research and practical examples

One of the pillars of the Green Deal for Sustainable Healthcare 2.0 is the Health-promoting Healthcare Environment (Gezondheidsbevorderende Zorgomgeving), or an effective care environment. Since 2018, RIVM has collected insights and practical examples on what a sustainable, health promoting healthcare environment looks like on behalf of the Ministry of Health, Welfare and Sport. Unlike the rest of this report, this is less about the environmental impact of healthcare, but about the opportunities to create a healthcare environment in which patients, residents, employees and visitors feel comfortable and are invited to adopt healthy behaviour. A healthy living and care environment – both now and in the future – likewise falls under sustainable healthcare and is connected to the environment and the climate through the three principal themes of nature, architecture and nutrition.

The purpose of the insights and practical examples collected is to provide administrators, managers, healthcare professionals and policymakers with specific prospects for action. This has been accomplished by:

- acquiring knowledge from literature and making it accessible in so-called background documents;
- drawing up What Works Files(Wat Werkt Dossiers) – an overview of the effectiveness of the various interventions;
- sharing inspiring, qualitatively substantiated examples of sustainable initiatives from practice and making them accessible.

In January 2022, the project 'Sustainable Healthcare Interventions' was combined with the project 'Green Deal for Sustainable Healthcare Knowledge Base'.

This chapter presents a brief summary of the results of the project from 2018 to May 2022. The objective of this report is not to provide an exhaustive overview of the background to the study, but to provide a brief summary of the key data and initial insights. The background documents referred to are presented on the RIVM website for the Green Deal for Sustainable Healthcare[17], alongside the What Works Files. These set out the scientific basis for the relationship between nature, architecture and nutrition on the one hand and health on the other. In addition, the practical examples collected have been organised and made publicly accessible on the aforementioned website.

Alongside the background documents, the What Works Files and the practical examples, three webinars were held, and exchanges and collaboration took place with various stakeholders in this field.

4.1 Method Background documents and What Works Files

A literature review was carried out for the three background documents on nature, architecture and nutrition, relying on both national and international literature. The What Works Files were drawn up on the basis of these background documents. The files set out to what extent – according to the literature – certain measures or changes contribute to the well-being and health of patients, residents, employees and visitors of healthcare institutions. 'What works' indicates that there is a sufficient amount of (high-quality) research available with a positive impact. 'What is likely to work' means that there is a lack of sufficient research, but that the studies that were available show positive effects. 'What doesn't work' means that the majority of studies retrieved shows that a specific element does not lead to a positive impact. 'What is uncertain or unknown' means that there is a lack of high-quality, consistent literature on this issue.

4.2 Method for practical examples

The practical examples came about through a web search and through RIVM correspondence with healthcare institutions (or umbrella organisations). In addition, healthcare institutions with inspiring examples were able to reach out by emailing duurzamezorg@rivm.nl. It was then determined whether the suggested example matched our specific pillar and the associated requirements. The following information was then ascertained through telephone interviews:

- The approach to the change, measure or activity (the method in question);
- The purpose and target group of the change, measure or activity (e.g. patients, (a group of) residents, employees or visitors);
- The impact (what effect has the measure or activity has; has individual research been conducted into that impact). In this context, reference is made to information available from the literature and the What Works Files.
- Alignment with other Green Deal aims: for example, does the measure or activity aimed at promoting health likewise contribute to reducing greenhouse gas emissions (e.g. by realising more green spaces indoors and outside the institution) or to the circular economy (e.g. because fruit and vegetables are cultivated at an allotment for use within the institution);
- Key areas of focus during implementation; are there are specific areas of focus? (framework conditions, success factors, lessons learned);
- Additional information (reference to the website of the institution or other sources, email address).

A draft text for the website was drawn up based on the interviews, which was then reviewed by the institution, edited further and provided with photos and/or videos and placed on the website.
The practical examples that have been collected so far (just like the background documents and What Work Files) have been grouped into three main categories: nature, architecture and nutrition. Within those categories, a distinction has been made between the various sectors:

- Hospitals and University Medical Centres (UMCs);
- Nursing and care;
- Mental health care (geestelijke gezondheidszorg, GGZ);
- Disability care.

4.3 Results

This section presents the principal results of the health-promoting healthcare environment project. The results of the literature review are set out in the three background documents on nature, architecture and nutrition. The What Works Files were drawn up based on these background documents. These What Works Files are shown here for the relation between Health and: Nature (Table 16), Architecture (Table 17) and Nutrition(Table 18). The files set out to what extent specific measures or changes contribute to the well-being and the health of patients, residents, employees and visitors of healthcare institutions.

Table 16 Overview of the What Works File for Nature and Health. A detailed outline is available in the background document [103].

What Works – Nature and Health

What works?

- Patients in hospitals are more satisfied with a room with plants than with a room without plants.
- Plants contribute to stress reduction and positive emotions.
- Posters of plants or other depictions of nature also contribute to stress reduction and a greater degree of satisfaction among patients and healthcare staff.
- A green environment has a positive impact on employees, because plants, among other things, contribute to recovery from a stressful working environment. A green environment, in this case, refers to nature in the immediate vicinity of the healthcare institution, such as a garden, roof terrace or forest.
- Sounds of nature, such as birds, a gentle breeze or water, contribute to stress relief for patients in hospitals.
- Rooms with views of nature can improve post-surgery recovery.

What is likely to work?

- Indoor plants have a positive impact on the physical health on patients in hospitals, such as blood pressure, pain, fatigue and length of stay at the hospital.
- Indoor plants can contribute to positive emotions, tranquillity, reduced stress and an increased perceived sense of well-being in hospital patients.
- Watching nature films can help patients recover from a stressful event and lower blood pressure.
- A green environment (such as a garden, roof terrace, forest) around a nursing home for people with dementia can improve the mental health of the residents. These effects relate to a reduction in agitation, a more positive mood and an improved quality of life.

  Sounds of nature can contribute to more positive emotions in hospital patients, reduced anxiety and agitation, lower blood pressure, less pain and less post-operative trauma.

What are the uncertainties or unknowns?

- It is unknown what the impact of indoor plants is on the health and perception of employees and visitors in various healthcare settings.
- It is unsure which factors exactly play a role in relation to the positive health effects of indoor plants on hospital patients. These factors include the specific types of plants, how striking the

plants feature in the space, the time of exposure, the duration of the effects and the type of target group.
- The relationship between indoor plants and the risk of developing infections or allergic reactions has not yet been studied sufficiently.
- Although there is a relatively large amount of information available on the positive impact of a green environment (such as a garden, roof terrace, forest) on human health, more research can be done into the use of green spaces within healthcare environments.
- Some studies have combined the effects of nature with other health-promoting factors. More research is needed on the isolated effect of nature and the underlying mechanisms to better understand aspects such as the degree of exposure (location, duration, etc.).

Table 17 What Works File on Architecture and Health. A detailed outline is available in the background document[104].

What Works – Architecture and Health

What works?

- Rooms with a view of nature have a positive effect on the health and well-being of patients and healthcare staff. Also see Table 6.
- Daylight and clear artificial light have a positive effect on the health and well-being of both patients and staff.
- The use of noise-reducing materials has a positive impact on the well-being of both patients and staff.

What is likely to work?

- For many patients, a single room has a positive impact on their well-being, such as reduced stress, more privacy and improved sleep. For other patients, a room with multiple occupants is more beneficial to their recovery.
- The use of single rooms can lead to a lower level of job satisfaction for healthcare staff, less of an overview of patient needs and concerns regarding the (social) isolation of the patient.
- The use of spaces where families can meet appears to increase the perceived social support of patients.
- Improved orientation within the building increases the satisfaction of the (healthcare) staff. A clear layout of the workplace or a floor plan may be beneficial in this regard. This also includes placing more patients in one room or implementing a uniform layout for single rooms.
- Fresh air or filtered air is associated with fewer infections.
- Sustainability aspects can likewise be taken into account in the architecture, such as the use of recycled materials.

What are the uncertainties?

- In general, it appears to be difficult to conduct research into the impact of environmental factors on health and well-being. This is because the impact of the architecture of a building are difficult to isolate from the effects of other environmental factors.
- The impact of the architecture will depend on the type of user (patient, visitor or employee) and the degree to which the user is exposed to it.

Table 18 What Works File on Nutrition and Health. A detailed outline is available in the background document[105].

What Works – Nutrition and Health

What works?

- For hospital patients or residents of nursing or care homes, flexibility in terms of menu choice or mealtimes helps prevent malnutrition – in addition, this has a positive effect on the energy and protein intake of patients and residents. It also reduces the likelihood of food wastage.
- For hospital patients or residents of nursing or care homes, the work of nutrition assistants to assist with menu choices contributes to a higher food, energy and protein intake.
- Several small (whether or not enriched) meals and/or additional (enriched) snacks have a positive impact on the energy and protein intake of hospital patients or residents of nursing and care homes.
- Combined lifestyle interventions accompanied by changes in the environment that encourage a healthy diet and exercise inter alia help reduce obesity among residents of mental healthcare institutions and in care institutions for the disabled.
- Among residents of mental healthcare institutions and disabled care institutions, active engagement and participation of the treating team in the intervention support the impact on aspects such as body weight.
- The use of priming nudges helps employees and visitors at healthcare institutions make healthier choices. This involves small changes to the environment that improve the visibility, accessibility and availability of healthy products.

What is likely to work?

- The use of (trained) volunteers to assist with meals contributes to preventing malnutrition in hospital patients and residents of nursing and care homes.
- A different way of serving meals (family style, buffet style, restaurant style) helps prevent malnutrition in hospital patients or residents of nursing and care homes.
- A homely environment contributes to preventing malnutrition in hospital patients or residents of nursing and care homes.
- Driving healthy choices, for example, through labelling of healthy products, such as using a colour coding system, encourages healthy nutrition among staff and visitors of healthcare institutions.

What doesn't work?

- Establishing protected mealtimes (‘do not disturb’ during mealtimes) prevents malnutrition among hospital patients or residents of nursing and care homes, if it is the only measure that is implemented.

What unknowns are there?

- It is as yet unknown whether the use of high-contrast dishes to serve meals helps prevent malnutrition in hospital patients or residents of nursing and care homes, if it is the only measure that is implemented.
- It is as yet unknown whether or not playing music during mealtimes helps prevent malnutrition in hospital patients or

residents of nursing and care homes, if it is the only measure that is implemented.

- Neither is it as yet known whether or not improving the smell and/or taste of foods helps prevent malnutrition in hospital patients or residents of nursing and care homes, if it is the only measure that is implemented.

In addition to the What Works Files, a total of 54 practical examples were collected. In the first few months of 2022, a start was made on updating and presenting the first examples from practice from 2020 in a more appealing manner. For example, the interviewees were asked to look back on the activity, elaborate on how the activity has developed up to now, and what the results have been.
The practical examples are highly diverse in terms of their objectives, target group, approach and scope. There are a number of aspects that stand out:

- The vast majority of examples from practice are aimed at residents/clients. Occasionally, employees and visitors are included in the initiatives and activities, however, they are less frequently the main target group.
- Most of the practical examples described are initiatives and activities at hospitals/UMCs and in nursing and care facilities, such as mental health care, disabled care and rehabilitation care.
- Almost all the professionals who were interviewed indicated that it is vital for an institution to have a vision statement that sets out what it considers essential in the area of a healthy living and working environment. In addition, support from management contributes to the success and continuity of the initiatives.
- It is crucial to the implementation of any measure, modifications to a building or changes in policy that there should be communication with experts in the field of a healthy environment and well-being, with patients/residents themselves and with staff and visitors. This ensures that any initiative will align with their requirements and needs and will ensure a greater support base for the introduction of those measures.
- The interviews and practical examples clearly show that the well-being of residents (and staff) has always been and continues to be a key priority and areas of focus for healthcare institutions. This certainly applies to institutions characterised by longer stays, such as care for the elderly and disabled care. Well-being not only leads to better health, but is a key indicator for the governance and management of the institution with regard to the proper functioning of the institutions.

By now, RIVM website on sustainable healthcare is visited by a large number of people. See Table 19.

Table 19 Number of visitors of the RIVM sustainable healthcare website between October 2021 to March 2022, including RIVM staff. During this period, around 1600 people per month visited the website.

Visitors to RIVM website Sustainable Healthcare[¥]		**Promoting health[#]**	**Sub sections**
No. total	10,330	5,850	
Average per week	341	93	
		34	*architecture*
		27	*nature*
		57	*nutrition*

[¥] www.rivm.nl/green-deal-duurzame-zorg
[#] Several pages under www.rivm.nl/green-deal-duurzame-zorg/gezondheid-bevorderen-door-goede-leefomgeving-zorginstellingen

The conversations, interviews and webinars show that there is a need for more scientifically substantiated examples from professional practice for the various pillars or themes, such as circular working practices and climate change (mitigation), and for bridging links to be established between the various pillars or themes. This is in line with previous findings, published in the RIVM letter report 'Review of the Monitoring Options for the Green Deal for Sustainable Healthcare '[12].

In addition to the examples cited on the RIVM website, organisations themselves have likewise collected examples on an effective healthcare environment, as well as about the other key themes of the Green Deal for Sustainable Healthcare. These are accessible to other outside of the organisation to a varying extent and therefore are not always public[12]. There is a website specifically dedicated to the issue of medicine residues, with examples and more information about the Chain Approach on Removal of Pharmaceutical Residues in Water (Ketenaanpak Medicijnresten uit Water) (www.medicijnresten.org).

More is nevertheless required in addition to continuing to structure and share science-backed examples. Initiatives and partnerships are needed to help (smaller) institutions in implementing, monitoring and evaluating sustainable interventions. Tools and instruments can be shared and custom-developed in partnership with the other institutions and knowledge partners, to ensure that all institutions can more effectively implement sustainable and healthy interventions[12,106].

Other activities

In addition to the background documents, What Works Files and practical examples, other activities have taken place to inspire the field and to share knowledge about the health-promoting healthcare environment. In June and November 2021 and in February 2022, three webinar specials were held in partnership with the Ministry of Health, Welfare and Sport about Nature, Architecture and Nutrition, in successive order, in the context of sustainable healthcare. Over 200 participants attended the Nature and Architecture webinars, with approx. 350 participants attending Nutrition. The participants primarily consisted of administrators and healthcare professionals and policymakers. The general component consisted of presentations on research and experiences centring on one of the key themes and on examples from professional practice. The Architecture & Sustainable

Healthcare and Nutrition & Sustainable Healthcare webinars also included a panel discussion with experts. The Nature & Sustainable Healthcare and Architecture & Sustainable Healthcare webinars included an opportunity for participants to carry on the discussion in sector-specific break-out rooms after the general section. In addition to the exchange of experiences, these events similarly revealed a great need for specific information and substantiation.

Furthermore, there has been an exchange of knowledge with parties such as ZonMw, Vilans, Eten+Welzijn, Alliantie Gezonde Voeding, the sustainability coordinators of the teaching hospitals and other stakeholders in the healthcare, architecture and food sectors.

4.4 Conclusions and recommendations for a health-promoting healthcare environment

There appears to be a need for knowledge and insights on and practical examples for a health-promoting healthcare environment. All the various institutions indicated that they are motivated to create an environment for their patients/clients, staff and visitors in which they feel good, are able to enjoy a healthy stay, exercise and eat and drink healthily. Regarding their own initiatives, the interviewees also stated that the changes, measures or activities had contributed to a positive impact, such as more flavoursome food and less general waste. In addition, various activities have been initiated in which patients or residents have become more active and independent.

It is precisely the need to create a healthy environment for residents, visitors and employees that underpins the desire to reach an accurate assessment in respect of measures to be taken and activities to be set up. Which activities or measures are suitable? What is an effective approach? What framework conditions need to be put in place? The practical examples and substantiation are subsequently beneficial in this context. People want to learn from one another and use both time and money as effectively and purposefully as possible in order to become more sustainable. This emphasises the importance of scientific substantiation and the accessibility of the examples from practice.

The collection and further structuring of more scientifically backed practical examples remains crucial – particularly for mental healthcare and care for the disabled. There is currently still little information available about these sectors and it is precisely there that residents will often remain for long stays. In such cases, the institution will no longer be a temporary place of residence but a living environment, which makes it particularly crucial to create a healthy and pleasant living environment. More examples are also needed for all healthcare professionals in the area of other sustainability themes, such as circularity and climate change mitigation.

In addition to more examples, initiatives and partnerships are needed to help (smaller) institutions to use, monitor and evaluate sustainable interventions. This may, for example, involve looking at the indicators as formulated by the Monitoring and Review Working Group of the Ministry of Health, Welfare and Sport.

5 Generic discussion, conclusion and recommendations

5.1 Discussion

5.1.1 Environmental footprint and monitoring

A method has been established in this RIVM report to measure the environmental footprint of the Dutch healthcare sector, which required a bespoke approach. The generic footprint was calculated using a (top-down) input-output analysis using the most recent data and key figures available. The outcome was supplemented with specific (bottom-up) data, such as the impact of propellants in inhalation medication. Thereafter, a bottom-up analysis was used to deepen the understanding of the product group that contributes most to the calculated environmental footprint of the healthcare sector: chemical products, which includes pharmaceuticals and medical consumables. This hybrid approach, in which the generic top-down analysis and the bottom-up analysis converge, lays the foundation for a baseline measurement of the environmental footprint of the Dutch healthcare sector. It was also examined what data is still missing, what needs to be specified further or requires better interpretation in follow-up research.

In order to actually establish a baseline measurement, it is necessary to analyse what the minimum amount of data required for this is, to examine whether all this data is available and to determine what the uncertainties are. In addition, it is crucial to review what the possibilities are for keeping data and key figures representative and up to date and what a useful monitoring frequency would be. This would allow a baseline measurement to be achieved, alongside an action plan for the monitoring of national developments of the environmental footprint of healthcare. A baseline and monitoring the environmental footpring of healthcare goes to fulfilling one of the commitments made by the Ministry of Health, Welfare and Sport at the COP26 UN climate summit[10]. It is vital to work with the Ministry of Health, Welfare and Sport and the organisations involved in healthcare to determine precisely what goals a monitor should serve or support, so that they can be calibrated where necessary. Any follow-up research, for example, can include more types of environmental impact, such as eutrophication and soil acidification, and relevant impacts for bio-based materials (often used for more sustainable plastics) and sustainable food respectively[107,108]. In addition, key areas of focus or hotspots can likewise be addressed in local, national and international policy aims.

An environmental footprint and a monitor allow the current status of and any changes in environmental impacts to be tracked. This will help identify, prioritise and monitor issues that require our attention in making the healthcare sector more sustainable. Parties in the healthcare sector, such as manufacturers, suppliers, industry associations and healthcare institutions, can themselves use this study to, for example, choose focus in annual plans on topics that (temporarily) require more attention[7]. Dutch and international stakeholders can also use the results of the environmental footprint in collaborative networks, such as for for pharmaceutical residues in the environment[109] or in a Green Deal for

Sustainable Healthcare[10] . For example, this report shows that chemicals, consumables and pharmaceuticals collectively account for a large share of the environmental impact. It is therefore vital that manufacturers of pharmaceuticals, medical devices and consumables share more data publicly for the benefit of sustainability analyses. This may relate to data on the manufacturing process, such as data on use of resources, energy consumption, water consumption. However, information on transport distances and product composition is equally required to gain a more accurate picture of how chemicals and pharmaceuticals can be made more sustainable. It is similarly of value that the results of sustainability studies, such as life cycle assessments, should be shared publicly. In addition, sustainable food in the healthcare sector can make a key contribution to reducing environmental impact.

Due to the complexity of the transition to a sustainable society, current and direct local impacts (environment and health) are still difficult to measure. Specific interim goals for sustainability improvements in the healthcare sector, however, can already be formulated for all the key pillars, alongside long-term aims. This can be achieved based on the forthcoming Green Deal for Sustainable Healthcare 3.0 or the international sustainable development goals. A range of practical examples and ongoing activities for all the various pillars can then be identified and tracked in a structured manner in the form of a transition or action monitoring programme[25]. This will provide an initial picture of how sustainability efforts in healthcare are progressing and where these efforts are headed[12]. In addition, a monitor for the environmental footprint at national scale can identify the more quantitative effects and will allow work to take place on knowledge development. This will involve key issues, such as greenhouse gas emissions, use of resources, waste, etc., being identified and monitored. By examining both impact and activities over the years, knowledge can be shared more effectively and better management of sustainability in healthcare can be achieved[12].

5.1.2 *From an overview to action prospects*

Establishing a generic overview for the Netherlands is a vital approach, given that it is impossible, in practical terms, to conduct an individual life cycle assessment or individual environmental impact assessment for each individual product. Singular or individual assessments take up a great deal of time and resources and, additionally, make it more difficult to gain a clear overview and identify any trends.

In the coming years, it will be necessary to elaborate this basic analysis to a higher level of detail, in order to be able to make a greater distinction between services and product groups, such as for chemicals, disposable products and pharmaceuticals. Specific analyses can provide specific information in a targeted manner, such as the improved measurements of the impact of analgesics and antibiotics on the environmental themes discussed in this study. This also requires transparency (data) and engagement (partnerships) from parties in value chains, such as pharmaceutical and packaging manufacturers. In addition to sustainability analyses, ecotoxicity risk assessments often have to be performed, for example, for surface water[110,111], given that a (regulatory) local assessment may be required to determine ecotoxicity and local exposure, and a method such as an LCA may not be sufficient in this regard.

Given that the practical landscape and action prospects of the individual institutions may be very different, for example in care for the disabled or in hospitals, being able to distinguish between the various sub-sectors in healthcare would be highly beneficial. In addition, this allows for the environmental footprint, including hotspots, to be determined more accurately. Analyses and practical examples for these various institutions are required to help healthcare professionals improve and evaluate sustainability at a local level[12]. Moreover, these practical examples can be fleshed out further and substantiated in order to ensure better alignment between climate change adaptation and mitigation and environmental quality and public health. For example, RIVM recognises that a greener healthcare environment can not only contribute to climate change mitigation and adaptation, but also to the well-being of patients and staff[103].

The environmental footprint of the Dutch healthcare sector and the activities of all the various healthcare professionals involved can lead to linking up with other sectors and serve an exemplary function. The Ministry of Economic Affairs and Climate Policy, the Ministry of Agriculture, Nature and Food Quality and the Ministry of Infrastructure and Water Management, for example, similarly work with footprint data. Although individual ministries are already looking at indirect emissions from the procurement of products, there is as yet no policy for the reduction of greenhouse gas emissions across the entire value chain, nor for the other types of environmental impact examined in this study. Furthermore, the ministerial departments are not yet jointly looking at value chain emissions[114]. Identifying and mapping out these emissions is crucial to obtaining a more accurate picture of the effects on health and the environment (both now and in the long term) and to providing action prospects. Examining multiple types of environmental impact simultaneously is likewise crucial to identifying win-win opportunities as well as to preventing the shift of climate change to other types of environmental impact, for example. The approach presented in this report, in which the direct environmental impact and the indirect impact (across the value chain) have been calculated for entire sector on behalf of the Ministry of Health, Welfare and Sport can contribute to the sharing of knowledge between sectors and ministerial departments and ensure greater cohesion.

Translating impact into costs (and benefits), such as in a social cost-benefit analysis[115], may be a way to more easily compare the outcomes of environmental impacts and support decision making. Another method would be to convert the various types of impact to health loss, for which purpose disability-adjusted life years (DALYs) may be used. A DALY is a year of life lost due to death or disease and, for example, is used in disease burden calculations. Given that climate change can lead to health effects in the long term, the emissions of greenhouse gases and particulate matters can be converted into DALY for the population, in order to express the long-term impact in health loss. This provides an indication of the extent to which health is linked to climate change or to air quality[116]. For example, it could be examined how many emissions are released for certain types of treatment and what the additional future disease burden would be in DALY. This approach was deliberately not chosen in this study, as the relationship with public health cannot yet be assessed for many types of environmental impact (such as pathogens, litter or microplastics). This study did not include ascertaining for what types of environmental impact a DALY could be calculated and how representative or accurate this would be. Moreover, this study is primarily concerned with the intrinsic question of how significant the various types of environmental impact are and where they come from, in order to subsequently identify how these types of impact can be reduced and prevented. The purpose of this study was not to weigh one type of (environmental) impact against another, which is an endeavour that involves social, economic, political and ethical aspects, in addition to health and the environment. The results of this study – or parts thereof – can be elaborated on further in any follow-research for social cost-benefit analyses or can be (partially) converted into DALY.

It has already become clear, even without conversion into DALY or costs and benefits, that healthcare professionals and policymakers can contribute to achieving the objectives in the field of climate and the circular economy – and thereby can contribute to public health in the long term. If measures are taken to make treatments, products or services more sustainable, with fewer emissions across the chain, this will also reduce the disease burden in the future. Sustainable healthcare therefore not only goes to benefit today's patients and residents, but the environmental and public health of the future.

5.1.3 Reliability and uncertainties

Both at policy level and at the level of the workplace, a better understanding of the life cycle of product groups, such as consumables, medical devices and protective equipment, helps ascertain which products need to be made more sustainable and where in the life cycle this is to be achieved[22]. This is likewise beneficial when making decisions or establishing priorities, so that time and resources can be used as effectively as possible to increase sustainability.
A (national) independent knowledge database with publicly available data for environmental impact assessment can additionally be effective for the broad development, sharing and harmonisation of such knowledge. A distinction must be made in this case between primary and raw data (such as data on the resources used in the manufacturing of pharmaceuticals or a so-called life cycle inventory (LCI) dataset) or results, for example, of life cycle analyses. It is therefore essential that we look at quality and transparency (e.g. CRED[112]), at the application of the FAIR data concept (*Findability Accessibility Interoperability Reusability*) and at opportunities to modify or expand existing data (such as the Raw Materials Information System[113] and/or DigiMV).[12]

Another example of a knowledge database with more primary data is www.co2emissiefactoren.nl, which is a partnership of Milieu Centraal, Stimular, SKAO, Connekt and Central Government, which provides an updated list of Dutch greenhouse gas emissions factors (CO2-eq) each year for various product groups, based on the assessment of a broad panel of experts and the most recent insights. The Environmental

Impact of Food Products database[108] is an example of a knowledge database that contains the results of LCA studies in which the environmental impact has been calculated for food products. The results include greenhouse gas emissions, eutrophication of salt and fresh water, acidification of the soil, land use and irrigation/water consumption. A public knowledge database of this type, containing data and/or results, could contribute to both improving footprint calculations at a local and national level and to establishing a common language and definitions. This is crucial, given that different studies and results can then be better validated and compared.

The most representative and current data and methods were used for the present sector-wide environmental footprint calculation. However, a degree of uncertainty is always associated with the data and the model used. In addition, the specific contributions of the individual products (or product groups) or other sources of environmental impact used at the generic level are uncertain. Combining generic (top-down) and specific (bottom-up) data and methods provides insight into optimal models and outcomes in terms of variation and uncertainties. While generic top-down results in the model contain more uncertainties due to the high level of aggregation, specific models may contain more uncertainties in the data. Furthermore, data cannot simply be extrapolated to or from other countries, other years or individual institutions or persons, given that it will often relate to averages and situations that may differ at a local level. Changes in reality can therefore lead to the data or key figures no longer being representative. In addition, although uncertainties in a specific comparison may be acceptable, upon extrapolation of the specific comparison to a greater magnitude these uncertainties will likewise scale up, resulting in the data no longer being representative or useful. An example of this may be the extrapolation of a comparison of two products to two entire product groups for the whole of the Netherlands. It is therefore vital that any follow-up research should remain committed to improving this hybrid approach by working towards a superior level of detail (e.g better distinction of product groups) and further identifying the degree of uncertainty and sensitivity (e.g. variation in time and space) of the approach.

The comparisons with the footprint results of various studies and the literature review into drug LCAs show that the various estimates are based on a large number of differences (in scope, data, method and results). However, there are equally similarities between the results, for example in order of magnitude, which means that some form of validation can sometimes be achieved. For a number of product groups, this helps identify where a more sustainable approach is needed in the life cycle as well as where more information is required. Finally, this study shows that the use of a uniform, unambiguous method to determine the environmental footprint is crucial to reducing variation and to making studies comparable.

5.2 Conclusion & recommendations

This report has calculated an first national environmental footprint for the healthcare sector that goes beyond climate change alone. The generic input-output analysis (top-down) was carried out for the study, using the most recent data available, with the calculated footprint subsequently being combined with additional (specific) data from life cycle assessments. The environmental impact categories examined in this study are greenhouse gas emissions, blue water consumption, the extraction of abiotic resources (minerals and metals), land use and total waste generation. The study shows that chemical products (which include consumables and pharmaceuticals) make the largest significant contribution to the environmental impact of the healthcare sector. The bottom-up research shows that it is currently not yet possible to gain a complete picture of which products or components of the value chain of chemical products are responsible for the impact calculated. Better data is needed to calculate the specific contribution of pharmaceuticals in the chemical products category. This approach lays the foundation for a baseline measurement of the environmental footprint of the Dutch healthcare sector, which can subsequently be used to monitor the environmental footprint in the years to come.

A review was also carried out to establish whether machine learning, in addition to other methods, such as life cycle assessment, could contribute to estimating additional bottom-up data for the environmental impact of pharmaceuticals. It is currently unknown whether enough existing and reliable data is available to be able to rely on machine learning.

In addition, this study reviewed professional practice and collected examples from that domain on how a health-promoting healthcare environment can be stimulated within the themes of nature, architecture and nutrition. Initial positive effects can be identified as a result of changes made in the healthcare environment that improve the well-being of patients, visitors and employees. The positive impact of a number of practical examples has been demonstrated by means of scientific research. In addition, there are indications that some of the practical examples contribute to sustainability. In the case of various examples, this is similarly demonstrated by studies carried out by the institutions themselves (e.g. by reducing food wastage).

This study contributes to the knowledge base for a sustainable healthcare sector. In order to improve the method and insights, and to be able to contribute to more specific action prospects, both in terms of policy and practical implementation, RIVM is putting forward the following recommendations to ministries, healthcare institutions, manufacturers and other relevant parties:

- Use less energy and resources (raw materials), as this will lead to a lower environmental impact. In concrete terms, limiting the unnecessary use of drugs (pharmaceuticals) and focusing on reusable materials will contribute to this endeavour directly;
- Manufacturers of pharmaceuticals, medical devices and consumables should share quality data publicly, to allow that data to be available for sustainability assessments. This may relate to data on the manufacturing process and product composition, as well as to the results of any sustainability studies, such as life cycle analyses, that have been carried out;

- Draw up a joint plan with healthcare institutions, industry associations, health insurers, knowledge institutions, the Ministry of Health, Welfare and Sport and other stakeholders for the sharing and maintenance of independent and accessible data in the public domain, such as through a knowledge database or an (existing) platform (e.g. data on resources, composition and use);
- Manufacturers, suppliers, transporters and healthcare providers should work together to ensure a greater degree of cooperation within (international) chains. Any partnerships should link up to the key themes of health, climate change, nature and circularity, for example, by making joint agreements on definitions and objectives, which can then be embedded in policy aims and annual plans;
- The ministries involved, such as Health, Welfare and Sport, Economic Affairs, Infrastructure and Water Management and Agriculture, should collaborate more closely with the aim of linking up the key themes of health, climate change, nature and circularity more effectively – for example, by driving the harmonisation of definitions and methods and focusing on a generic, open access and valid approach for the calculation of the sectoral footprint;
- Have an action plan drawn up for a baseline measurement of the environmental footprint of the Dutch healthcare sector. Identify the requirements, uncertainties and frequency for monitoring. A baseline measurement and monitor will allow the Netherlands to fulfil one of the commitments of the COP26 UN climate summit and will allow the progress of the goals in the area of the circular economy to be monitored;
- Facilitate the continued development of the footprint calculation method, whereby a more accurate distinction can be made in the environmental footprint with regard to products and services, such as chemicals, pharmaceuticals, consumables and potential treatments;
- Facilitate any follow-up research in which a more specific distinction is made within the environmental footprint for various sub-sectors, by way of explicit specification in the input-output analysis and by distinguishing between hospitals, nursing and care homes, mental healthcare and care for the disabled;
- Facilitate more scientifically backed practical examples relating to various environmental issues and of the health-promoting healthcare environment for the various sub-sectors: hospitals, nursing and care homes, mental healthcare and care of the disabled – with a specific focus on long-term care. Any quantitative outcomes can then be used in the sustainability policy of institutions – whether as a new standard or as an achievable goal.

6 Glossary, terms and abbreviations

Active (pharmaceutical) ingredient See: API – active pharmaceutical ingredient
AD – applicability domain
The range of data to which a model can be applied. In this case, the term relates to the chemical data for which the training set of a model (such as QSAR or ANN) has been developed. The term indicates the range within which predictions can be made about material properties.
AI – artificial intelligence
Field of science concerned with creating an artificial, man-made phenomenon that exhibits a form of intelligence.
API – active pharmaceutical ingredient
The substance that provides a pharmaceutical with its beneficial effect. The term refers to the substance that inhibits stomach acid, for example, provides relief against headaches, hay fever or helps lower blood pressure. Pharmaceuticals also contain excipients in addition to their active ingredient.[1]
Applicability domain See: AD – applicability domain
ANN – artificial neural network
Machine learning model based on regression. An ANN is similar to a biological nervous system (such as the brain) in that it is able to process information and is made up of multiple layers.
Artificial intelligence See: AI – artificial intelligence
Greenhouse gas
See: GHG – greenhouse gas
BUA – bottom-up analysis
An approach or method that examines one part or several parts of a whole in detail. This detailed information provides an understanding of larger processes. A BUA provides additional insight in sub-categories, due to the fact that they are examined more specifically.
Carbon footprint
The aggregated contribution of a product, service or sector to climate change, caused by the emission of greenhouse gases across the entire life cycle and expressed in CO_2 equivalent.
CED – cumulative energy demand
The primary energy requirements throughout the entire life cycle of a product, service or sector. Used as an impact indicator in LCAs. CED is also known as 'primary energy consumption'.
CEENE – cumulative exergy extracted from the natural environment
LCIA method (Life Cycle Impact Assessment) that quantifies exergy extracted from natural ecosystems over the entire life cycle of a product, service or sector. Used as an impact indicator in LCAs.
Characterisation
Determining the impact on the environment, divided across the various impact categories in midpoint or endpoint indicators.
Characterisation factors
A factor that determines the extent to which an intervention contributes to environmental impact.
Climate footprint See: carbon footprint

Contribution analysis
A contribution analysis calculates the indirect effect based on purchased goods or services (the embedded effect of the total value chain per product).
CO_2 equivalent (CO_2-eq)
Unit of measure used to compare various greenhouse gases based on their global warming potential (GWP), by converting the amounts of other gases into the equivalent amount of carbon dioxide with the same global warming potential.[1]
Cradle-to-gate
A partial life cycle assessment of a product – from the extraction of raw materials (cradle) to the factory gate. The utilisation phase and waste phase are excluded from the scope of the impact assessment.
Cradle-to-grave
A comprehensive life cycle assessment of a product, from the extraction of raw materials (cradle), manufacturing, transport, product use and, ultimately, disposal.
Cumulative energy demand See: CED – cumulative energy demand
DDD – defined daily dose
Unit of measure used to compare pharmaceuticals based on dos equivalent amounts. The World Health Organization (WHO) has established this dose per pharmaceutical for the treatment of certain (key) indications.
Defined daily dose See: DDD – defined daily dose
DPI – dry powder inhaler
Used for the delivery of inhaled medications against asthma or COPD. A dry powder inhaler contains inhalation powder, which usually consists of a mixture of small drug particles mixed with lactose.
Endpoint indicators
A number indicating the environmental impact at the level of human health, loss of biodiversity and use of raw materials.
Environmental footprint
The aggregated contribution of all life cycles of a product, service or
Environmental impact
The impact of anthropogenic interventions, such as economic activities, on the environment, whereby substances are extracted from the environment (e.g. resource extraction) or substances are emitted into the environment (e.g. the emission of greenhouse gases.
EE-IOA – environmentally extended input output analysis
An IOA expanded with environmental extensions in order to be able to calculate the environmental impact of global value chains.
Exiobase
A harmonised multi-regional environmentally extended input-output table to be used in input-output analyses.
FU – functional unit
The basis (quantity and unit) on which two alternatives can be compared, for example, in an LCA.
GHG – greenhouse gas
A gas that contributes to global warming and climate change by trapping heat within the atmosphere.
Global warming potential
See: GWP – global warming potential

GWP – global warming potential
A relative measure that shows the greenhouse effect over a certain period of time of the release of 1 kg of a substance into the atmosphere compared to the release of 1 kg of CO2 into the atmosphere. The GWPs that are currently most commonly used have been calculated over a 100-year period.
Healthcare expenditure in the broad sense
All expenditure on the Dutch healthcare sector for the provision of healthcare to residents and non-residents.
Hotspot analysis
A hotspot analysis allows the indirect impact to be calculated for the location (sector and/or geography) in which the impact physically occurs.
Inventory data See: LCI – life cycle inventory
IOA – input output analysis
A macroeconomic method with which the network between industries can be analysed. IOAs are used to calculate how much production value is needed from individual industries in a value chain to generate a particular output.
LCA – life cycle assessment/analysis
A method in which the environmental impact is examined throughout the entire life cycle of a process, product or material.
LCI – life cycle inventory
The second step in an LCA – a collection of all environmental interventions (emissions into and extractions from the environment) that occur in a defined system.
LCIA – life cycle impact assessment
The third step in an LCA, in which environmental interventions are quantified according to environmental impact scores (mid and endpoints) based on so-called characterisation factors.
Machine learning
See: ML – machine learning
Metered dose inhaler
See: PMDI – pressurised metered dose inhaler
Midpoint indicator
A number that indicates the environmental impact at the level of individual environmental issues, such as climate change, acidification and ecotoxicity. An environmental intervention, such as the release of a certain substance into the air, can be taken into account in one or more midpoints.
MIP – mixed-integer programming
A calculation method where the unknown variables must be whole numbers (integers). In this case, the method is used to predict the environmental impact of chemicals.
ML – machine learning
Field of research within the artificial intelligence domain aimed at the development of techniques to allow computers to learn.
MSM – molecular-structure-based model
A model in which molecular descriptors deter the outcomes (environmental impact). The FineChem tool is an example of an MSM, which is able to predict the environmental impact of chemicals based on molecular descriptors.

Molecular descriptors / molecular characteristics
A structure or physicochemical property of a molecule or molecular particle, such as the molecular mass or percentage of N atoms.
(EE) MRIO - (environmentally extended) Multiregional Input Output table
An input output table which tracks data on the economies of various (groups of) countries, unlike a single-region table which only tracks the data of one national economy.
Neural Network See: ANN
OTC medicines / over-the-counter pharmaceuticals Over-the-counter drugs; over-the-counter medicines available at the supermarket and pharmacy.
PCA – principal component analysis
A statistical analysis method used to describe a large amount of data with a small number of relevant quantities, the main components of the dataset.
PCR – product category rule
Standardisation of the approach used to asses and compare environmental properties of a properties in a specific category. E.g. agreements on the functional unit to be used.
pMDI – pressurised metered dose inhaler
Inhaled medication for asthma or COPD. A pressurised metered dose inhaler contains active ingredients combined with a propellant.
PMI – process mass intensity
The mass required to be able to carry out a process. Often expressed in kg of raw materials / kg of product from the process.
Powder inhaler
See: DPI – dry powder inhaler
QSAR – quantitative structure-activity relationship models
A mathematical relationship between a molecular descriptor or a chemical and its toxic effect.
ReCiPe
A commonly used life cycle impact assessment method (LCIA) with characterisation factors at midpoint and endpoint level.
SHA – System of Health Accounts
An international system used for the classification of expenditure on healthcare goods and services.
Synthesis pathway descriptors
The characteristics / descriptors of the synthesis process that can be used as predictor variables for environmental impacts. E.g. the reaction temperature or duration of the synthesis process.
Top-down analysis
An approach or method that initially focuses on the larger whole (generic) and then becomes more specific.
UPR – unit process data
An element in an LCA which involves the quantification of the input and output of a process.
What Works Dossier
A summary of the effective elements, identified in the scientific literature, of a specific approach or intervention with regard to a specific target group, which briefly outlines what works, what does not work, what is most likely to work and what the uncertainties or unknowns are.

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Appendix A

Different databases have different delineation in their datasets and thus different data available. Dawkins et al.[27] created a table to illustrate this in 2019 in which the similarities and differences have been identified for the databases by Statistics Sweden (SCB), the Global Trade Analysis Project (GTAP), Eora, Exiobase, World Input-Output Database (WIOD) and the OECD's input-output database. Below is a list of the possible different contents of the databases, these may differ in:

- Most recent data & frequency of updating
- Time series of data that are available
- Available environmental impact categories
- Data representative of certain countries and/or regions
- Type of input-output tables and sources for these tables
- Sources and availability of environmental extensions
- Product/sector detail level
- Classification scheme
- Accessibility (public) For the table and more background information, see Dawkins et al.[27]

Appendix B

Health expenditure 2016 (CBS Statistics Netherlands)

Healthcare financing regimes Healthcare functions	Total of all financing regimes millions of euros	Total of financing of residents millions of euros	Abroad; output millions of euros
Total expenditure on healthcare and welfare	94842	94634	208
Total healthcare expenditure	73032	72918	114
HC1: Medical care	34699	34616	83
HC11: Inpatient medical care	13024	12988	37
HC12: Day treatment medical care	3685	3676	9
HC13: Outpatient/ambulatory medical care	17399	17362	37
HC14: Medical care at home	590	590	0
HC2: Rehabilitation care	3170	3170	0
HC21: Inpatient rehabilitation care	1030	1030	0
HC22: Day treatment rehabilitation care	35	35	0
HC23: Outpatient/ambulatory rehabilitation	2106	2106	0
HC3: Long-term healthcare	18896	18885	11
HC31: Long-term inpatient healthcare	14535	14524	11
HC32: Long-term day-treatment care	148	148	0
HC33: Long-term ambulatory care	173	173	0
HC34: Home care - long term	4040	4040	0
HC4: Support services	1365	1364	1
HC41: Medical laboratory analysis	641	641	0
HC42: Medical imaging	104	104	0
HC43: Patient transport	620	619	1
HC5: Pharmaceutical and devices	8746	8727	19
HC51: Pharmaceuticals, consumables	5639	5620	19
HC52: Therapeutic devices	3107	3107	0
HC6: Preventive care	2561	2561	0
HC7: Governance, system and financial admin	2905	2905	0
HC71: Healthcare policy and provision	847	847	0
HC72: Organisation of financing	2058	2058	0
HC9: Healthcare (not referred to previously)	690	690	0
Total healthcare-related expenditure	9317	9317	0
HCR1: Long-term care (well-being)	8984	8984	0
HCR11: Long-term care, well-being, in kind	7079	7079	0
HCR12: Long-term care, benefits	1905	1905	0
HCR2: Health promotion, multisector	333	333	0
M1(HC): Other care and welfare	12493	12399	94

Appendix C

Import distribution of Chemicals n.e.c. and Medical precision and optical instruments, watches and clocks in the Dutch overall final demand in 2016. RoW = Rest of world. Table adapted from Steenmeijer et al. (2022) (link).

Country/Region	% for Chemicals n.e.c.	% for Medical precision and optical instruments, watches and clocks
Australia	0.57	0.90
Austria	0.01	0.18
Belgium	0.63	0.61
Brazil	1.19	0.05
Bulgaria	0.05	0.06
Canada	0.55	0.23
China	4.46	2.39
Croatia	0.00	0.00
Cyprus	0.00	0.00
Czech Republic	0.46	0.17
Denmark	0.02	0.52
Estonia	0.00	0.00
Finland	0.01	0.10
France	0.07	5.52
Germany	0.39	10.62
Greece	0.00	0.02
Hungary	0.03	0.13
India	1.69	0.12
Indonesia	1.37	0.02
Ireland	0.58	0.93
Italy	0.01	1.16
Japan	0.81	0.00
Latvia	0.00	0.00
Lithuania	0.00	0.01
Luxembourg	0.00	0.00
Malta	0.00	0.01
Mexico	0.36	0.37
Netherlands	2.36	45.55
Norway	0.03	0.54
Poland	0.25	0.26
Portugal	0.00	0.06
RoW Africa	12.02	0.16

Country/Region	% for Chemicals n.e.c.	% for Medical precision and optical instruments, watches and clocks
RoW America	1.33	1.85
RoW Asia and Pacific	36.82	2.16
RoW Europe	0.81	0.17
RoW Middle East	8.97	1.61
Romania	0.08	0.03
Russia	2.79	0.04
Slovakia	0.00	0.34
Slovenia	0.12	0.04
South Africa	0.39	0.04
South Korea	0.49	0.00
Spain	0.06	0.50
Sweden	0.00	0.82
Switzerland	2.75	2.60
Taiwan	1.62	0.76
Turkey	0.21	0.03
United Kingdom	0.12	3.22
United States	15.54	15.09
Total	100	100

Appendix D

The table below sets out the available data from existing studies on climate footprint calculations for the national healthcare sectors of other countries. The figures have been calculated for different definitions, regions and years. The values for the EU scale and the global scale are likely to be lower estimates due to incomplete data[6] and the value of Austria per hospital bed is likely to be low due to the highest number of hospital admissions, the highest number of beds and the longest hospital stays in the EU[22]. The values of Tennison et al.[24] were calculated for a footprint that does not include the impact of pressurised metered dose inhalers' emissions and the impact of individual travel movements. The System of Health Accounts (SHA; defined by the OECD) provides an internationally comparable definition for healthcare, which takes into account healthcare provided to residents (local or abroad), excluding welfare services and care provision to non-residents).

Available data for anaesthetic gases from existing studies on climate footprint calculations for foreign healthcare sectors in other countries. SHA = System of Health Accounts.

Source	Gases	Definition of healthcare sector	Region	Unit	Value	Year
HCWH & Arup, 2019	N_2O	Internationally comparable (SHA)	EU	Percentage of healthcare sector climate footprint	1%	2014
	N_2O	Internationally comparable (SHA)	World	Percentage of healthcare sector climate footprint	0.6%	2014
	N_2O, F gases	Internationally comparable (SHA)	World	Percentage of scope 1 greenhouse gases	2.5%	2014
Weisz et al., 2020	N_2O, F gases	Internationally comparable (SHA)	Austria	Greenhouse gases per hospital bed	329 kg CO_2-eq	2015
	N_2O, F gases	Internationally comparable (SHA)	Austria	Percentage of healthcare sector climate footprint	0.3%	2014/ 2015
Tennison et al., 2021	N_2O, F gases	Healthcare (NHS), broad definition	United Kingdom	Percentage of healthcare sector climate footprint	2.24%	2016
	N_2O, F gases	Healthcare (NHS) and welfare services, broad definition	United Kingdom	Percentage of healthcare sector climate footprint	1·78 %	2016

Appendix E

Product name	Doses (puffs) per pack from preparation texts of the Pharmacotherapeutic Compass	Propellant in g/package from MEB dossiers
AIROMIR AEROSOL 100MCG/DO	200	5.30
SALBUTAMOL AEROSOL 100MCG/DO	200	7.50
VENTOLIN AEROSOL 100MCG/DO	200	17.98
SEREVENT AEROSOL 25MCG/DO	120	11.99
ATIMOS AEROSOL 12MCG/DO	100	9.09
ATIMOS AEROSOL 12MCG/DO	120	10.40
FORADIL AEROSOL 12MCG/DO	100	9.09
AIRFLUSAL AEROSOL 25/125UG/DO	120	12.47
AIRFLUSAL AEROSOL 25/250UG/DO	120	12.42
SERETIDE AEROSOL 25/125MCG/DO	120	11.95
SERETIDE AEROSOL 25/250MCG/DO	120	11.95
SERETIDE AEROSOL 25/50MCG/DO	120	11.95
salmeterol/fluticason AEROSOL 25/125MCG/DO	120	12.50
salmeterol/fluticason AEROSOL 25/250MCG/DO	120	12.48
SYMBICORT AEROSOL 100/3UG/DO	120	10.95
SYMBICORT AEROSOL 200/6UG/DO	120	10.80
SYMBICORT AEROSOL 6/200MCG/DO	120	10.80
FORMODUAL AEROSOL 100/6UG/DO	180	11.20
FORMODUAL AEROSOL 6/100MCG/DO	180	11.20
FOSTER AEROSOL 100/6UG/DO	180	11.20
FOSTER AEROSOL 200/6UG/DO	120	10.36
FOSTER AEROSOL 6/100MCG/DO	180	8.14
FOSTER AEROSOL 6/200MCG/DO	120	14.24
FUTIFORM AEROSOL 10/250MCG/DO	120	10.90
FUTIFORM AEROSOL 125/5UG/DO	120	10.90
FUTIFORM AEROSOL 250/10UG/DO	120	10.90
FUTIFORM AEROSOL 5/125MCG/DO	120	10.90
FUTIFORM AEROSOL 5/50MCG/DO	120	10.90
BERODUAL AEROSOL 50/20MCG/DO	200	10.16
TRIMBOW AEROSOL 87/5/9UG/DO	120	10.40

Product name	Doses (puffs) per pack from preparation texts of the Pharmacotherapeutic Compass	Propellant in g/package from MEB dossiers
TRIMBOW AEROSOL 87/5/9UG/DO	180	14.30
QVAR AEROSOL 100MCG/DO	200	10.89
QVAR AEROSOL 50MCG/DO	200	10.90
beclomethasone AEROSOL 100MCG/DO	200	12.13
beclomethasone AEROSOL 250MCG/DO	200	11.78
beclomethasone AEROSOL 50MCG/DO	200	12.13
budesonide AEROSOL 200MCG/DO	200	11.21
FLIXOTIDE AEROSOL 125MCG/DO	60	7.99
FLIXOTIDE AEROSOL 125MCG/DO	120	11.98
FLIXOTIDE AEROSOL 250MCG/DO	60	7.99
FLIXOTIDE AEROSOL 250MCG/DO	120	11.98
FLIXOTIDE AEROSOL 50MCG/DO	120	10.59
fluticasone AEROSOL 250MCG/DO	120	12.48
fluticasone AEROSOL 125MCG/DO	120	12.50
ALVESCO AEROSOL 160MCG/DO	60	5.59
ALVESCO AEROSOL 160MCG/DO	120	8.80
ALVESCO AEROSOL 80MCG/DO	60	5.60
ALVESCO AEROSOL 80MCG/DO	120	8.82
ATROVENT AEROSOL 20MCG/DO	200	9.48
ipratropium AEROSOL 20MCG/DO	200	12.30
LOMUDAL AEROSOL 5MG/DO	112	15.90
TILADE AEROSOL 2MG/DO	112	20.04

Appendix F

Appendix F.1 Characterisation factors for climate change. Table adapted from Steenmeijer et al. (2022) (link).

Stressor	Unit	kg CO2-eq
CO2 - combustion - air	kg	1
CH4 - combustion - air	kg	25
N2O - combustion - air	kg	298
CH4 - non-combustion - Extraction/production of (natural) gas - air	kg	25
CH4 - non-combustion - Extraction/production of crude oil - air	kg	25
CH4 - non-combustion - Mining of anthracite - air	kg	25
CH4 - non-combustion - Mining of bituminous coal - air	kg	25
CH4 - non-combustion - Mining of coking coal - air	kg	25
CH4 - non-combustion - Mining of lignite (brown coal) - air	kg	25
CH4 - non-combustion - Mining of sub-bituminous coal - air	kg	25
CH4 - non-combustion - Oil refinery - air	kg	25
CO2 - non-combustion - Cement production - air	kg	1
CO2 - non-combustion - Lime production - air	kg	1
SF6 - air	kg	26087
HFC - air	kg CO2-eq	1
PFC - air	kg CO2-eq	1
CH4 - agriculture - air	kg	25
CO2 - agriculture - peat decay - air	kg	1
N2O - agriculture - air	kg	298
CH4 - waste - air	kg	25
CO2 - waste - biogenic - air	kg	1
CO2 - waste - fossil - air	kg	1

Appendix F.2 Characterisation factors for abiotic resource use. Table adapted from Steenmeijer et al. (2022) (link).

Stressor	Unit	kt
Domestic Extraction Used - Metal Ores - Bauxite and aluminium ores	kt	1
Domestic Extraction Used - Metal Ores - Copper ores	kt	1
Domestic Extraction Used - Metal Ores - Gold ores	kt	1
Domestic Extraction Used - Metal Ores - Iron ores	kt	1
Domestic Extraction Used - Metal Ores - Lead ores	kt	1
Domestic Extraction Used - Metal Ores - Nickel ores	kt	1
Domestic Extraction Used - Metal Ores - Other non-ferrous metal ores	kt	1
Domestic Extraction Used - Metal Ores - PGM ores	kt	1

Stressor	Unit	kt
Domestic Extraction Used - Metal Ores - Silver ores	kt	1
Domestic Extraction Used - Metal Ores - Tin ores	kt	1
Domestic Extraction Used - Metal Ores - Uranium and thorium ores	kt	1
Domestic Extraction Used - Metal Ores - Zinc ores	kt	1
Domestic Extraction Used - Non-Metallic Minerals - Building stones	kt	1
Domestic Extraction Used - Non-Metallic Minerals - Chemical and fertilizer minerals	kt	1
Domestic Extraction Used - Non-Metallic Minerals - Clays and kaolin	kt	1
Domestic Extraction Used - Non-Metallic Minerals - Gravel and sand	kt	1
Domestic Extraction Used - Non-Metallic Minerals - Limestone, gypsum, chalk, dolomite	kt	1
Domestic Extraction Used - Non-Metallic Minerals - Other minerals	kt	1
Domestic Extraction Used - Non-Metallic Minerals - Salt	kt	1
Domestic Extraction Used - Non-Metallic Minerals - Slate	kt	1

Appendix F.3 Characterisation factors for blue water consumption. Table adapted from Steenmeijer et al. (2022) (link).

Stressor	Eenheid	Mm3
Water Consumption Blue - Agriculture - rice	Mm3	1
Water Consumption Blue - Agriculture - wheat	Mm3	1
Water Consumption Blue - Agriculture - other cereals	Mm3	1
Water Consumption Blue - Agriculture - roots and tubers	Mm3	1
Water Consumption Blue - Agriculture - sugar crops	Mm3	1
Water Consumption Blue - Agriculture - pulses	Mm3	1
Water Consumption Blue - Agriculture - nuts	Mm3	1
Water Consumption Blue - Agriculture - oil crops	Mm3	1
Water Consumption Blue - Agriculture - vegetables	Mm3	1
Water Consumption Blue - Agriculture - fruits	Mm3	1
Water Consumption Blue - Agriculture - fibres	Mm3	1
Water Consumption Blue - Agriculture - other crops	Mm3	1
Water Consumption Blue - Agriculture - fodder crops	Mm3	1
Water Consumption Blue - Livestock - dairy cattle	Mm3	1
Water Consumption Blue - Livestock - nondairy cattle	Mm3	1
Water Consumption Blue - Livestock - pigs	Mm3	1
Water Consumption Blue - Livestock - sheep	Mm3	1
Water Consumption Blue - Livestock - goats	Mm3	1
Water Consumption Blue - Livestock - buffaloes	Mm3	1
Water Consumption Blue - Livestock - camels	Mm3	1
Water Consumption Blue - Livestock - horses	Mm3	1
Water Consumption Blue - Livestock - chickens	Mm3	1
Water Consumption Blue - Livestock - turkeys	Mm3	1
Water Consumption Blue - Livestock - ducks	Mm3	1

Stressor	Eenheid	Mm3
Water Consumption Blue - Livestock - geese	Mm3	1
Water Consumption Blue - Manufacturing - Products of meat cattle	Mm3	1
Water Consumption Blue - Manufacturing - Products of meat pigs	Mm3	1
Water Consumption Blue - Manufacturing - Products of meat poultry	Mm3	1
Water Consumption Blue - Manufacturing - Meat products n.e.c.	Mm3	1
Water Consumption Blue - Manufacturing - products of vegetable oils and fats	Mm3	1
Water Consumption Blue - Manufacturing - Dairy products	Mm3	1
Water Consumption Blue - Manufacturing - Processed rice	Mm3	1
Water Consumption Blue - Manufacturing - Sugar	Mm3	1
Water Consumption Blue - Manufacturing - Food products n.e.c.	Mm3	1
Water Consumption Blue - Manufacturing - Beverages	Mm3	1
Water Consumption Blue - Manufacturing - Fish products	Mm3	1
Water Consumption Blue - Manufacturing - Tobacco products (16)	Mm3	1
Water Consumption Blue - Manufacturing - Textiles (17)	Mm3	1
Water Consumption Blue - Manufacturing - Wearing apparel; furs (18)	Mm3	1
Water Consumption Blue - Manufacturing - Leather and leather products (19)	Mm3	1
Water Consumption Blue - Manufacturing - Pulp	Mm3	1
Water Consumption Blue - Manufacturing - Secondary paper for treatment, Re-processing of secondary paper into new pulp	Mm3	1
Water Consumption Blue - Manufacturing - Paper and paper products	Mm3	1
Water Consumption Blue - Manufacturing - Printed matter and recorded media (22)	Mm3	1
Water Consumption Blue - Manufacturing - Plastics, basic	Mm3	1
Water Consumption Blue - Manufacturing - Secondary plastic for treatment, Re-processing of secondary plastic into new plastic	Mm3	1
Water Consumption Blue - Manufacturing - N-fertiliser	Mm3	1
Water Consumption Blue - Manufacturing - P- and other fertiliser	Mm3	1
Water Consumption Blue - Manufacturing - Chemicals n.e.c.	Mm3	1
Water Consumption Blue - Manufacturing - Rubber and plastic products (25)	Mm3	1
Water Consumption Blue - Manufacturing - Glass and glass products	Mm3	1
Water Consumption Blue - Manufacturing - Secondary glass for treatment, Re-processing of secondary glass into new glass	Mm3	1
Water Consumption Blue - Manufacturing - Ceramic goods	Mm3	1
Water Consumption Blue - Manufacturing - Bricks, tiles and construction products, in baked clay	Mm3	1
Water Consumption Blue - Manufacturing - Cement, lime and plaster	Mm3	1
Water Consumption Blue - Manufacturing - Ash for treatment, Re-processing of ash into clinker	Mm3	1

Stressor	Eenheid	Mm3
Water Consumption Blue - Manufacturing - Other non-metallic mineral products	Mm3	1
Water Consumption Blue - Manufacturing - Basic iron and steel and ferro-alloys and first products thereof	Mm3	1
Water Consumption Blue - Manufacturing - Secondary steel for treatment, Re-processing of secondary steel into new steel	Mm3	1
Water Consumption Blue - Manufacturing - Precious metals	Mm3	1
Water Consumption Blue - Manufacturing - Secondary precious metals for treatment, Re-processing of secondary precious metals into new preciuos metals	Mm3	1
Water Consumption Blue - Manufacturing - Aluminium and aluminium products	Mm3	1
Water Consumption Blue - Manufacturing - Secondary aluminium for treatment, Re-processing of secondary aluminium into new aluminium	Mm3	1
Water Consumption Blue - Manufacturing - Lead, zinc and tin and products thereof	Mm3	1
Water Consumption Blue - Manufacturing - Secondary lead for treatment, Re-processing of secondary lead into new lead	Mm3	1
Water Consumption Blue - Manufacturing - Copper products	Mm3	1
Water Consumption Blue - Manufacturing - Secondary copper for treatment, Re-processing of secondary copper into new copper	Mm3	1
Water Consumption Blue - Manufacturing - Other non-ferrous metal products	Mm3	1
Water Consumption Blue - Manufacturing - Secondary other non-ferrous metals for treatment, Re-processing of secondary other non-ferrous metals into new other non-ferrous metals	Mm3	1
Water Consumption Blue - Manufacturing - Fabricated metal products, except machinery and equipment (28)	Mm3	1
Water Consumption Blue - Manufacturing - Machinery and equipment n.e.c. (29)	Mm3	1
Water Consumption Blue - Manufacturing - Office machinery and computers (30)	Mm3	1
Water Consumption Blue - Manufacturing - Electrical machinery and apparatus n.e.c. (31)	Mm3	1
Water Consumption Blue - Manufacturing - Radio, television and communication equipment and apparatus (32)	Mm3	1
Water Consumption Blue - Manufacturing - Medical, precision and optical instruments, watches and clocks (33)	Mm3	1
Water Consumption Blue - Manufacturing - Motor vehicles, trailers and semi-trailers (34)	Mm3	1
Water Consumption Blue - Manufacturing - Other transport equipment (35)	Mm3	1
Water Consumption Blue - Manufacturing - Furniture; other manufactured goods n.e.c. (36)	Mm3	1
Water Consumption Blue - Electricity - tower - Electricity by coal	Mm3	1
Water Consumption Blue - Electricity - tower - Electricity by gas	Mm3	1
Water Consumption Blue - Electricity - tower - Electricity by nuclear	Mm3	1

Stressor	Eenheid	Mm3
Water Consumption Blue - Electricity - tower - Electricity by hydro	Mm3	1
Water Consumption Blue - Electricity - tower - Electricity by wind	Mm3	1
Water Consumption Blue - Electricity - tower - Electricity by petroleum and other oil derivatives	Mm3	1
Water Consumption Blue - Electricity - tower - Electricity by biomass and waste	Mm3	1
Water Consumption Blue - Electricity - tower - Electricity by solar photovoltaic	Mm3	1
Water Consumption Blue - Electricity - tower - Electricity by solar thermal	Mm3	1
Water Consumption Blue - Electricity - tower - Electricity by tide, wave, ocean	Mm3	1
Water Consumption Blue - Electricity - tower - Electricity by geothermal	Mm3	1
Water Consumption Blue - Electricity - tower - Electricity n.e.c.	Mm3	1
Water Consumption Blue - Electricity - once-through - Electricity by coal	Mm3	1
Water Consumption Blue - Electricity - once-through - Electricity by gas	Mm3	1
Water Consumption Blue - Electricity - once-through - Electricity by nuclear	Mm3	1
Water Consumption Blue - Electricity - once-through - Electricity by hydro	Mm3	1
Water Consumption Blue - Electricity - once-through - Electricity by wind	Mm3	1
Water Consumption Blue - Electricity - once-through - Electricity by petroleum and other oil derivatives	Mm3	1
Water Consumption Blue - Electricity - once-through - Electricity by biomass and waste	Mm3	1
Water Consumption Blue - Electricity - once-through - Electricity by solar photovoltaic	Mm3	1
Water Consumption Blue - Electricity - once-through - Electricity by solar thermal	Mm3	1
Water Consumption Blue - Electricity - once-through - Electricity by tide, wave, ocean	Mm3	1
Water Consumption Blue - Electricity - once-through - Electricity by geothermal	Mm3	1
Water Consumption Blue - Electricity - once-through - Electricity n.e.c.	Mm3	1
Water Consumption Blue - Domestic - domestic Water Consumption Blue	Mm3	1

Appendix F.4 Characterisation factors for land use. Table adapted from Steenmeijer et al. (2022) (link).

Stressor	Unit	km2
Cropland - Cereal grains n.e.c.	km2	1
Cropland - Crops n.e.c.	km2	1
Cropland - Fodder crops - Cattle	km2	1

Stressor	Unit	km2
Cropland - Fodder crops - Meat animals n.e.c.	km2	1
Cropland - Fodder crops - Pigs	km2	1
Cropland - Fodder crops -Poultry	km2	1
Cropland - Fodder crops - Raw milk	km2	1
Cropland - Oil seeds	km2	1
Cropland - Paddy rice	km2	1
Cropland - Plant-based fibres	km2	1
Cropland - Sugar cane, sugar beet	km2	1
Cropland - Vegetables, fruit, nuts	km2	1
Cropland - Wheat	km2	1
Forest area - Forestry	km2	1
Other land Use: Total	km2	1
Permanent pastures – Grazing - Cattle	km2	1
Permanent pastures – Grazing - Meat animals n.e.c.	km2	1
Permanent pastures – Grazing - Raw milk	km2	1
Infrastructure land	km2	1
Forest area - Marginal use	km2	1

Appendix G

Aggregation table for Exiobase v3. Table adapted from Steenmeijer et al. (2022) (link).

Code	Name	Aggregate description	Aggregate description contribution analysis	Scope GHGP	Aggregate description hotspot analysis
i01.a	Cultivation of paddy rice	Food, tobacco and agricultural products	Food and food services	Scope 3	Agricultural sector
i01.b	Cultivation of wheat	Food, tobacco and agricultural products	Food and food services	Scope 3	Agricultural sector
i01.c	Cultivation of cereal grains n.e.c.	Food, tobacco and agricultural products	Food and food services	Scope 3	Agricultural sector
i01.d	Cultivation of vegetables, fruits, nuts	Food, tobacco and agricultural products	Food and food services	Scope 3	Agricultural sector
i01.e	Cultivation of oil seeds	Food, tobacco and agricultural products	Food and food services	Scope 3	Agricultural sector
i01.f	Cultivation of sugar cane, sugar beet	Food, tobacco and agricultural products	Food and food services	Scope 3	Agricultural sector
i01.g	Cultivation of plant-based fibres	Textile	Other	Scope 3	Other
i01.h	Cultivation of crops n.e.c.	Food, tobacco and agricultural products	Food and food services	Scope 3	Agricultural sector
i01.i	Cattle farming	Food, tobacco and agricultural products	Food and food services	Scope 3	Agricultural sector
i01.j	Pig farming	Food, tobacco and agricultural products	Food and food services	Scope 3	Agricultural sector
i01.k	Poultry farming	Food, tobacco and agricultural products	Food and food services	Scope 3	Agricultural sector
i01.l	Meat animals n.e.c.	Food, tobacco and agricultural products	Food and food services	Scope 3	Agricultural sector
i01.m	Animal products n.e.c.	Food, tobacco and agricultural products	Food and food services	Scope 3	Agricultural sector

Code	Name	Aggregate description	Aggregate description contribution analysis	Scope GHGP	Aggregate description hotspot analysis
i01.n	Raw milk	Food, tobacco and agricultural products	Food and food services	Scope 3	Agricultural sector
i01.o	Wool, silk-worm cocoons	Textile	Other	Scope 3	Other
i01.w.1	Manure treatment (conventional), storage and land application	Food, tobacco and agricultural products	Food and food services	Scope 3	Agricultural sector
i01.w.2	Manure treatment (biogas), storage and land application	Food, tobacco and agricultural products	Food and food services	Scope 3	Agricultural sector
i02	Forestry, logging and related service activities (02)	Food, tobacco and agricultural products	Food and food services	Scope 3	Agricultural sector
i05	Fishing, operating of fish hatcheries and fish farms; service activities incidental to fishing (05)	Food, tobacco and agricultural products	Food and food services	Scope 3	Agricultural sector
i10	Mining of coal and lignite; extraction of peat (10)	Coal and Petroleum	Other	Scope 3	Fossil fuel industry
i11.a	Extraction of crude petroleum and services related to crude oil extraction, excluding surveying	Coal and Petroleum	Other	Scope 3	Fossil fuel industry
i11.b	Extraction of natural gas and services related to natural gas extraction, excluding surveying	Natural gas and gaseous fuels	Other	Scope 3	Fossil fuel industry
i11.c	Extraction, liquefaction, and regasification of other petroleum and gaseous materials	Natural gas and gaseous fuels	Other	Scope 3	Fossil fuel industry
i12	Mining of uranium and thorium ores (12)	Minerals and Metals	Other	Scope 3	Mining of minerals and metals
i13.1	Mining of iron ores	Minerals and Metals	Other	Scope 3	Mining of minerals and metals
i13.20.11	Mining of copper ores and concentrates	Minerals and Metals	Other	Scope 3	Mining of minerals and metals

Code	Name	Aggregate description	Aggregate description contribution analysis	Scope GHGP	Aggregate description hotspot analysis
i13.20.12	Mining of nickel ores and concentrates	Minerals and Metals	Other	Scope 3	Mining of minerals and metals
i13.20.13	Mining of aluminium ores and concentrates	Minerals and Metals	Other	Scope 3	Mining of minerals and metals
i13.20.14	Mining of precious metal ores and concentrates	Minerals and Metals	Other	Scope 3	Mining of minerals and metals
i13.20.15	Mining of lead, zinc and tin ores and concentrates	Minerals and Metals	Other	Scope 3	Mining of minerals and metals
i13.20.16	Mining of other non-ferrous metal ores and concentrates	Minerals and Metals	Other	Scope 3	Mining of minerals and metals
i14.1	Quarrying of stone	Minerals and Metals	Other	Scope 3	Mining of minerals and metals
i14.2	Quarrying of sand and clay	Minerals and Metals	Other	Scope 3	Mining of minerals and metals
i14.3	Mining of chemical and fertilizer minerals, production of salt, other mining and quarrying n.e.c.	Minerals and Metals	Other	Scope 3	Mining of minerals and metals
i15.a	Processing of meat cattle	Food, tobacco and agricultural products	Food and food services	Scope 3	Agricultural sector
i15.b	Processing of meat pigs	Food, tobacco and agricultural products	Food and food services	Scope 3	Agricultural sector
i15.c	Processing of meat poultry	Food, tobacco and agricultural products	Food and food services	Scope 3	Agricultural sector
i15.d	Production of meat products n.e.c.	Food, tobacco and agricultural products	Food and food services	Scope 3	Agricultural sector
i15.e	Processing vegetable oils and fats	Food, tobacco and agricultural products	Food and food services	Scope 3	Agricultural sector
i15.f	Processing of dairy products	Food, tobacco and agricultural products	Food and food services	Scope 3	Agricultural sector
i15.g	Processed rice	Food, tobacco and agricultural products	Food and food services	Scope 3	Agricultural sector

Code	Name	Aggregate description	Aggregate description contribution analysis	Scope GHGP	Aggregate description hotspot analysis
i15.h	Sugar refining	Food, tobacco and agricultural products	Food and food services	Scope 3	Agricultural sector
i15.i	Processing of Food products n.e.c.	Food, tobacco and agricultural products	Food and food services	Scope 3	Agricultural sector
i15.j	Manufacture of beverages	Food, tobacco and agricultural products	Food and food services	Scope 3	Agricultural sector
i15.k	Manufacture of fish products	Food, tobacco and agricultural products	Food and food services	Scope 3	Agricultural sector
i16	Manufacture of tobacco products (16)	Food, tobacco and agricultural products	Food and food services	Scope 3	Agricultural sector
i17	Manufacture of textiles (17)	Textile	Other	Scope 3	Other
i18	Manufacture of wearing apparel; dressing and dyeing of fur (18)	Textile	Other	Scope 3	Other
i19	Tanning and dressing of leather; manufacture of luggage, handbags, saddlery, harness and footwear (19)	Textile	Other	Scope 3	Other
i20	Manufacture of wood and of products of wood and cork, except furniture; manufacture of articles of straw and plaiting materials (20)	Furniture and timber	Other	Scope 3	Other
i20.w	Re-processing of secondary wood material into new wood material	Furniture and timber	Other	Scope 3	Other
i21.1	Pulp	Paper Products	Other	Scope 3	Other
i21.2	Re-processing of secondary paper into new pulp	Paper Products	Other	Scope 3	Other
i21.w.1	Paper	Paper Products	Other	Scope 3	Other
i22	Publishing, printing and reproduction of recorded media (22)	Paper Products	Other	Scope 3	Other
i23.1	Manufacture of coke oven products	Coal and Petroleum	Other	Scope 3	Fossil fuel industry

Code	Name	Aggregate description	Aggregate description contribution analysis	Scope GHGP	Aggregate description hotspot analysis
i23.2	Petroleum Refinery	Coal and Petroleum	Other	Scope 3	Fossil fuel industry
i23.3	Processing of nuclear fuel	Chemical	Pharmaceuticals and chemical products	Scope 3	Pharmaceutical and chemical industry
i24.a	Plastics, basic	Chemical	Pharmaceuticals and chemical products	Scope 3	Pharmaceutical and chemical industry
i24.a.w	Re-processing of secondary plastic into new plastic	Chemical	Pharmaceuticals and chemical products	Scope 3	Pharmaceutical and chemical industry
i24.b	N-fertiliser	Chemical	Pharmaceuticals and chemical products	Scope 3	Pharmaceutical and chemical industry
i24.c	P- and other fertiliser	Chemical	Pharmaceuticals and chemical products	Scope 3	Pharmaceutical and chemical industry
i24.d	Chemicals nec	Chemical	Pharmaceuticals and chemical products	Scope 3	Pharmaceutical and chemical industry
i25	Manufacture of rubber and plastic products (25)	Chemical	Pharmaceuticals and chemical products	Scope 3	Other
i26.a	Manufacture of glass and glass products	Non-metallic mineral products	Other	Scope 3	Other
i26.a.w	Re-processing of secondary glass into new glass	Non-metallic mineral products	Other	Scope 3	Other
i26.b	Manufacture of ceramic goods	Non-metallic mineral products	Other	Scope 3	Other
i26.c	Manufacture of bricks, tiles and construction products, in baked clay	Non-metallic mineral products	Other	Scope 3	Other
i26.d	Manufacture of cement, lime and plaster	Non-metallic mineral products	Other	Scope 3	Other
i26.d.w	Re-processing of ash into clinker	Non-metallic mineral products	Other	Scope 3	Other
i26.e	Manufacture of other non-metallic mineral products n.e.c.	Non-metallic mineral products	Other	Scope 3	Other
i27.41	Manufacture of basic iron and steel and of ferro-alloys and first products thereof	Metal Products	Other	Scope 3	Other

Code	Name	Aggregate description	Aggregate description contribution analysis	Scope GHGP	Aggregate description hotspot analysis
i27.41.w	Re-processing of secondary steel into new steel	Metal Products	Other	Scope 3	Other
i27.42	Precious metals production	Metal Products	Other	Scope 3	Other
i27.42.w	Re-processing of secondary precious metals into new precious metals	Metal Products	Other	Scope 3	Other
i27.43	Aluminium production	Metal Products	Other	Scope 3	Other
i27.43.w	Re-processing of secondary aluminium into new aluminium	Metal Products	Other	Scope 3	Other
i27.44	Lead, zinc and tin production	Metal Products	Other	Scope 3	Other
i27.44.w	Re-processing of secondary lead into new lead, zinc and tin	Metal Products	Other	Scope 3	Other
i27.45	Copper production	Metal Products	Other	Scope 3	Other
i27.45.w	Re-processing of secondary copper into new copper	Metal Products	Other	Scope 3	Other
i27.5	Other non-ferrous metal production	Metal Products	Other	Scope 3	Other
i27.a	Re-processing of secondary other non-ferrous metals into new other non-ferrous metals	Metal Products	Other	Scope 3	Other
i27.a.w	Casting of metals	Metal Products	Other	Scope 3	Other
i28	Manufacture of fabricated metal products, except machinery and equipment (28)	Metal Products	Other	Scope 3	Other
i29	Manufacture of machinery and equipment n.e.c. (29)	General and special Machinery	Other	Scope 3	Other
i30	Manufacture of office machinery and computers (30)	General and special Machinery	Other	Scope 3	Other
i31	Manufacture of electrical machinery and apparatus n.e.c. (31)	Electrical, electronic and measuring equipment	Therapeutic, electrical equipment and machinery	Scope 3	Other
i32	Manufacture of radio, television and communication	Electrical, electronic and	Therapeutic, electrical	Scope 3	Other

Code	Name	Aggregate description	Aggregate description contribution analysis	Scope GHGP	Aggregate description hotspot analysis
	equipment and apparatus (32)	measuring equipment	equipment and machinery		
i33	Manufacture of medical, precision and optical instruments, watches and clocks (33)	Electrical, electronic and measuring equipment	Therapeutic, electrical equipment and machinery	Scope 3	Other
i34	Manufacture of motor vehicles, trailers and semi-trailers (34)	Transport Equipment	Other	Scope 3	Other
i35	Manufacture of other transport equipment (35)	Transport Equipment	Other	Scope 3	Other
i36	Manufacture of furniture; manufacturing n.e.c. (36)	Furniture and timber	Other	Scope 3	Other
i37	Recycling of waste and scrap	Waste management and disposal	Other	Scope 3	Other
i37.w.1	Recycling of bottles by direct reuse	Waste management and disposal	Other	Scope 3	Other
i40.11.a	Production of electricity by coal	Electricity	Heat and electricity	Scope 2	Electricity sector
i40.11.b	Production of electricity by gas	Electricity	Heat and electricity	Scope 2	Electricity sector
i40.11.c	Production of electricity by nuclear	Electricity	Heat and electricity	Scope 2	Electricity sector
i40.11.d	Production of electricity by hydro	Electricity	Heat and electricity	Scope 2	Electricity sector
i40.11.e	Production of electricity by wind	Electricity	Heat and electricity	Scope 2	Electricity sector
i40.11.f	Production of electricity by petroleum and other oil derivatives	Electricity	Heat and electricity	Scope 2	Electricity sector
i40.11.g	Production of electricity by biomass and waste	Electricity	Heat and electricity	Scope 2	Electricity sector
i40.11.h	Production of electricity by solar photovoltaic	Electricity	Heat and electricity	Scope 2	Electricity sector
i40.11.i	Production of electricity by solar thermal	Electricity	Heat and electricity	Scope 2	Electricity sector

Code	Name	Aggregate description	Aggregate description contribution analysis	Scope GHGP	Aggregate description hotspot analysis
i40.11.j	Production of electricity by tide, wave, ocean	Electricity	Heat and electricity	Scope 2	Electricity sector
i40.11.k	Production of electricity by Geothermal	Electricity	Heat and electricity	Scope 2	Electricity sector
i40.11.l	Production of electricity nec	Electricity	Heat and electricity	Scope 2	Electricity sector
i40.12	Transmission of electricity	Electricity	Heat and electricity	Scope 2	Electricity sector
i40.13	Distribution and trade of electricity	Electricity	Heat and electricity	Scope 2	Electricity sector
i40.2	Manufacture of gas; distribution of gaseous fuels through mains	Natural gas and gaseous fuels	Other	Scope 3	Fossil fuel industry
i40.3	Steam and hot water supply	Steam, hot water supply and water distribution	Heat and electricity	Scope 2	Other
i41	Collection, purification and distribution of water (41)	Steam, hot water supply and water distribution	Other	Scope 3	Other
i45	Construction (45)	Construction	Other	Scope 3	Other
i45.w	Re-processing of secondary construction material into aggregates	Construction	Other	Scope 3	Other
i50.a	Sale, maintenance, repair of motor vehicles, motor vehicles parts, motorcycles, motor cycles parts and accessories	Services	Services	Scope 3	Other
i50.b	Retail sale of automotive fuel	Services	Services	Scope 3	Other
i51	Wholesale trade and commission trade, except of motor vehicles and motorcycles (51)	Services	Services	Scope 3	Other
i52	Retail trade, except of motor vehicles and motorcycles; repair of personal and household goods (52)	Services	Services	Scope 3	Other

Code	Name	Aggregate description	Aggregate description contribution analysis	Scope GHGP	Aggregate description hotspot analysis
i55	Hotels and restaurants (55)	Food, tobacco and agricultural products	Food and food services	Scope 3	Agricultural sector
i60.1	Transport via railways	Transport	Other	Scope 3	Other
i60.2	Other land transport	Transport	Other	Scope 3	Other
i60.3	Transport via pipelines	Transport	Other	Scope 3	Other
i61.1	Sea and coastal water transport	Transport	Other	Scope 3	Other
i61.2	Inland water transport	Transport	Other	Scope 3	Other
i62	Air transport (62)	Transport	Other	Scope 3	Other
i63	Supporting and auxiliary transport activities; activities of travel agencies (63)	Services	Services	Scope 3	Other
i64	Post and telecommunications (64)	Services	Services	Scope 3	Other
i65	Financial intermediation, except insurance and pension funding (65)	Services	Services	Scope 3	Other
i66	Insurance and pension funding, except compulsory social security (66)	Services	Services	Scope 3	Other
i67	Activities auxiliary to financial intermediation (67)	Services	Services	Scope 3	Other
i70	Real estate activities (70)	Services	Services	Scope 3	Other
i71	Renting of machinery and equipment without operator and of personal and household goods (71)	Services	Services	Scope 3	Other
i72	Computer and related activities (72)	Services	Services	Scope 3	Other
i73	Research and development (73)	Services	Services	Scope 3	Other
i74	Other business activities (74)	Services	Services	Scope 3	Other
i75	Public administration and defence; compulsory social security (75)	Services	Services	Scope 3	Other
i80	Education (80)	Services	Services	Scope 3	Other

Code	Name	Aggregate description	Aggregate description contribution analysis	Scope GHGP	Aggregate description hotspot analysis
i85	Health and social work (85)	Services	Services	Scope 3	Other
i90.1.a	Incineration of waste: Food	Waste management and disposal	Other	Scope 3	Other
i90.1.b	Incineration of waste: Paper	Waste management and disposal	Other	Scope 3	Other
i90.1.c	Incineration of waste: Plastic	Waste management and disposal	Other	Scope 3	Other
i90.1.d	Incineration of waste: Metals and Inert materials	Waste management and disposal	Other	Scope 3	Other
i90.1.e	Incineration of waste: Textiles	Waste management and disposal	Other	Scope 3	Other
i90.1.f	Incineration of waste: Wood	Waste management and disposal	Other	Scope 3	Other
i90.1.g	Incineration of waste: Oil/Hazardous waste	Waste management and disposal	Other	Scope 3	Other
i90.2.a	Biogasification of food waste, incl. land application	Waste management and disposal	Other	Scope 3	Other
i90.2.b	Biogasification of paper, incl. land application	Waste management and disposal	Other	Scope 3	Other
i90.2.c	Biogasification of sewage sludge, incl. land application	Waste management and disposal	Other	Scope 3	Other
i90.3.a	Composting of food waste, incl. land application	Waste management and disposal	Other	Scope 3	Other
i90.3.b	Composting of paper and wood, incl. land application	Waste management and disposal	Other	Scope 3	Other
i90.4.a	Waste water treatment, food	Waste management and disposal	Other	Scope 3	Other
i90.4.b	Waste water treatment, other	Waste management and disposal	Other	Scope 3	Other
i90.5.a	Landfill of waste: Food	Waste management and disposal	Other	Scope 3	Other

Code	Name	Aggregate description	Aggregate description contribution analysis	Scope GHGP	Aggregate description hotspot analysis
i90.5.b	Landfill of waste: Paper	Waste management and disposal	Other	Scope 3	Other
i90.5.c	Landfill of waste: Plastic	Waste management and disposal	Other	Scope 3	Other
i90.5.d	Landfill of waste: Inert/metal/hazardous	Waste management and disposal	Other	Scope 3	Other
i90.5.e	Landfill of waste: Textiles	Waste management and disposal	Other	Scope 3	Other
i90.5.f	Landfill of waste: Wood	Waste management and disposal	Other	Scope 3	Other
i91	Activities of membership organisation n.e.c. (91)	Services	Services	Scope 3	Other
i92	Recreational, cultural and sporting activities (92)	Services	Services	Scope 3	Other
i93	Other service activities (93)	Services	Services	Scope 3	Other
i95	Private households with employed persons (95)	Services	Services	Scope 3	Other
i99	Extra-territorial organisations and bodies	Services	Services	Scope 3	Other

Appendix H

The contribution analysis for the five environmental impact categories, classified according to the terminology of the GHGP. Scope 1 relates to direct impact, scope 2 relates to indirect impact through the purchase of energy (heat and electricity), while scope 3 relates to all other indirect types of impact. The aggregation of the 163 Exiobase sectors by the grouped categories is available in Appendix G. Due to rounding, the sum of the rows may not correspond to the total. Table adapted from Steenmeijer et al. (2022) (link).

Scope	Source (grouped)	Global warming (kt CO_2-eq)	Material extraction (kt)	Blue water consumption (Mm^3)	Land use (km^2)	Waste generation (kt)
Scope 1	Operational impacts by healthcare sector (incl anaesthetic gases)	1588 (9.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	190 (4.0%)
Scope 2	Electricity	1848 (10.5%)	135 (0.4%)	6 (1.5%)	108 (0.5%)	72 (1.5%)
	Steam and hot water supply	109 (0.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.0%)
Scope 3	Coal & Petroleum	189 (1.1%)	71 (0.2%)	1 (0.3%)	37 (0.2%)	10 (0.2%)
	Construction	269 (1.5%)	755 (2.2%)	2 (0.5%)	172 (0.7%)	133 (2.8%)
	Electrical, electronic & measuring equipment	1336 (7.6%)	1408 (4.2%)	12 (3.0%)	620 (2.6%)	378 (7.9%)
	Food, tobacco & agricultural products	1018 (5.8%)	517 (1.5%)	94 (23.9%)	5645 (23.7%)	641 (13.3%)
	Furniture & timber	26 (0.1%)	20 (0.1%)	1 (0.3%)	225 (0.9%)	4 (0.1%)
	General and special Machinery	182 (1.0%)	267 (0.8%)	2 (0.5%)	120 (0.5%)	75 (1.6%)
	Metal Products	48 (0.3%)	83 (0.2%)	0 (0.0%)	16 (0.1%)	40 (0.8%)
	Minerals & metals	108 (0.6%)	1380 (4.1%)	1 (0.3%)	32 (0.1%)	162 (3.4%)

Scope	Source (grouped)	Global warming (kt CO_2-eq)	Material extraction (kt)	Blue water consumption (Mm^3)	Land use (km^2)	Waste generation (kt)
	Natural gas & gaseous fuels	108 (0.6%)	13 (0.0%)	0 (0.0%)	4 (0.0%)	1 (0.0%)
	Non-metallic mineral products	53 (0.3%)	242 (0.7%)	0 (0.0%)	17 (0.1%)	6 (0.1%)
	Paper Products	202 (1.1%)	195 (0.6%)	3 (0.8%)	849 (3.6%)	73 (1.5%)
	Pharmaceuticals & chemical products	7239 (41.2%)	26936 (79.7%)	249 (63.2%)	14326 (60.1%)	2609 (54.3%)
	pMDI Propellant Releases	77 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Private travel by patients & visitors	573 (3.3%)	24 (0.1%)	0 (0.0%)	2 (0.0%)	0 (0.0%)
	Services	1176 (6.7%)	1397 (4.1%)	18 (4.6%)	1301 (5.5%)	279 (5.8%)
	Textile	76 (0.4%)	64 (0.2%)	2 (0.5%)	109 (0.5%)	11 (0.2%)
	Transport	647 (3.7%)	175 (0.5%)	2 (0.5%)	188 (0.8%)	46 (1.0%)
	Transport Equipment	25 (0.1%)	34 (0.1%)	0 (0.0%)	17 (0.1%)	9 (0.2%)
	Waste management & disposal	276 (1.6%)	56 (0.2%)	1 (0.3%)	49 (0.2%)	58 (1.2%)
	Water distribution	42 (0.2%)	12 (0.0%)	0 (0.0%)	7 (0.0%)	3 (0.1%)
Non-protocol	Private travel by patients & visitors	359 (2.0%)	19 (0.1%)	0 (0.0%)	1 (0.0%)	0 (0.0%)
Total		17575 (100.0%)	33801 (100.0%)	394 (100.0%)	23845 (100.0%)	4803 (100.0%)

Appendix I

The hotspot analysis for the five environmental impact categories. The aggregation of the 163 Exiobase sectors by the grouped categories is available in Appendix G. Due to rounding, the sum of the rows may not correspond to the total. Table adapted from Steenmeijer et al. (2022) (link).

Scope	Sector/source	Global warming (kt CO_2-eq)	Material extraction (kt)	Blue water consumption (Mm^3)	Land use (km^2)	Waste generation (kt)
Direct	Operational impacts (incl anaesthetic gases)	1588 (9.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	190 (4.0%)
Indirect	Chemical	2174 (12.4%)	211 (0.6%)	15 (3.8%)	3 (0.0%)	229 (4.8%)
	Coal & Petroleum	1636 (9.3%)	15 (0.0%)	0 (0.0%)	1 (0.0%)	39 (0.8%)
	Construction	108 (0.6%)	13 (0.0%)	0 (0.0%)	1 (0.0%)	119 (2.5%)
	Electrical, electronic & measuring equipment	555 (3.2%)	3 (0.0%)	4 (1.0%)	0 (0.0%)	11 (0.2%)
	Electricity	3969 (22.6%)	1 (0.0%)	7 (1.8%)	4 (0.0%)	95 (2.0%)
	Food, tobacco & agricultural products	2074 (11.8%)	92 (0.3%)	350 (88.8%)	23418 (98.2%)	1434 (29.9%)
	Furniture & timber	63 (0.4%)	0 (0.0%)	1 (0.3%)	78 (0.3%)	7 (0.1%)
	General & special machinery	21 (0.1%)	1 (0.0%)	1 (0.3%)	1 (0.0%)	6 (0.1%)
	Metal Products	504 (2.9%)	9 (0.0%)	5 (1.3%)	2 (0.0%)	46 (1.0%)
	Minerals & metals	451 (2.6%)	33107 (97.9%)	2 (0.5%)	18 (0.1%)	2444 (50.9%)
	Natural gas & gaseous fuels	522 (3.0%)	18 (0.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Scope	Sector/source	Global warming (kt CO_2-eq)	Material extraction (kt)	Blue water consumption (Mm^3)	Land use (km^2)	Waste generation (kt)
	Non-metallic mineral products	468 (2.7%)	23 (0.1%)	0 (0.0%)	1 (0.0%)	8 (0.2%)
	Paper Products	114 (0.6%)	1 (0.0%)	2 (0.5%)	32 (0.1%)	72 (1.5%)
	pMDI Propellant Releases	77 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Private travel	553 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Private travel, occurring in other sectors (not distributed)	379 (2.2%)	42 (0.1%)	0 (0.0%)	3 (0.0%)	0 (0.0%)
	Services	412 (2.3%)	248 (0.7%)	2 (0.5%)	93 (0.4%)	21 (0.4%)
	Steam, hot water supply & water distribution	545 (3.1%)	0 (0.0%)	0 (0.0%)	1 (0.0%)	5 (0.1%)
	Textile	115 (0.7%)	0 (0.0%)	4 (1.0%)	150 (0.6%)	6 (0.1%)
	Transport	844 (4.8%)	7 (0.0%)	0 (0.0%)	26 (0.1%)	3 (0.1%)
	Transport Equipment	11 (0.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.0%)
	Waste management & disposal	391 (2.2%)	10 (0.0%)	0 (0.0%)	12 (0.1%)	67 (1.4%)
Total		17575 (100.0%)	33801 (100.0%)	394 (100.0%)	23845 (100.0%)	4803 (100.0%)

Appendix J

The geographical hotspot analysis for the various countries and regions in Exiobase for the five environmental impact categories. Due to rounding, the sum of the rows may not correspond to the total. Table adapted from Steenmeijer et al. (2022) (link).

		Global warming (kt CO2-eq)	Material extraction (kt)	Blue water consumption (Mm3)	Land use (km2)	Waste generation (kt)
Africa	Rest of World Africa	389 (2.2%)	298 (0.9%)	25,9 (6.6%)	3098 (13.0%)	191 (4.0%)
	South Africa	399 (2.3%)	159 (0.5%)	2,6 (0.7%)	812 (3.4%)	94 (2.0%)
America	Brazil	281 (1.6%)	299 (0.9%)	8,5 (2.2%)	1478 (6.2%)	432 (9.0%)
	Canada	106 (0.6%)	104 (0.3%)	0,4 (0.1%)	575 (2.4%)	45 (0.9%)
	Mexico	74 (0.4%)	104 (0.3%)	2,5 (0.6%)	145 (0.6%)	52 (1.1%)
	USA	839 (4.8%)	639 (1.9%)	335 (8.5%)	1780 (7.5%)	313 (6.5%)
	Rest of World Americas	362 (2.1%)	603 (1.8%)	10,8 (2.7%)	2905 (12.2%)	943 (19.6%)
Asia and Pacific	Australia	197 (1.1%)	416 (1.2%)	6,1 (1.5%)	2743 (11.5%)	291 (6.1%)
	China	2150 (12.2%)	7300 (21.6%)	37,4 (9.5%)	1198 (5.0%)	412 (8.6%)
	Indonesia	407 (2.3%)	912 (2.7%)	1.1 (0.3%)	630 (2.6%)	152 (3.2%)
	India	484 (2.8%)	16031 (47.4%)	52.6 (13.3%)	423 (1.8%)	130 (2.7%)
	Japan	156 (0.9%)	54 (0.2%)	0.2 (0.1%)	11 (0.0%)	6 (0.1%)
	Korea	104 (0.6%)	25 (0.1%)	0.3 (0.1%)	9 (0.0%)	7 (0.1%)
	Taiwan	186 (1.1%)	41 (0.1%)	0.1 (0.0%)	47 (0.2%)	0 (0.0%)
	Rest of World Asia and Pacific	766 (4.4%)	463 (1.4%)	61.5 (15.6%)	1673 (7.0%)	228 (4.7%)

		Global warming (kt CO2-eq)	Material extraction (kt)	Blue water consumption (Mm3)	Land use (km2)	Waste generation (kt)
Europe	Austria	15 (0.1%)	33 (0.1%)	0.1 (0.0%)	28 (0.1%)	6 (0.1%)
	Belgium	119 (0.7%)	113 (0.3%)	1.1 (0.3%)	36 (0.2%)	33 (0.7%)
	Bulgaria	11 (0.1%)	41 (0.1%)	0,2 (0.0%)	59 (0.2%)	13 (0.3%)
	Switzerland	25 (0.1%)	97 (0.3%)	0.1 (0.0%)	22 (0.1%)	4 (0.1%)
	Czech Republic	37 (0.2%)	29 (0.1%)	0.1 (0.0%)	30 (0.1%)	4 (0.1%)
	Germany	317 (1.8%)	329 (1.0%)	1,6 (0.4%)	201 (0.8%)	70 (1,4%)
	Denmark	27 (0.2%)	21 (0.1%)	0.1 (0.0%)	18 (0.1%)	6 (0.1%)
	Spain	80 (0.5%)	70 (0.2%)	4,1 (1.1%)	273 (1.1%)	32 (0.7%)
	Estonia	7 (0.0%)	4 (0.0%)	0,0 (0.0%)	38 (0.2%)	1 (0.0%)
	Finland	13 (0.1%)	61 (0.2%)	0.1 (0.0%)	75 (0.3%)	12 (0.2%)
	France	123 (0.7%)	174 (0.5%)	1.4 (0.4%)	190 (0.8%)	29 (0.6%)
	UK	134 (0.8%)	91 (0.3%)	0.5 (0.1%)	96 (0.4%)	14 (0.3%)
	Greece	28 (0.2%)	50 (0.1%)	0.6 (0.2%)	75 (0.3%)	8 (0.2%)
	Croatia	6 (0.0%)	7 (0.0%)	0,0 (0.0%)	7 (0.0%)	0 (0.0%)
	Hungary	19 (0.1%)	14 (0.0%)	0.2 (0.1%)	55 (0.2%)	5 (0.1%)
	Ireland	73 (0.4%)	20 (0.1%)	0.4 (0.1%)	86 (0.4%)	22 (0.5%)
	Italy	61 (0.3%)	70 (0.2%)	0.8 (0.2%)	60 (0.3%)	8 (0.2%)
	Lithuania	9 (0.1%)	5 (0.0%)	0,0 (0.0%)	59 (0.2%)	2 (0.0%)
	Luxembourg	9 (0.1%)	1 (0.0%)	0,0 (0.0%)	2 (0.0%)	1 (0.0%)
	Latvia	6 (0.0%)	1 (0.0%)	0,0 (0.0%)	71 (0.3%)	1 (0.0%)
	Malta	1 (0.0%)	1 (0.0%)	0,0 (0.0%)	0 (0.0%)	0 (0.0%)
	Norway	58 (0.3%)	46 (0.1%)	0.1 (0.0%)	102 (0.4%)	6 (0.1%)
	Poland	55 (0.3%)	150 (0.4%)	0.8 (0.2%)	86 (0.4%)	38 (0.8%)

		Global warming (kt CO2-eq)	Material extraction (kt)	Blue water consumption (Mm3)	Land use (km2)	Waste generation (kt)
	Portugal	18 (0.1%)	47 (0.1%)	0.3 (0.1%)	21 (0.1%)	5 (0.1%)
	Romania	33 (0.2%)	18 (0.1%)	2.1 (0.5%)	219 (0.9%)	15 (0.3%)
	Russia	766 (4.4%)	361 (1.1%)	5.7 (1.4%)	2353 (9.9%)	151 (3.2%)
	Slovakia	9 (0.1%)	7 (0.0%)	0.1 (0.0%)	20 (0.1%)	2 (0.0%)
	Slovenia	5 (0.0%)	4 (0.0%)	0,0 (0.0%)	3 (0.0%)	1 (0.0%)
	Sweden	22 (0.1%)	107 (0.3%)	0,2 (0.0%)	260 (1.1%)	40 (0.8%)
	Rest of World Europe	284 (1.6%)	101 (0.3%)	5.4 (1.4%)	861 (3.6%)	56 (1.2%)
Middle East	Cyprus	3 (0.0%)	3 (0.0%)	0.1 (0.0%)	6 (0.0%)	1 (0.0%)
	Turkey	49 (0.3%)	172 (0.5%)	4.6 (1.2%)	56 (0.2%)	14 (0.3%)
	Rest of World Middle East	1861 (10.6%)	3227 (9.5%)	109.3 (27.7%)	599 (2.5%)	237 (4.9%)
The Netherlands	The Netherlands, operational	1588 (9.0%)	0 (0.0%)	0,0 (0.0%)	0 (0.0%)	190 (4.0%)
	The Netherlands, not operational	4420 (25.2%)	832 (2.5%)	9.9 (2.5%)	247 (1.0%)	482 (10.0%)
All	Global	379 (2.2%)	42 (0.1%)	0.3 (0.1%)	3 (0.0%)	0 (0.0%)
Grand Total		17575 (100.0%)	33801 (100.0%)	394.2 (100.0%)	23845 (100.0%)	4803 (100.0%)

Appendix K

Number of daily doses (DDDs) of acetylsalicylic acid, ibuprofen, naproxen and paracetamol for 2016-2020 from the GIPdatabank. Table adapted from Steenmeijer et al. (2022) (link).

ATC code, active ingredient (product name)	2016	2017	2018	2019	2020
B01AC06 Acetylsalicylic acid (Aspirin protect ®)	229,614,250	228,458,377	222,647,634	214,055,325	211,497,137
B01AC30 Clopidogrel/acetylsalicylic acid	3,652,600	3,086,300	2,556,300	2,326,400	44,536
N02BA01 Acetylsalicylic acid	504	560	449	435	1,151
N02BA51 Acetylsalicylic combination preparations	67,020	59,713	52,808	48,575	44,181
M01AE01 Ibuprofen	13,683,339	13,002,748	12,476,929	11,122,066	10,211,585
M01AE02 Naproxen	34,339,518	36,268,704	34,444,170	38,734,549	36,748,218
M01AE52 Naproxen with esomeprazole	163,980	140,570	139,860	119,350	100,870
N02BE01 Paracetamol	31,588,498	35,797,614	41,646,223	.	.
N02AJ13 Tramadol with paracetamol	7,995,524	7,896,189	7,633,794	7,484,338	7,275,684

Number of daily doses (DDDs) of amoxicillin and combination preparations for 2016-2020 from the GIPdatabank. Table adapted from Steenmeijer et al. (2022) (link).

ATC code, active ingredient (product name)	2016	2017	2018	2019	2020
J01CA04 Amoxicillin	11,861,520	11,346,147	11,847,568	7,555,534	5,858,768
J01CA04 Amoxicillin	15,240	20,628	19,959	9,107	11,357
A02BD04 Pantoprazole Amoxicillin and Clarithromycin	155,401	132,146	186,238	189,666	129,893
J01CR02 Amoxicillin with beta-lactamase inhibitor	8,813,606	8,463,926	8,462,251	5,609,649	4,862,614
J01CR02 Amoxicillin with beta-lactamase inhibitor	2,385	2,544	2,382	2,302	2,185

RIVM

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