Final Report

Health economic study on impact of reverse-switching antifungal and antiviral non-prescription medicines

Submitted by:

IQVIA

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Final Report of Health Economic Study on Impact of Reverse-Switching Antifungal and Antiviral Non-Prescription Medicines

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Table of Contents

List of Tables

List of Figures

Acronyms

AT : Austria

BE : Belgium

BG : Bulgaria

CR : Croatia

CY : Cyprus

CZ : Czech Republic

DK : Denmark

EE : Estonia

FI : Finland

FR : France

DE : Germany

GR : Greece

HU : Hungary

IE : Ireland

IT : Italy

LV : Latvia

LT : Lithuania

LU : Luxembourg

MT : Malta

NL : Netherlands

PL : Poland

PT : Portugal

RO : Romania

SK : Slovakia

SI : Slovenia

ES : Spain

SE : Sweden

UK : United Kingdom

NPM : Non-prescription medicines

Executive summary

Background

Non-prescription antimicrobial medicines play a crucial role in public health by providing accessible treatment options for common conditions such as cold sores, dermatomycosis and vaginal thrush. These medicines enable timely and effective self-care, reducing the burden on healthcare systems and allowing individuals to manage their health independently.

The European Commission (EC) is proposing a reform of the pharmaceutical legislation framework within the European Union (EU). Central to this reform, which aims to mitigate antimicrobial resistance (AMR), is the classification of all antimicrobial medicinal products for human use - including antifungals and antivirals - as prescription only medicines. This policy shift targets a wide array of antimicrobial medicines, many of which are currently available as non-prescription medicines (NPMs).

Objective

The primary objective of this health economic study is to analyse and quantify the socio-economic implications and health outcomes associated with the potential reclassification of currently available non-prescription antifungal and antiviral medicines to prescription-only status.

Methodology

We conducted literature review by constructing search strings based on the research question, retrofitted and optimised using a set of known results of reverse-switches. The search results were manually screened by 3 reviewers and DistillerSR automation. We estimated the burden of disease using IQVIA OTCIMS data, defined as the number of symptomatic individuals receiving NPM treatment for dermatomycosis (including athlete's foot), vaginal thrush, and herpes labialis in the last 12 months. This definition was selected to reflect the population that will be directly impacted by the reverse-switch of antifungals and antivirals NPM.

We hypothesised three options for patients' action upon reverse switching, whether they visit a doctor to get a prescription, or switch to an alternate treatment available for self-purchase or do nothing and wait for the symptoms to self-resolve. A total of 378 people from 5 countries (France, Germany, Italy, Poland and the United Kingdom) were surveyed to understand their course of action. Based on these findings and the natural history obtained from the literature, we constructed a decision tree and outlined the assumptions for the model.

We estimated the impact of reverse-switching by modelling the excess demand for healthcare through excess appointments to doctor's practice, including emergency visits across 28 countries. The total costs of reverse-switching, consisting of health system-related spendings (outpatient and prescription costs) and productivity losses, were projected over the next five years, leveraging historical growth rates for burden and costs. The volume impact of antifungals and antivirals use before and after reverse switch was also estimated.

Result

Overall, 67.4% of the population surveyed indicated that they would seek outpatient care to get a prescription while the remaining will seek alternative treatment available for self-purchase (28.7%) or do nothing and wait for the symptoms to resolve on its own (3.9%) in the event of a reverse-switch of antifungal and antiviral NPMs. This will result in ~59 million additional visits to doctor's practice in a single year as people seek treatment across these 28 countries, in which approximately 11 million of them are emergency visits**.**

Cumulatively, the total cost of reverse-switching for a single year is 9.68 billion and projected to cumulatively amount to €50,1 billion in five years, increasing by 1.98% year-on-year. Approximately 81% of these costs, equivalent to €40.7 billion, are healthcare-related expenditures which are mainly driven by the doctor visits. Of these healthcare costs, 81% are borne by public payers, followed by 14% by individuals, and 5% by private health insurance. The remaining 19% of the total costs, equivalent to €9.4 billion, are attributed to productivity losses due to individuals seeking care at doctors' practices and to a lesser extent, disability due to severity of the diseases. The largest costs are attributed to vaginal thrush (€20.4 billion), followed by herpes labialis (€19 billion), and dermatomycosis (€10.7 billion).

The volume impact results reveal that reverse-switching may not reduce the use of antifungal and antiviral medicines. Based on our detailed assumptions and factors, the volume impact of antivirals shows a potential 58% increase, with consumption rising from 21.1 million units to 33.2 million units. Meanwhile, antifungals show a potential 32% increase, with consumption jumping from 35.5 million units to 46.8 million units.

Implications of Reverse-Switching

The reclassification of antifungal and antiviral NPMs to prescription-only status carries significant socio-economic and healthcare implications in four key areas:

1. Delay in seeking care: Reverse-switching may cause individuals to delay seeking appropriate treatment, opting instead to either use an alternative treatment or do nothing, due to existing physical and social barriers in accessing healthcare. This delay can lead to the exacerbation of conditions, resulting in an estimated 19,2 million of unresolved cases and increased severity of illnesses over time.
2. Additional Burden and Costs to the Healthcare System: The shift of patients to the healthcare system will create substantial additional burdens and costs. It is anticipated that there will be a major increase of 59 million excess visits to doctors, including 11 million emergency care visits. This surge in healthcare utilisation will strain resources, reduce the availability of consultation time for each patient, and necessitate an additional €7.8 billion healthcare related spending expected to happen in a single year, whereby 81% will be borne by the public payer.
3. Productivity Loss to Individuals: The economic impact on individuals includes €1.8 billion productivity losses due to time spent seeking outpatient care and dealing with the disabilities caused by worsening conditions. These productivity losses highlight the broader socio-economic implications of reverse-switching, outside of the healthcare system related costs.
4. Unintended Consequences: Contrary to the intended outcome, reverse-switching may not have the desired impact in reducing the volume of antiviral and antifungal medicines use. There is a potential increase of 58% and 32% respectively. Patients who choose to visit a doctor will receive a prescription, whereas patients who explore alternative options or take no action, may experience delay in appropriate treatment, which could lead to worsened symptoms. Eventually, they may require a doctor's appointment and a prescription for a more severe condition. Additionally, this unintended consequence could shift prescribing practices, such as moving from topical/external treatment to oral/systemic treatment. Therefore, the proposal for reverse-switching may not only fall short of its aim in reducing consumption of antifungals and antivirals but could also introduce new complexities in managing public health.

Introduction

Antimicrobial resistance (AMR) is a major public health challenge, responsible for approximately 35,000 deaths annually in the EU. The European Commission (EC), in an effort to reduce AMR, as it relates to human health specifically, seeks to restrict access to antimicrobials by focusing on several key measures including reclassification of non-prescription antimicrobial medicines, such as antibiotic, antifungal, and antiviral, to prescription-only medicines by amending the Directive 2001/83/EC relating to medicinal products for human use [1,2].

In addition, the EC has also set specific targets to reduce the overall consumption of antibiotics by 20% and ensure that at least 65% of antibiotic use in humans is appropriate. These targets are part of a broader effort to reduce the risk of developing resistant strains[1,2].

By introducing prescription-only status in these medicines, the EC aims to reduce their consumption, preserve their effectiveness, and slow down the development of resistance. Introducing a prescription-only status for antibiotics to mitigate proven resistance is reasonable, given that antibiotics are often overused, incorrectly prescribed, and frequently involve broad-spectrum antibiotics that contribute to resistance. However, applying the same restriction to antiviral and antifungal non-prescription medicines (NPMs) is the wrong approach, due to reasons outlined below.

1. **Health outcomes:** Currently, many common infections and conditions are managed effectively with NPMs. Restricting access to these treatments could result in delayed care, leading to more severe health issues and excess incidence in the population.
2. **Health systems impact:** As people transition from self-care to seeking medical advice from doctors to resolve their conditions, it is also expected that visits to health facilities will be increased. This adds further strain on the health care system and shifts resources to non-critical conditions.
3. **Economic impact:** Consequently, healthcare-related spendings will increase, as well as indirect costs to individuals such as lost productivity, due to time loss in disability and seeking care.
4. **Effectiveness of AMR Reduction:** Reclassifying NPMs primarily focuses only on restricting access and shifting care, without addressing the burden of diseases. Therefore, it remains unclear whether such policy change is the most effective approach for reducing consumption of antifungals and antivirals.

In view of this, AESGP has commissioned a study to explore the impact of reverse switching NPM antifungals and antivirals. The study evaluates the potential health outcomes, socioeconomic consequences and the impact to the volume of antifungals and antivirals use as a result of the proposed reclassification. The findings from this study will provide valuable insights to the regulators and policymakers, balancing the need to protect public health while minimizing negative impacts from unintended consequences.

[1] EU Action on Antimicrobial Resistance - European Commission (https://health.ec.europa.eu/antimicrobial-resistance/eu-action-antimicrobial-resistance_en)

[2] European Health Union: EU steps up the fight against antimicrobial resistance - European Commission (https://cyprus.representation.ec.europa.eu/news/european-health-union-eu-steps-fight-against-antimicrobial-resistance-2023-06-13_en)

Objectives

The primary objective of this health economic study is to analyse and quantify the socio-economic implications and health outcomes associated with the potential reclassification of currently available antifungal and antiviral non-prescription medicines (NPM) to prescription-only status. This analysis is critical to inform the EC's proposed reform of the pharmaceutical legislation framework, which aims to reduce antimicrobial resistance by restricting access to these medicines.

Specifically, the study will focus on the following key areas:

1. **Social and Economic Costs:** Calculate the social and economic costs associated with a reverse-switch of currently available antiviral and antifungal NPMs. This assessment will encompass both direct costs (such as increased healthcare expenditures due to additional medical consultations and prescriptions) and indirect costs (such as productivity losses and economic impact due to untreated or delayed treatment of infections).
2. **Health Outcomes:** Evaluate the health outcomes resulting from the reclassification, considering the potential increase in untreated or inadequately treated infections. The study will analyse the implications for public health, including the burden on healthcare systems and the potential for exacerbating health inequalities, particularly among vulnerable populations.
3. **Effectiveness of Reducing Antifungals and Antivirals Use:** Assess whether the proposed reverse-switch would achieve the desired outcome of reducing the volume of use of antifungals and antivirals active pharmaceutical ingredients (APIs). This includes evaluating alternative scenarios and the feasibility of achieving the EC's objectives through different strategies.

In addressing the above key areas, this study will focus on the following markets and indications:

1. **Countries: European Union countries** (Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxemburg, Malta, Netherlands, Poland, Portugal, Republic of Cyprus, Romania, Slovakia, Slovenia, Spain, and Sweden) and the **United Kingdom**.
2. **Indications:**
    a. Fungal diseases: Vaginal thrush, dermatomycosis including athlete's foot
    b. Viral disease: Herpes labialis

Methodology

1. Literature review

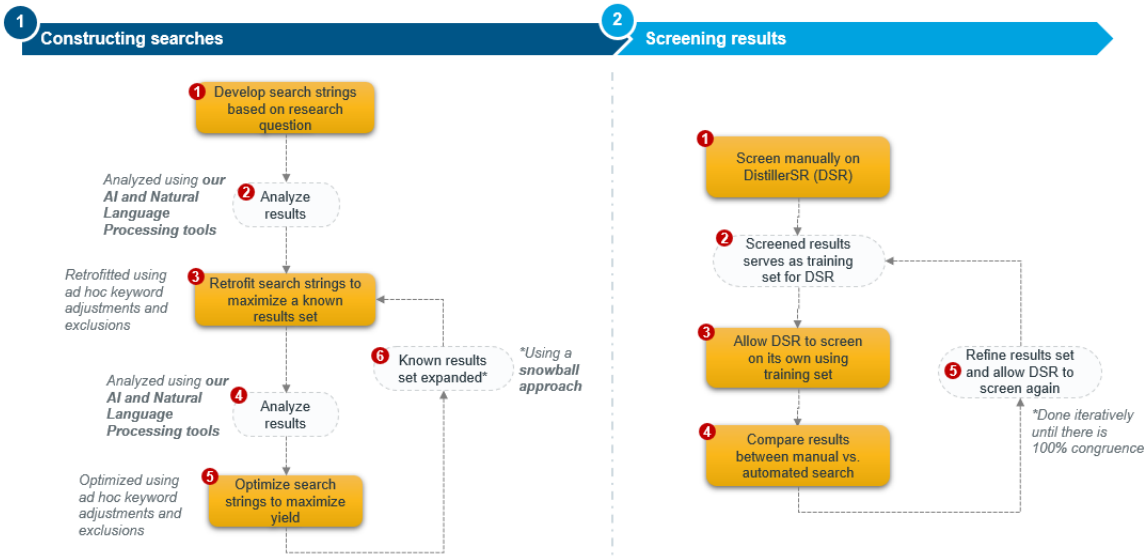

Figure 1 Literature review

A.1. Constructing searches

First, we developed a search vocabulary that encapsulates the broadest scope of the research question. This preliminary step resulted in 162 search outcomes (refer to Table 1). Upon evaluation of these results, we retrofitted and enhanced the search strings to align with a set of known results on switches and reverse-switches. This was achieved by adjusting the keywords to increase the number of hits and adding exclusions to minimize irrelevant results. The final yield for screening was 2,502 search results (refer to Table 2).

A.2. Literature Screening

The screening process was initiated by manually reviewing all 2502 pieces of literature using Distiller SR, which served as a training set for the tool. This manual review was carried out by 3 reviewers. Subsequently, we executed an automated second screening of the same 2502 literature using Distiller SR, guided by the training set. A comparison was then drawn between the results of the manual screening and the automated screening, and any conflicts were scrutinized and resolved. The screening process was further refined by allowing Distiller SR to conduct additional screenings until a 100% congruence was achieved between the two sets of results, yielding 135 articles as the final set of reverse-switch literature. We have furnished this set separately in an Excel document.

Table 1 Preliminary search string and number of hits

String No.	Searches	Hits
1	(Over the counter or Over-the-counter or OTC or OTC* or OTC-Rx or self-medication or nonprescription or non-prescription or without prescription or self-medication or self medication or without a prescription or prescription-free or prescription free or pharmacist-led medication or pharmacist led medication or non-prescribed or prescription-only-medicine or prescription only medicine or pharmacist* only or prescription* only).mp.	83,637
2	(Up-schedul* or up schedul* or re schedul* or re-schedul* or reschedul* or Upschedul* or reverse-switch* or reverse switch* or new schedule or schedule change or reverse switch* or market disruption or designated substance* or controlled substance).mp.	10,104
3	1 and 2	**266**
4	Limit 3 to human	217
5	Limit 4 to yr="2000 -Current"	208
6	Remove duplicates from 5	**162**

Table 2 Final search strings and number of hits

String	Search strings	Hits
1	(Over the counter or Over-the-counter or OTC or OTC* or OTC-Rx or self-medication or nonprescription or non-prescription or without prescription or self-medication or self medication or without a prescription or prescription-free or prescription free or pharmacist-led medication or pharmacist led medication or non-prescribed or prescription-only-medicine or prescription only medicine or pharmacist* only or prescription* only or designated substance* or controlled substance or prescribed or prescription or prescriptions or regulatory or medicines or drug or drugs).mp. or medicine.ti.	21,732,318
2	(Up-schedul* or up schedul* or re schedul* or re-schedul* or reschedule or rescheduled or rescheduling or Upschedul* or reverse-switch* or reverse switch* or new schedule or schedule change or reverse switch* or market disruption or market withdrawal).mp.	6,880
3	1 and 2	2,512
4	limit 3 to human	2,242
5	limit 4 to yr="2000 -Current"	2,088
6	remove duplicates from 5	1,597
7	(Over the counter or Over-the-counter or OTC or OTC-Rx).ti.	8,219

8	(designated substance* or controlled substance or prescribed or prescription or prescriptions or regulatory or medicines or drug or drugs or self-medication or nonprescription or non-prescription or without prescription or self-medication or self medication or without a prescription or prescription-free or prescription free or pharmacist-led medication or pharmacist led medication or non-prescribed or prescription-only-medicine or prescription only medicine or pharmacist* only or prescription* only or (medicine or impact or pharmac*)).ti.	3,239,181
9	(Up-schedul* or up schedul* or re schedul* or re-schedul* or reschedule or rescheduled or rescheduling or Upschedul* or reverse-switch* or reverse switch* or new schedule or schedule change or reverse switch* or market disruption or market withdrawal).ti.	694
10	7 or 9	8,888
11	8 and 10	3,256
12	limit 11 to human	2,551
13	limit 12 to yr="2000 -Current"	2,076
14	limit 13 to yr="2010 -Current"	1,413
15	remove duplicates from 5	1,597
16	remove duplicates from 14	995
17	6 or 16 (duplicates removed)	2,521
18	6 or 13 (duplicates removed)	2,907
19	(cancer* or vaccin* or immuni?ation* or antidepressant* or malignant neoplasia or malignant tumour or neoplastic malignancy or oncologic malignancy or neoplasmic malignancy or reimmuni?ation* or neurothymoleptic or psychoenergizer or thymoleptic).ti,ab.	6,707,938
20	17 not 19 (duplicates removed)	2,122
21	18 not 19 (duplicates removed)	2,502
22	After 3 independent reviews conducted manually and using DSR automation arm, 135 articles were included in the final list	135

2. Estimating burden

B.1. Burden estimates calculation

We define the burden of disease as the number of individuals infected with any of the specified indications—dermatomycosis including athlete's foot, vaginal thrush, and herpes labialis—who exhibit symptoms and receive antifungal or antiviral NPMs as treatment. This definition is selected as reverse switching will directly impact this population segment who are already accessing and using NPMs to treat these conditions.

For this reason, we have utilized IQVIA's proprietary OTC sales data to estimate the annual disease burden. We outline the following steps to derive the burden estimates.

Step 1: Identification of Relevant Molecules

For each in-scope indication we identified the relevant consumer health classification (CHC) from OTC database. Secondly, we filtered for the relevant molecules by excluding herbal formulations and medicines for systemic use. This process narrowed down the list of molecules that will be used for burden estimation.

Step 2: Isolation of Sales Data

We isolated sales data for relevant molecules from IQVIA's OTC database, focusing on those contributing to the top ~90% of 2023 sales of suitable CHCs for each indication.

Step 3: Identification of Top Molecules

We identified the top molecules for each market based on sales volumes, ensuring that our analysis targets the most impactful market contributors for each indication.

Step 4: Estimation of SKUs Sold

From the OTC database, we aggregated the sales data at product level to calculate the total number of stock-keeping units (SKUs) sold in each quarter directly.

Step 5: Splitting SKUs by Persona

The total SKUs sold are split into each identified persona (see Section "Natural History") using the same percentage share approach.

Step 6: Conversion to Patient Numbers

Conversion of SKUs: The split SKUs are converted to patient numbers, estimating the number of people who used the total SKUs for primary and recurrent infections.

Patient Conversion Model

The number of people infected with the indication in a year (X) is calculated, considering the percentage share of infected people with recurrences (p), the duration and chronicity of the recurrent conditions based on the natural history which is obtained from the literature. The natural history is described in greater details in Section 4. The SKUs used for primary infections (α) and recurrent infections (β) are summed to determine the total SKUs used in a year.

$$X = \frac{SKUs\ used\ in\ a\ year}{\alpha + p \times (\beta - \alpha)}$$

Step 7: Total Disease Burden Validation

The calculated total burden of disease for each country and indication is validated by triangulating with additional data sources to ensure accuracy and completeness. The data triangulation process is elaborated in the following sections.

B.2. Burden estimates triangulation: Herpes labialis

To ensure the accuracy of our burden estimates, we triangulated our data by comparing and integrating different data sources to enhance the reliability of our estimates. Specifically for Herpes Labialis, we triangulated our burden estimates with those derived from natural history and epidemiology studies for HSV-1.

From Langenberg et al. (1999)[3] and Bernstein et al. (2013)[4], this funnel provides a detailed breakdown of disease progression and prevalence for oral HSV-1:

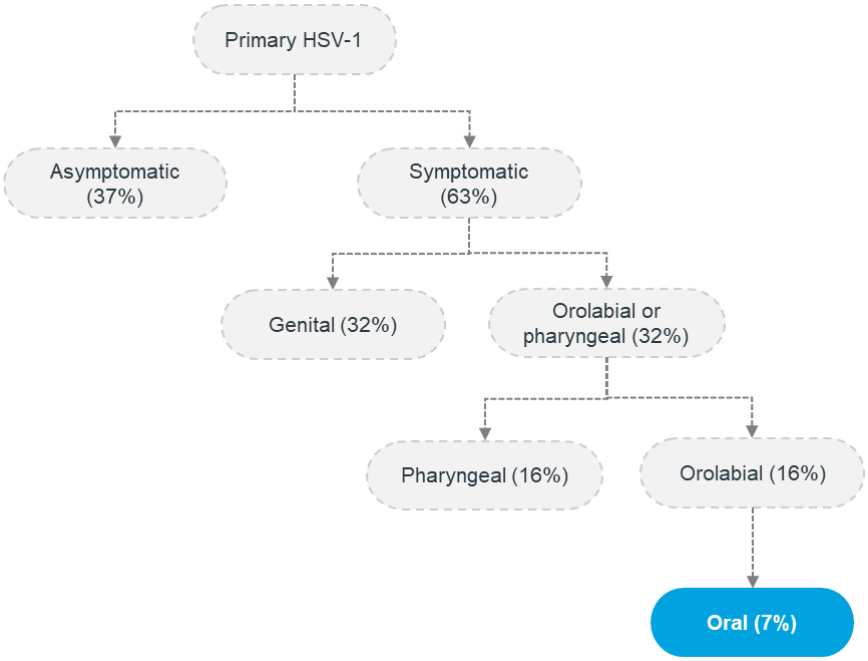

Figure 2 Estimates for oral HSV-1 based on natural history/epidemiology funnel

We validated our herpes labialis burden estimates by comparing them to oral HSV-1 prevalence of each country, based on the epidemiology funnel above. Our estimates consistently fell below the latter, confirming their validity.

B.3. Burden estimates triangulation: Vaginal Thrush

We employed a 4-step approach to triangulate the burden of vaginal thrush across the in-scope countries, as follows:

1. Identify the MeSH Term[5]
   We began by identifying the relevant Medical Subject Headings (MeSH) term to categorize our target condition. This process involved:
   - Navigating through all MeSH categories, starting from the broader diseases category down to infections, bacterial infections and mycoses, mycoses, and finally, candidiasis.
   - Focusing on Candidiasis, Vulvovaginal as the specific condition, which refers to infections of the vulva and vagina caused by fungi of the genus *Candida*.

[3] Langenberg AG, Corey L, Ashley RL, Leong WP, Straus SE. A prospective study of new infections with herpes simplex virus type 1 and type 2. Chiron HSV Vaccine Study Group. N Engl J Med. 1999 Nov 4;341(19):1432-8. doi: 10.1056/NEJM199911043411904. PMID: 10547406.

[4] Bernstein DI, Bellamy AR, Hook EW 3rd, Levin MJ, Wald A, Ewell MG, Wolff PA, Deal CD, Heineman TC, Dubin G, Belshe RB. Epidemiology, clinical presentation, and antibody response to primary infection with herpes simplex virus type 1 and type 2 in young women. Clin Infect Dis. 2013 Feb;56(3):344-51. doi: 10.1093/cid/cis891. Epub 2012 Oct 19. PMID: 23087395; PMCID: PMC3540038.

[5] NCBI MeSH Database (https://www.ncbi.nlm.nih.gov/mesh/?term=Vaginal+thrush)

2. Obtain Prevalence Rates
   Next, we sourced the prevalence rates for vulvovaginal candidiasis (VVC) from established literature. Specifically, we used the prevalence rates reported by Foxman et al.[6] in their study on recurrent vulvovaginal candidiasis in five European countries and the United States, published in the Journal of Lower Genital Tract Disease. Based on this journal, the average prevalence of VVC is 44% for the 5 in-scope European countries.
3. Calculate 2023 Prevalence (based on prevalence rate in step 2)
   We applied the average prevalence rates by Foxman et al[6] to the 2023 female population for each country[7] to estimate the prevalence of vaginal thrush in 2023. This calculation assumes that the prevalence rate remains constant, and any potential underestimation is acknowledged.
4. Compare Estimates
   Finally, we compared our estimated burden of vaginal thrush with the calculated prevalence in (3). Our estimates consistently fell below the latter, confirming their validity.

The following table shows the burden estimates triangulation for Vaginal Thrush.

Table 3 Data Triangulation for Vaginal Thrush

Country	Women Population 2023[8]	Women average prevalence rate (2018)[9]	Prevalence 2023[10]	IQVIA Burden Estimates	% estimation out of prevalence[11]
France	34,388,807	44%	15,131,075	6,275,003	41%
Germany	43,087,751	44%	18,958,610	4,516,657	24%
Italy	30,472,769	44%	13,408,019	3,423,639	26%
Poland	19,682,162	44%	8,660,151	1,364,306	16%
Spain	23,118,652	44%	10,172,207	1,172,809	12%
United Kingdom	34,945,231	44%	15,375,901	1,451,875	9%

B.4. Burden estimates triangulation: Dermatomycosis (including Athlete's Foot)

Data triangulation process for burden disease estimation for dermatomycosis follows a 4-step approach similar to vaginal thrush.

1. Identify the MeSH Term for Dermatomycosis[12]
   a. Definition: Dermatomycosis is defined as "Superficial infections of the skin or its appendages by any of various fungi."
   b. MeSH Term: "Dermatomycosis" is derived from "Derma" (skin) and "Mycosis" (fungal infection).

[6] Foxman B, Muraglia R, Dietz JP, Sobel JD, Wagner J. Prevalence of recurrent vulvovaginal candidiasis in 5 European countries and the United States: results from an internet panel survey. J Low Genit Tract Dis. 2013 Jul;17(3):340-5.

[7] Institute for Health Metrics and Evaluation (IHME)

[8] GBD Results. (n.d.). Institute for Health Metrics and Evaluation. https://vizhub.healthdata.org/gbd-results/?params=gbd-api-2021-public/5869e3f79e49a11949060d13e0b1c7d4

[9] Prevalence rate obtained from Foxman et al, assumption is made that prevalence remains constant for 2023 population.

[10] Population multiplied by average prevalence rate

[11] IQVIA burden estimates divided by calculated prevalence 2023

[12] Dermatomycoses - MeSH - NCBI. (n.d.). https://www.ncbi.nlm.nih.gov/mesh/?term=Dermatomycosis

2. Obtain Prevalence Rates[13]
    a. Resource: We used the Global Burden of Disease (GBD) database provided by the Institute for Health Metrics and Evaluation (IHME).
    b. Filter:
        i. Choose "Fungal Skin Disease" as the filter segmentation to find relevant data.
        ii. Choose “rate” as the metrics.
        iii. Choose latest year available (2021)
        iv. Choose all European countries in scope.
3. Calculate the 2023 Prevalence (based on prevalence rate in step 2)
    a. Obtain the 2023 population for each European country.
    b. Multiply each country's 2023 population by the 2021 prevalence rate to estimate the number of individuals with dermatomycosis in 2023.
    c. Assumption: 2021 prevalence rate remains constant
4. Compare estimates
    a. We compared our estimated burden with the calculated prevalence in (3). Our estimates consistently fell below the latter, confirming their validity.

The following table shows the burden estimates triangulation for dermatomycosis.

Table 4 Data triangulation for Dermatomycosis

Country	Population 2023[14]	Prevalence rate 2021[15]	Prevalence 2023[16]	IQVIA Burden Estimates	% estimation out of prevalence[17]
Austria	9,079,172	11%	974,688	84,692	9%
Belgium	11,545,599	11%	1,243,235	249,146	20%
Bulgaria	6,665,339	8%	528,724	21,986	4%
Croatia	4,171,250	8%	334,428	50,420	15%
Czechia	10,645,359	8%	827,186	174,358	21%
Estonia	1,309,237	8%	104,476	3,525	3%
Finland	5,546,701	11%	633,818	33,064	5%
France	66,732,724	11%	7,335,336	1,451,757	20%
Germany	86,134,855	11%	9,859,926	1,050,292	11%
Greece	10,046,434	12%	1,183,789	131,226	11%
Hungary	9,521,807	8%	745,952	170,679	23%
Ireland	4,983,996	9%	470,859	81,652	17%
Italy	59,459,557	12%	7,194,280	686,848	10%
Latvia	1,831,152	8%	148,387	18,520	12%
Lithuania	2,666,783	8%	215,851	769	0%
Netherlands	17,302,251	11%	1,843,875	150,745	8%
Poland	38,145,389	8%	2,927,281	786,219	27%

[13] GBD Results. (n.d.). Institute for Health Metrics and Evaluation. https://vizhub.healthdata.org/gbd-results/?params=gbd-api-2021-public/5869e3f79e49a11949060d13e0b1c7d4

[14] GBD Results. (n.d.). Institute for Health Metrics and Evaluation. https://vizhub.healthdata.org/gbd-results/?params=gbd-api-2021-public/5869e3f79e49a11949060d13e0b1c7d4

[15] Obtained from IHME as “Fungal Skin Disease”, assumption is made that prevalence remains constant for 2023 population.

[16] Population multiplied by average prevalence rate

[17] IQVIA burden estimates divided by calculated prevalence 2023

Portugal	10,560,882	12%	1,223,476	171,596	14%
Romania	18,652,554	8%	1,434,295	175,646	12%
Slovakia	5,429,950	7%	387,226	124,100	32%
Slovenia	2,069,354	8%	168,326	43,264	26%
Spain	45,145,713	8%	3,602,367	58,524	2%
United Kingdom	68,593,669	11%	7,218,327	472,057	7%

3. Building decision trees

In this section, we outline the methodology used to build decision trees for the reverse-switch scenario. The primary tool to finalize the decision trees was through a survey conducted across multiple countries. The survey discussion guide and detailed results can be found in the appendices for further reference.

C.1. Decision trees

C.1.1 Patient options

This section presents the decision pathways for patients in the event of a reverse switch.

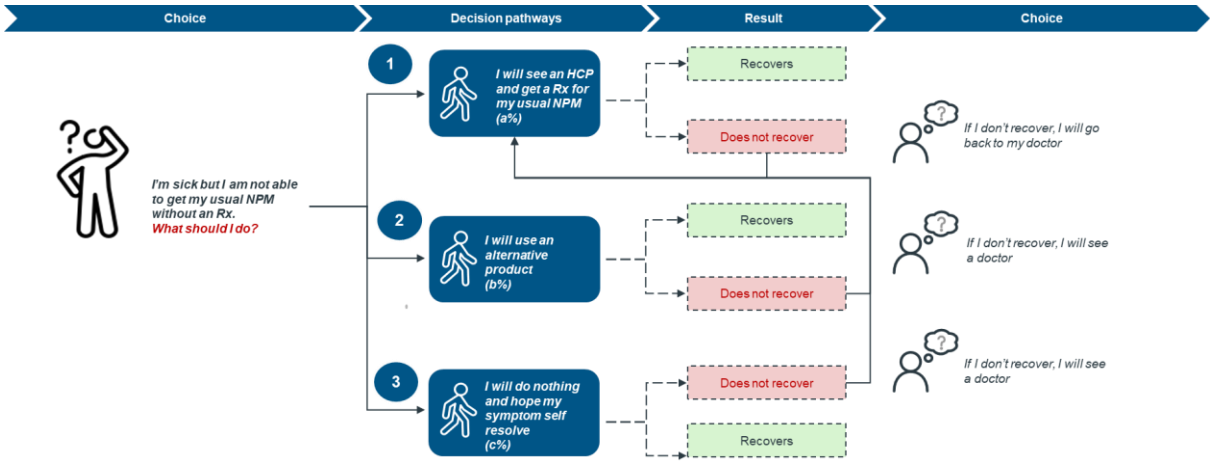

Figure 3 Decision tree: Patient options

The decision tree diagram above visually represents the decision-making process for a patient in the event of a reverse switch, whereby one is unable to access the previously assigned NPM antifungal or antiviral without a prescription. We hypothesized three options available for the patient population as outlined below, of which a%, b% and c% values were obtained based on the survey conducted. These values are detailed in the "Survey Results" section.

The patient chooses one of the three options:

1. Option 1: Switch to Prescription (Rx) Medicines:
    a. Action: The patient sees a healthcare professional (HCP) and obtains a prescription for their usual NPM antifungal or antiviral (a%)

   b. Result: The outcome can be recovery or no recovery. If the patient does not recover, they will see their GP again.

2. Option 2: Switch to an Alternate Treatment:
   a. Action: The patient uses an alternative treatment (b%)
   b. Result: The outcome can be recovery or no recovery. If the patient does not recover, they will see a GP and eventually switch to Rx.

3. Option 3: Do Nothing:
   a. Action: The patient does nothing and allows their symptoms to self-resolve (c%)
   b. Result: The outcome can be recovery or no recovery. If the patient does not recover, they will see a GP and eventually switch to Rx.

Assumptions

Additionally, the following assumptions have been made in building the decision tree:

1. Reverse-Switching Entire Class of NPMs: The analysis assumes that reverse-switching affects the entire class of antifungal and antiviral NPMs, reclassifying them as prescription-only (Rx-only).
2. Patient Options in Event of Reverse Switch: In the event of a reverse switch, patients/consumers choose one of three options:
   a. Switch to the Rx Medicine: Obtain a prescription for the reverse switched medicine.
   b. Switch to an Alternate Treatment (excluding Rx): Use an alternative treatment not classified as Rx.
   c. Do Nothing: Opt to manage without any treatment, waiting symptoms to self-resolve.
3. Choice Distribution Based on Survey Results: The distribution of patients choosing any of the three options is based on the survey results, which provide insights into the preferences and behaviours of the different population segments.
4. Eventual Switch to Rx:
   a. Seek Rx: All patients who switch to Rx will do so immediately, without delay.
   b. Alternate Treatment Users: All patients who initially switch to an alternate medicine will eventually switch to Rx. They are assumed to have one outpatient visit per year and one prescription refill.
   c. Do Nothing: All patients who initially do nothing will eventually switch to Rx. They are assumed to have one outpatient visit per year.

C.1.2 Scenario 1: Patient switches to a Rx medicine

In this scenario, patients who cannot access their usual antifungal or antiviral NPM without a prescription choose to visit a doctor to obtain a prescription. This decision pathway and its outcomes are illustrated in the decision tree diagram below.

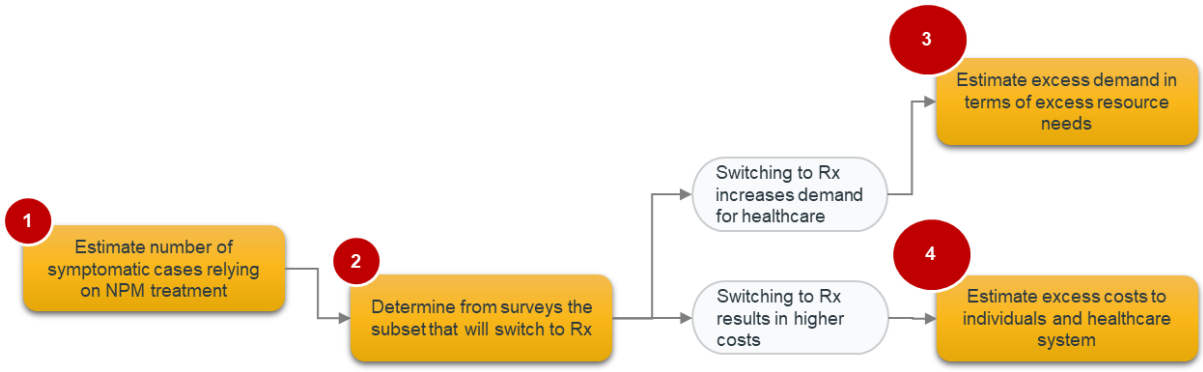

Figure 4 Decision tree of scenario 1: Patient switches to a Rx medicine

Decision Tree Breakdown

1. Estimate Number of Symptomatic Cases Relying on NPM Treatment: The first step is to estimate the number of symptomatic cases that rely on NPM treatments, as outlined in Methodology Section 2.
2. Determine Subset Switching to Rx: We determined the subset of patients who will switch to prescription from the survey results.
3. Estimate Excess Demand in Terms of Excess Resource Needs: Health losses lead to excess demand for healthcare resources. We estimated the number of additional visits, including emergency visits, upon reverse switching. The detailed methodology is elaborated under Methodology Section 4.
4. Estimate Excess Costs: Excess costs are estimated in terms of health costs and productivity losses, which will be elaborated under Methodology Section 5. The breakdown of excess costs includes:
    a. Health Costs:
        i. Excess costs estimated in terms of health costs and productivity losses.
        ii. Excess health costs estimated in terms of the share incident on individual vs. public payer vs. private insurance.
        iii. Cost contributors are cost of prescription drugs and outpatient care.
        iv. Excess prescription and outpatient costs estimated based on excess episodes.
    b. Productivity Losses: Productivity losses estimated in terms of wage losses to patient due to exacerbations and outpatient visits (not hospitalizations).

Assumptions

1. Same Medicine: We assume that the Rx medicine is the same as the reverse switched antifungal or antiviral NPM.
2. Dosage: If switched to the Rx medicine, there will not be a dosage change. The dose will be the same as the NPM.
3. Formulation:
    a. The Rx medicine will be available in the same formulation as the reverse-switched NPM.
    b. The price of the Rx medicine will remain unchanged with reverse switching, but the allocation of costs will be greater for the government if the medicine is reimbursed.
4. Outpatient Visits:
    a. All patients who switch to Rx will have at least one outpatient visit.
    b. Patients who have recurrences will have one additional visit within a year.

c. This additional visit will provide prescriptions for the rest of the year.
d. A prescription refill is needed for each recurrent episode.
e. All patients who switch to Rx will do so immediately, without delay.

5. Recurrent Episodes: The lower bound of recurrent episodes is assumed for patients who switch to Rx.

C.1.3 Scenario 2: Patient switches to an alternate treatment (excluding Rx)

In this scenario, patients who cannot access their known NPM without a prescription, choose to switch to an alternate medicine available for self-purchase. This decision pathway and its outcomes are illustrated below.

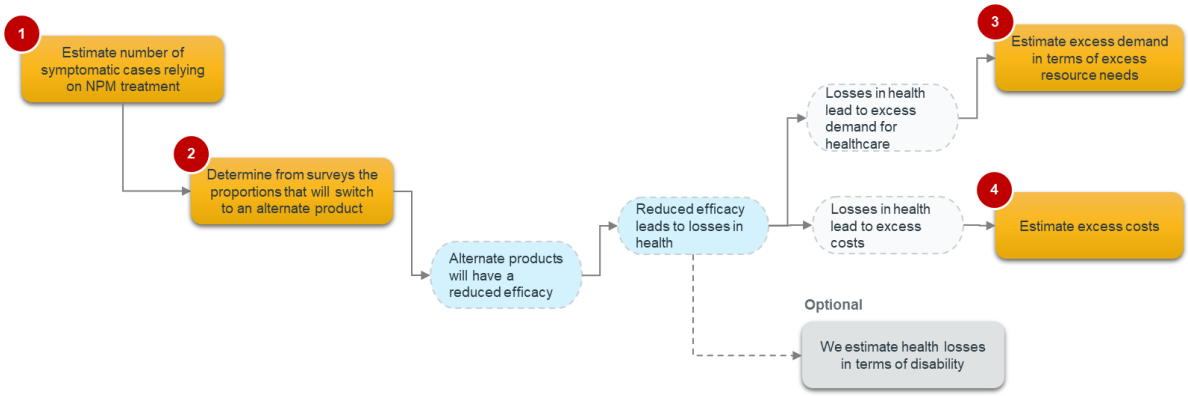

Figure 5 Decision tree for scenario 2: Patient switches to an alternate treatment

Decision tree breakdown:

1. Estimate Number of Symptomatic Cases Relying on NPM Treatment: The first step is to estimate the number of symptomatic cases that rely on NPM treatments, as outlined in Methodology Section 2.

2. Determine Proportions Switching to an Alternate Treatment: We determined the subset of patients who will switch to an alternative from the survey results.

3. Estimate Excess Demand in Terms of Excess Resource Needs: Health losses lead to excess demand for healthcare resources. We estimated the number of additional visits, including emergency visits, upon reverse switching. The detailed methodology is elaborated under Methodology Section 4.

4. Estimate Excess Costs: Excess costs are estimated in terms of healthcare related costs and productivity losses, which will be elaborated under "Estimating cost" methodology section. The breakdown of excess costs includes:
    a. Health Costs:
        i. Excess costs estimated in terms of health costs and productivity losses.
        ii. Excess health costs estimated in terms of the share incident on individual vs. public payer vs. private insurance.
        iii. Cost contributors are cost of prescription drugs and outpatient care.
        iv. Excess prescription and outpatient costs estimated based on excess episodes.
    b. Productivity Losses: Productivity losses estimated in terms of wage losses to patient due to exacerbations and outpatient visits (not hospitalizations).

5. Health Losses in Terms of Disability (optional): Reduced efficacy of alternate treatments lead to losses in health. These health losses are estimated in terms of disability, which impacts the patient's quality of life. The disability methodology and calculation are elaborated in the appendices as additional consideration.

Assumptions

1. Reduced Efficacy of Alternate Treatments:
    a. As we assumed that reverse-switching entails switching the entire class of antifungal and antiviral NPMs, the alternate treatments available for self-purchase are assumed to have lesser efficacy. They are mostly meant to provide symptom relief rather than treat the underlying infection and even if some herbal formulations might have natural antifungal or antiviral properties, their effectiveness varies. This reduced efficacy leads to health losses.
    b. Switching to an alternate treatment is assumed to be as effective as doing nothing in managing the condition.
2. Upper Bound of Recurrent Episodes: For patients who switch to alternate treatments, the upper bound of recurrent episodes is assumed, reflecting a higher likelihood of recurrence due to the reduced efficacy.

C.1.4 Scenario 3: Patients do nothing

In this scenario, patients who cannot access the reverse-switched medicine without a prescription choose to do nothing and wait for the symptoms to self-resolve. This decision pathway and its outcomes are illustrated in the decision tree diagram below.

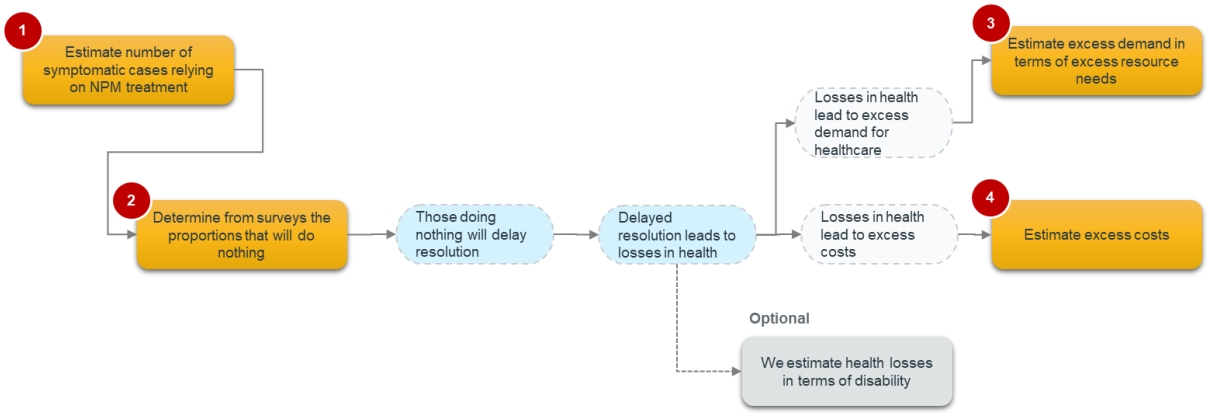

Figure 6 Decision tree of scenario 3: Patient does nothing

Decision tree breakdown:

1. Estimate Number of Symptomatic Cases Relying on NPM Treatment: The first step is to estimate the number of symptomatic cases that rely on NPM treatments, as outlined in Methodology Section 2.

2. Determine Proportions Who Do Nothing: We determined the subset of patients who will do nothing from the survey results.
3. Estimate Excess Demand in Terms of Excess Resource Needs: Health losses lead to excess demand for healthcare resources. We estimated the number of additional visits, including emergency visits, upon reverse switching. The detailed methodology is elaborated under Methodology Section 4.
4. Estimate Excess Costs: Excess costs are estimated in terms of health costs and productivity losses, which will be elaborated under "Estimating cost" methodology section. The breakdown of excess costs includes:
    a. Health Costs:
        i. Excess costs estimated in terms of health costs and productivity losses.
        ii. Excess health costs estimated in terms of the share incident on individual vs. public payer vs. private insurance.
        iii. Cost contributors are cost of prescription drugs and outpatient care.
        iv. Excess prescription and outpatient costs estimated based on excess episodes.
    b. Productivity Losses: Productivity losses estimated in terms of wage losses to patient due to exacerbations and outpatient visits (not hospitalizations).
5. Health Losses in Terms of Disability (optional): Reduced efficacy of alternate treatments leads to losses in health. These health losses are estimated in terms of disability, which impacts the patient's quality of life. The disability methodology and calculation are elaborated in the appendices as additional consideration.

Assumptions

In building the overall patient options decision tree, the following assumptions have been made:

1. Worsening symptoms if not seeking treatment: If a patient does nothing, their symptoms are likely to worsen. The worsening will be characterized as episodic.
2. Upper Bound of Recurrent Episodes: For patients who do nothing, the upper bound of recurrent episodes is assumed, reflecting a higher likelihood of recurrence due to worsening symptoms.

C.2. Survey

C.2.1. Survey methodology

This section outlines the survey methodology used to design and conduct the research. The methodology involves deriving survey questions through two parallel pathways, recruiting respondents, collecting profile information, and gathering quantitative data inputs.

Objectives

1. **Validation of Hypotheses:** The survey questions were designed to validate the hypotheses developed during the initial research phases.
2. **Estimation of Model Parameter Values:** The responses allow for the estimation of model parameter values crucial for the analysis.
3. **Stratification of Respondents:** The data collected enables the stratification of respondents based on vulnerability and demographic characteristics, ensuring a comprehensive analysis.

Derivation of Survey Questions

The survey questions were developed using two parallel pathways:

1. **Pathway 1: Demographic, Socioeconomic, and Health Questions**
    a. Data Sources:
        i. NHANES Survey (US): The National Health and Nutrition Examination Survey (NHANES) is a program of studies designed to assess the health and nutritional status of adults and children in the United States.
        ii. EHIS Survey (Europe): The European Health Interview Survey (EHIS) aims to measure the health status, health determinants, and use of health services of the EU population.
    b. Steps:
        i. Extract and reconcile relevant demographic, socioeconomic, and health questions from NHANES and EHIS surveys.
        ii. Apply relevant vulnerability criteria based on desk research to ensure the inclusion of appropriate questions.
    c. Output: A comprehensive set of demographic, socioeconomic, and health questions tailored for the survey.

2. **Pathway 2: Patient Journey Change Hypotheses and Questions**
    a. Data Sources:
        i. Guidelines (NICE): The National Institute for Health and Care Excellence (NICE) provides evidence-based guidance and advice for health, public health, and social care practitioners in the UK.
        ii. Literature: Reviewed existing literature on patient journeys and behavior changes.
    b. Step (continuing the steps in Pathway 1): Apply assumptions regarding behavior changes to standard patient journeys.
    c. Output: A set of questions focused on patient journey changes and hypotheses.

Survey Design

1. **Research Design:**
    a. Type: Self-administered online survey.
    b. In-scope countries: UK, Germany, Italy, Poland, and France.
2. **Recruit Respondents:**
    a. Sample Size[18]: 100 per country, with a fair distribution across in-scope indications.
3. **Collect Profile Information:** To understand the demographic, socioeconomic, and health profiles of respondents.
4. **Collect Quantitative Data Inputs:** To elicit individual preferences by asking respondents to state their choices among different hypothetical alternatives.

The complete design of the survey is detailed in the discussion guide elaborated in the Appendix 1.

[18] To derive the sample size, we used this formula: $n= (z^2 p (q))/d^2$, where z = 1.96 at 95% confidence level, d (the precision around the population mean) = 10%, p = 50% (assuming unknown prevalence of choice); and q = (1-p), which resulted in ~96 per country.

C.2.2. Survey results extrapolation

As the survey was conducted in 5 out of 28 in-scope countries, we needed to extrapolate parameter values obtained via the survey to the remaining 23 countries. We employed an extrapolation methodology based on several key factors. This approach ensures that the results are representative and applicable across the countries in scope.

The countries surveyed are:

1. Italy
2. Germany
3. France
4. Poland
5. United Kingdom

Extrapolation Methodology

To extrapolate the survey results from these 5 countries to the remaining 23, we utilized a three-filter approach.

1. Health System Similarities (Filter 1)
    - We assigned each country to a health system typology using prior characterizations from literature and data from the World Health Organization (WHO) and the Organisation for Economic Co-operation and Development (OECD).
    - The health system cluster is based on the following factors:
        - Healthcare supply
        - Public-private mix
        - Access regulation
        - Primary care orientation
        - Healthcare system performance
    - This filter ensures that countries with similar health system structures are grouped together, reflecting comparable regulatory environments and healthcare practices.

2. Affordability Similarities (Filter 2)
    a. Extracted from OECD Health Data, this filter uses per capita out-of-pocket health spending similarities to group countries.
    b. By considering affordability, we account for the economic capacity of populations to access and utilize NPM medications and ensuring that extrapolated data reflects financial accessibility.

3. Geographic Proximity (Filter 3)
    - This filter is based on the geographic distance, which we used as a proxy to assess similarities in population behavior and decision-making patterns.
    - Geographic proximity often correlates with cultural and social similarities, affecting health-seeking behavior and the utilization of healthcare services.

Assignment of Non-Surveyed Countries

Each non-surveyed country was matched to one of the five surveyed countries based on the combined results of the three filters. The following table details the implementation of the filters:

Table 5 Country extrapolation details

Countries	Country in scope of Survey?	Healthcare system match	Per capita OOP spending on health	Health spending group	Geographical group	Final classification
Austria	No	France, Germany	1148	Italy	Germany	**Germany**
Belgium	No	France, Germany	1075	Italy	France, Germany	**Germany**
Bulgaria	No	Germany	842	Germany	Italy	**Germany**
Croatia	No	Poland	245	Poland	Italy	**Poland**
Cyprus	No	Italy	383	Poland	Italy	**Italy**
Czechia	No	France, Germany	548	France	Poland, Germany	**France**
Denmark	No	UK	812	UK	Germany, UK	**UK**
Estonia	No	Poland	686	UK	Poland	**Poland**
Finland	No	United Kingdom	846	Germany, UK	Poland, UK, Germany	**UK**
France	Yes		545			
Germany	Yes		883			
Greece	No	Italy	912	Italy	Italy	**Italy**
Hungary	No	Poland	785	United Kingdom	Poland, Germany	**Poland**
Ireland	No	France, Germany	646	France	United Kingdom, France	**France**
Italy	Yes		920			
Latvia	No	Poland	842	Germany	Poland, Germany	**Poland**
Lithuania	No	Poland	1082	Italy	Poland, Germany	**Poland**
Luxembourg	No	France, Germany	567	France	France, Germany	**France**
Malta	No	Italy	1308	Italy	Italy	**Italy**
Netherlands	No	UK	658	UK	Germany, UK, France	**UK**
Poland	Yes		535			
Portugal	No	UK, Italy	1190	Italy	France	**Italy**
Romania	No	Poland	499	Poland	Poland	**Poland**
Slovakia	No	Poland	489	Poland	Poland	**Poland**
Slovenia	No	France, Germany	522	France	Italy, Germany, France	**France**
Spain	No	Italy	858	Germany	France	**Italy**
Sweden	No	United Kingdom	846	Germany	Poland, Germany	**UK**

UK	Yes	764

This matching process ensures that the extrapolated results are contextually relevant to the specific characteristics of each non-surveyed country.

4. Modelling excess demand in healthcare

D.1. Natural history

The natural history of the in-scope indications—Herpes Labialis, Vaginal Thrush, and Dermatomycosis including Athlete's Foot —is divided into personas, reflecting different patient experiences and disease progression patterns. The following sections detail the characteristics and assumptions for each persona across these conditions.

Athlete's foot

1. Persona 1: First episode[19]:
    a. Approximately 55% of patients experience a first episode of Athlete's Foot[20].
    b. Duration: 1 episode lasting up to 4-6 weeks[21].
2. Persona 2: Recurrent episodes
    a. Approximately 45% of patients experience recurrent episodes[22].
    b. Frequency: 3-4 episodes per year[23].
    c. Duration: Each episode lasts up to 2 months[24].

Dermatomycosis

1. Persona 1: First episodes
    a. Tinea Corporis/Cruris: About 9% of patients experience a first episode, which is derived from average in Sweden[25] and Lithuania[26].
    b. Duration: 1 episode lasting up to 1-4 weeks[27] [28] [29].
2. Persona 2: Recurrent episodes

[19] Costa, F., & Costa, F. (2023, December 18). Fluconazole: What It's For, How to Use & Side Effects. Tua Saúde. https://www.tuasaude.com/en/fluconazole/

[20] Terbinafine (Oral Route). (2024, May 2). https://www.mayoclinic.org/drugs-supplements/terbinafine-oral-route/proper-use/drg-20066265

[21] Terbinafine (Oral Route). (2024, May 2). https://www.mayoclinic.org/drugs-supplements/terbinafine-oral-route/proper-use/drg-20066265

[22] Bodman, M. (n.d.). Treatment Principles For Tinea Pedis. Hmpgloballearningnetwork.com. https://www.hmpgloballearningnetwork.com/site/podiatry/treatment-principles-tinea-pedis

[23] Singh, S., Verma, P., Chandra, U., & Tiwary, N. K. (2019). Risk factors for chronic and chronic-relapsing tinea corporis, tinea cruris and tinea faciei: Results of a case–control study. Indian Journal of Dermatology, Venereology, and Leprology, 85(2), 197. https://doi.org/10.4103/ijdvl.ijdvl_807_17

[24] Singh, S., Verma, P., Chandra, U., & Tiwary, N. K. (2019). Risk factors for chronic and chronic-relapsing tinea corporis, tinea cruris and tinea faciei: Results of a case–control study. Indian Journal of Dermatology, Venereology, and Leprology, 85(2), 197. https://doi.org/10.4103/ijdvl.ijdvl_807_17

[25] Drakensjö, I. T., & Chryssanthou, E. (2010). Epidemiology of dermatophyte infections in Stockholm, Sweden: a retrospective study from 2005–2009. Medical Mycology, 1–5. https://doi.org/10.3109/13693786.2010.540045

[26] Paškevičius A, Švedienė J. Distribution and species composition of causative agents of dermatophytoses in Lithuania. Acta Dermatovenerol Croat. 2013;21(2):99-104. PMID: 24001417.

[27] Terbinafine (Oral Route). (2024b, May 2). https://www.mayoclinic.org/drugs-supplements/terbinafine-oral-route/proper-use/drg-20066265

[28] Itraconazole. (2023, June 14). DermNet®. https://dermnetnz.org/topics/itraconazole

[29] Betamethasone And Clotrimazole (Topical Route). (2024, May 2). https://www.mayoclinic.org/drugs-supplements/betamethasone-and-clotrimazole-topical-route/proper-use/drg-20061704

   a. Onychomycosis and Tinea Unguium: Around 80% of patients experience recurrent episodes, which is derived from average in Sweden[30] and Lithuania[31].
   b. Frequency: 3-4 episodes per year[32].
   c. Duration: Each episode lasts up to 2-6 weeks[33] [34] [35].
3. Persona 3: Other recurrent cases
   a. Tinea Capitis: Approximately 11% of patients experience recurrent episodes which is derived from average in Sweden[36] and Lithuania[37].
   b. Frequency: We assumed 3-4 episodes per year[38].
   c. Duration: Each episode lasts up to 6 weeks[39].

Herpes Labialis

1. Persona 1: First episode
   a. Approximately 73% of patients experience a first episode of Herpes Labialis[40].
   b. Duration: We assumed 1 episode lasting 7-10 days[41].
2. Persona 2: Recurrent episodes:
   a. About 27% of patients experience recurrent episodes[42].
   b. Frequency: 2-6 episodes per year[43].
   c. Duration: We assumed each episode lasts 4-5 days on average[44].

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[30] Drakensjö, I. T., & Chryssanthou, E. (2010). Epidemiology of dermatophyte infections in Stockholm, Sweden: a retrospective study from 2005–2009. Medical Mycology, 1–5. https://doi.org/10.3109/13693786.2010.540045

[31] Paškevičius A, Švedienė J. Distribution and species composition of causative agents of dermatophytoses in Lithuania. Acta Dermatovenerol Croat. 2013;21(2):99-104. PMID: 24001417.

[32] Singh, S., Verma, P., Chandra, U., & Tiwary, N. K. (2019b). Risk factors for chronic and chronic-relapsing tinea corporis, tinea cruris and tinea faciei: Results of a case–control study. Indian Journal of Dermatology, Venereology, and Leprology, 85(2), 197. https://doi.org/10.4103/ijdvl.ijdvl_807_17

[33] Terbinafine (Oral Route). (2024b, May 2). https://www.mayoclinic.org/drugs-supplements/terbinafine-oral-route/proper-use/drg-20066265

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[35] NHS.uk. (2022, November 10). About clotrimazole cream, spray and solution. nhs.uk. https://www.nhs.uk/medicines/clotrimazole/about-clotrimazole-cream-spray-and-solution/

[36] Drakensjö, I. T., & Chryssanthou, E. (2010). Epidemiology of dermatophyte infections in Stockholm, Sweden: a retrospective study from 2005–2009. Medical Mycology, 1–5. https://doi.org/10.3109/13693786.2010.540045

[37] Paškevičius A, Švedienė J. Distribution and species composition of causative agents of dermatophytoses in Lithuania. Acta Dermatovenerol Croat. 2013;21(2):99-104. PMID: 24001417.

[38] Singh, S., Verma, P., Chandra, U., & Tiwary, N. K. (2019c). Risk factors for chronic and chronic-relapsing tinea corporis, tinea cruris and tinea faciei: Results of a case–control study. Indian Journal of Dermatology, Venereology, and Leprology, 85(2), 197. https://doi.org/10.4103/ijdvl.ijdvl_807_17

[39] Terbinafine (Oral Route). (2024b, May 2). https://www.mayoclinic.org/drugs-supplements/terbinafine-oral-route/proper-use/drg-20066265

[40] De Melo, J. R., Pivovar, L., Cossul, M. F., Gil, F. B. D., & De Lima, A. a. S. (n.d.-b). Exuberant recurrent herpes labialis in immunocompromised patient - case report. http://revodonto.bvsalud.org/scielo.php?script=sci_arttext&pid=S1984-56852015000200012#:~:text=The%20recurrent%20herpes%20labialis%20affects,%2C%20affecting%2010.2%25%20of%20patients.

[41] Cedars-sinai.org (n.d.). https://www.cedars-sinai.org/health-library/diseases-and-conditions/h/herpes-simplex-virus-hsv-mouth-infection.html#:~:text=Herpes%20simplex%20virus%20is%20the,after%20a%20day%20or%202

[42] De Melo, J. R., Pivovar, L., Cossul, M. F., Gil, F. B. D., & De Lima, A. a. S. (n.d.-b). Exuberant recurrent herpes labialis in immunocompromised patient - case report. http://revodonto.bvsalud.org/scielo.php?script=sci_arttext&pid=S1984-56852015000200012#:~:text=The%20recurrent%20herpes%20labialis%20affects,%2C%20affecting%2010.2%25%20of%20patients.

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[44] Usatine, R. P., & Tinitigan, R. (2010, November 1). Nongenital Herpes Simplex Virus. AAFP. https://www.aafp.org/pubs/afp/issues/2010/1101/p1075.html

Vaginal Thrush

1. Persona 1: First episode
    a. Around 95% of patients experience a first episode of Vaginal Thrush[45].
    b. Duration: 1 episode lasting up to 2 weeks[46] [47].
2. Persona 2: Recurrent episode
    a. Approximately 5% of patients experience recurrent episodes[48].
    b. Frequency: More than 4 episodes, collectively lasting around 6 months[49].

Our natural history framework provides a thorough overview of the typical progression and recurrence patterns for each condition. This facilitates better understanding and management of these in-scope indications to estimate cost impact.

D.2. Symptomatic and recurrent cases

This section details the methodology for calculating symptomatic and recurrent cases for three indications within the scope of our project:

1. Herpes Labialis
2. Vaginal Thrush
3. Dermatomycosis (including Athlete's foot)

Symptomatic Cases

The calculation of symptomatic cases aligns directly with the burden estimates for each indication (please refer to Methodology Section 2 for more details).

Recurrent Cases

The estimation of recurrent cases involves an additional step, utilizing the burden estimates in conjunction with the recurrence rate. This percentage represents the proportion of symptomatic cases that experience recurrence, as determined by a thorough review of natural history literature for each indication.

The calculation is as follows:

$$Recurrent\ cases = Burden\ estimates\ \times Recurrence\ rate$$

Where:

- Burden estimates: The number of individuals infected with any of the specified indications who exhibit symptoms and receive NPM treatment.

[45] Vaginal thrush. (n.d.-b). Better Health Channel. https://www.betterhealth.vic.gov.au/health/conditionsandtreatments/vaginal-thrush#managing-recurrent-vaginal-thrush

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[49] Cooke G, Watson C, Deckx L, Pirotta M, Smith J, van Driel ML. Treatment for recurrent vulvovaginal candidiasis (thrush). Cochrane Database Syst Rev. 2022 Jan 10;1(1):CD009151. doi: 10.1002/14651858.CD009151.pub2. PMID: 35005777; PMCID: PMC8744138.

- Recurrence rate: The estimated % share of total burden who experience recurrences based on the natural history. The following table details the recurrence rate across the indications:

Table 6 Recurrence rate percentages

Indication	Recurrence rate
Herpes Labialis[50]	27%
Vaginal Thrush [51]	5%
Dermatomycosis[52] [53]	80%
Athlete's foot[54]	45%

D.3. Excess appointments and Emergency visits

We assumed that in the event of a reverse switch, the affected persons may choose one of three decision pathways below.

1. Choose the obtain Rx for the reverse switched medicine
2. Choose an alternate treatment, other than antivirals and antifungals.
3. Do nothing

The proportion of patients choosing any of these three decision pathways were obtained based on the survey conducted as detailed in Methodology Section 3.

Excess Appointments

We define excess appointments as additional visits made in results of reverse-switching. To calculate the excess appointments, we consider both symptomatic and recurrent cases across the three decision pathways identified in the "Survey Results" section. The formulas used are:

1. For Seek Prescription decision pathway:

$$Excess\ appointments_{Seek\ Rx} = (Symptomatic\ cases \times a\%) + (Recurrent\ cases \times a\%)$$

Where:

- Symptomatic cases: Burden estimates of each indication
- a%: The % of total burden who chose to Seek Rx as their decision pathway in case of reverse-switch.
- Recurrent cases: The burden who experience more than 1 episode.

2. For Seek alternative treatment decision pathway:

$$Excess\ appointments_{Seek\ alternative\ treatment} = (Symptomatic\ cases \times b\%)$$

[50] *De Melo, J. R., Pivovar, L., Cossul, M. F., Gil, F. B. D., & De Lima, A. a. S. (n.d.). Exuberant recurrent herpes labialis in immunocompromised patient - case report. http://revodonto.bvsalud.org/scielo.php?script=sci_arttext&pid=S1984-56852015000200012#:~:text=The%20recurrent%20herpes%20labialis%20affects,%2C%20affecting%2010.2%25%20of%20patients.*

[51] Vaginal thrush. (n.d.). Better Health Channel. https://www.betterhealth.vic.gov.au/health/conditionsandtreatments/vaginal-thrush#managing-recurrent-vaginal-thrush

[52] Iara Trocoli Drakensjö, Erja Chryssanthou, Epidemiology of dermatophyte infections in Stockholm, Sweden: a retrospective study from 2005–2009, Medical Mycology, Volume 49, Issue 5, July 2011, Pages 484–488, https://doi.org/10.3109/13693786.2010.540045

[53] Paškevičius A, Švedienė J. Distribution and species composition of causative agents of dermatophytoses in Lithuania. Acta Dermatovenerol Croat. 2013;21(2):99-104. PMID: 24001417.

[54] Singh S, Verma P, Chandra U, Tiwary NK. Risk factors for chronic and chronic-relapsing tinea corporis, tinea cruris and tinea faciei: Results of a case–control study. Indian J Dermatol Venereol Leprol 2019;85:197-200

Where:

- Symptomatic cases: Burden estimates of each indication
- b%: The % of total burden who chose to Seek alternative treatment as their decision pathway in case of reverse-switch.

3. For Do nothing decision pathway:

$$Excess\ appointments_{Do\ nothing} = (Symptomatic\ cases\ \times c\%)$$

Where:

- Symptomatic cases: Burden estimates of each indication
- c%: The % of total burden who chose to do nothing as their decision pathway in case of reverse-switch.

For each decision pathway, we apply the corresponding population parameter percentage that derived from survey results to both symptomatic and recurrent cases to determine the total excess appointments.

Emergency Visits

We define emergency visits as the number of visits to emergency departments. To estimate the emergency visits resulting from these excess appointments, we use the following formula:

$$Emergency\ visits = (Excess\ appointments\ \times \%\ of\ Emergency\ visits)$$

Where:

- Excess appointments: The additional visits made as a result of reverse-switching.
- % of Emergency visits: The % share of total visits expected to be in emergency departments

The percentage of emergency visits is derived from OECD data[55], as outlined in the following table.

Table 7 Emergency visits

Country	2021 Emergency visits %
Portugal	63.0%
Spain	59.1%
England (UK)	43.1%
Estonia	33.0%
Denmark	29.5%
Average OECD25	26.6%
Ireland	25.8%
Italy	24.5%
Lithuania	23.9%
Belgium	23.3%
Finland	21.1%
Germany	19.8%

[55] OECD. (n.d.). https://www.oecd-ilibrary.org/sites/0de600bb-en/index.html?itemId=/content/component/0de600bb-en#:~:text=Across%2025%20OECD%20countries%20with,ED%20visits%20per%20100%20people.

Latvia	19.6%
Sweden	16.8%
Netherlands	9.7%
Poland	9.0%
Slovak Republic	9.0%
Austria	8.0%
Czech Republic	6.4%

5. Estimating costs

E.1. Prescription (Rx) cost

This section outlines the methodology for estimating the prescription cost for the three decision pathways identified in the event of a reverse switch. The calculation incorporates the burden of disease, share of population for each decision pathway, recurrence rates, and prescription drug prices.

Formula for Prescription Cost:

1. Seek Prescription decision pathway

$$Prescription\ cost_{Seek\ Rx} = \big((Burden \times a\%) + (Burden \times a\% \times Recurrence\ rate \times Number\ of\ episodes_{lower\ bound})\big) \times Mean\ Rx\ price$$

Where:

- Burden: The number of individuals infected with any of the specified indications who exhibit symptoms and receive Non-prescription medicine (NPM) treatment.
- a%: the % of total burden who chose to Seek Rx as their decision pathway in case of reverse-switch.
- Recurrence rate: The estimated % share of total burden who experience recurrences based on the natural history.
- $Number\ of\ episodes_{lower\ bound}$: The least number of bound episode range based on the natural history[56].
- Mean Rx price: The average prescription price within each country in Euro currency.

2. Seek alternative treatment decision pathway

$$Prescription\ cost_{Seek\ Alternative\ treatment} = \big(Burden \times b\% \times Recurrence\ rate \times Number\ of\ episodes_{upper\ bound}\big) \times Mean\ Rx\ price$$

[56] It is assumed that individuals who seek prescription medication immediately, resulting in better-controlled conditions and fewer number of episodes.

Where:

- Burden: The number of individuals infected with any of the specified indications who exhibit symptoms and receive Non-prescription medicine (NPM)treatment.
- b%: The % of total burden who chose to Seek alternative treatment as their decision pathway in case of reverse-switch.
- Recurrence rate: The estimated % share of total burden who experience recurrences based on the natural history.
- Upper bound episode: The greatest number of bound episode range based on the natural history[57].
- Mean Rx price: The average prescription price within each country in Euro currency.

3. Do nothing decision pathway

$$Prescription\ cost_{Do\ nothing} = \left(Burden \times c\% \times Recurrence\ rate \times Number\ of\ episodes_{upper\ bound}\right) \times Mean\ Rx\ price$$

Where:

- Burden: The number of individuals infected with any of the specified indications who exhibit symptoms and receive NPM treatment.
- c%: The % of total burden who chose to Seek alternative treatment as their decision pathway in case of reverse-switch.
- Recurrence rate: The estimated % share of total burden who experience recurrences based on the natural history.
- Upper bound episode: The greatest number of bound episode range based on the natural history[58].
- Mean Rx price: The average prescription price within each country in Euro currency.

This prescription cost was then detailed as per expenditure share to the four stakeholders:

1. Public payer
2. Individual
3. Private insurance
4. Others

This expenditure share % data is derived from OECD statistics[59]. The following table details the contribution share %:

Table 8 Prescription and outpatient cost contribution share

Country	Public payer share	Individual share	Private insurance share	Other

[57] It is assumed that individuals who seek alternative and do nothing are more likely to experience higher episodes due to delayed or alternative treatments.

[58] It is assumed that individuals who seek alternative and do nothing are more likely to experience higher episodes due to delayed or alternative treatments.

[59] Health expenditure and financing. (n.d.). © OECD. https://stats.oecd.org/index.aspx?DataSetCode=SHA

Austria	78.30%	15.80%	5.90%	0.00%
Belgium	77.60%	17.90%	4.50%	0.00%
Bulgaria	64.70%	34.00%	1.30%	0.00%
Croatia	85.00%	9.00%	5.10%	0.90%
Czech Republic	86.40%	12.70%	0.90%	0.00%
Estonia	76.20%	22.10%	1.70%	0.00%
Finland	79.80%	16.10%	4.10%	0.00%
France	84.80%	8.90%	6.30%	0.00%
Germany	85.50%	12.00%	2.50%	0.00%
Greece	62.10%	33.30%	4.40%	0.20%
Hungary	72.50%	24.60%	2.90%	0.00%
Ireland	77.40%	10.70%	11.90%	0.00%
Italy	75.50%	21.90%	2.60%	0.00%
Latvia	69.40%	27.00%	3.60%	0.00%
Lithuania	68.50%	30.20%	1.30%	0.00%
Netherlands	84.90%	9.40%	5.70%	0.00%
Norway	85.50%	14.10%	0.40%	0.00%
Poland	72.50%	19.80%	7.70%	0.00%
Portugal	63.20%	29.00%	7.80%	0.00%
Romania	78.00%	21.00%	0.70%	0.30%
Serbia	78.00%	21.00%	0.70%	0.30%
Slovakia	79.70%	19.40%	0.90%	0.00%
Slovenia	73.70%	12.90%	13.40%	0.00%
Spain	71.60%	21.00%	7.40%	0.00%
Switzerland	67.70%	22.30%	8.60%	1.40%
United Kingdom	83.00%	12.70%	4.30%	0.00%

E.2. Outpatient cost

This section outlines the methodology for estimating the outpatient costs for the three decision pathways identified in the event of a reverse switch. The calculation incorporates the burden of disease, share of population for each decision pathway, recurrence rates, and mean outpatient costs.

Formula for Outpatient Cost:

1. Seek Prescription decision pathway

$$Outpatient\ cost_{Seek\ Rx} = \big((Burden \times a\%) + (Burden \times a\% \times Recurrence\ rate)\big) \times Mean\ Outpatient\ cost$$

Where:

- Burden: The number of individuals infected with any of the specified indications who exhibit symptoms and receive Non-prescription medicine (NPM)treatment.
- a%: The % of total burden who chose to Seek Rx as their decision pathway in case of reverse-switch.
- Recurrence rate: The estimated % share of total burden who experience recurrences based on the natural history.
- Mean Outpatient cost: The average cost of an outpatient visit derived from IHME data[60]

2. Seek Alternative treatment decision pathway

$$Outpatient\ cost_{Seek\ alternative\ treatment} = Burden\ \times b\%\ \times Recurrence\ rate \times Mean\ Outpatient\ cost$$

Where:

- Burden: The number of individuals infected with any of the specified indications who exhibit symptoms and receive Non-prescription medicine (NPM)treatment.
- b%: The % of total burden who chose to Seek alternative treatment as their decision pathway in case of reverse-switch.
- Recurrence rate: The estimated % share of total burden who experience recurrences based on the natural history.
- Mean Outpatient cost: The average cost of an outpatient visit derived from IHME data[61]

3. Do nothing decision pathway

$$Outpatient\ cost\ _{Do\ nothing} = Burden\ \times c\%\ \times Recurrence\ rate \times Mean\ Outpatient\ cost$$

Where:

- Burden: The number of individuals infected with any of the specified indications who exhibit symptoms and receive Non-prescription medicine (NPM)treatment.
- c%: The % of total burden who chose to do nothing as their decision pathways in case of reverse-switch.
- Recurrence rate: The estimated % share of total burden who experience recurrences based on the natural history.
- Mean Outpatient cost: The average cost of an outpatient visit derived from IHME data[62]

This prescription cost was then detailed as per expenditure share to the four stakeholders:

1. Public payer
2. Individual
3. Private insurance

[60] Global Inpatient and Outpatient Health Care Utilization, Unit Costs, and Costs and Services Needed to Achieve Universal Health Coverage 1990-2016 | GHDx. (n.d.). https://ghdx.healthdata.org/record/ihme-data/UHC-cost-and-services-2016

[61] Global Inpatient and Outpatient Health Care Utilization, Unit Costs, and Costs and Services Needed to Achieve Universal Health Coverage 1990-2016 | GHDx. (n.d.). https://ghdx.healthdata.org/record/ihme-data/UHC-cost-and-services-2016

[62] Global Inpatient and Outpatient Health Care Utilization, Unit Costs, and Costs and Services Needed to Achieve Universal Health Coverage 1990-2016 | GHDx. (n.d.). https://ghdx.healthdata.org/record/ihme-data/UHC-cost-and-services-2016

4. Others

This expenditure share % data is elaborated within "Prescription cost" section.

E.3. Productivity cost

This section outlines the methodology for estimating the productivity costs for the three decision pathways identified in the event of a reverse switch. The calculation incorporates the burden of disease, share of population for each decision pathway, recurrence rates, and average wage per hour of each country. This productivity cost represents wage losses due to lost time from work either due to physician consultations or due to the severity of the disease.

Formula for Outpatient Cost:

1. Seek Prescription decision pathway

$$Productivity\ cost_{Seek\ Rx} = \big((Burden\ \times a\%) + (Burden\ \times a\% \times Recurrence\ rate\ )\big) \times Average\ wage\ per\ hour\ \times 1\ hours$$[63]

Where:

- Burden: The number of individuals infected with any of the specified indications who exhibit symptoms and receive Non-prescription medicine (NPM)treatment.
- a%: The % of total burden who chose to Seek Rx as their decision pathways in case of reverse-switch.
- Recurrence rate: The estimated % share of total burden who experience recurrences based on the natural history.
- Average wage per hour: Average wage per hour derived from the OECD data[64]. For those countries that do not have the data available, we applied the average wage per hour of OECD European countries.

2. Seek Alternative treatment decision pathway

$$Productivity\ cost_{Seek\ Alternative\ Product} = Burden\ \times b\%\ \times Recurrence\ rate \times Average\ wage\ per\ hour\ \times 0.5\ hours$$[65]

Where:

- Burden: The number of individuals infected with any of the specified indications who exhibit symptoms and receive Non-prescription medicine (NPM)treatment.
- b%: The % of total burden who chose to Seek alternative treatment as their decision pathways in case of reverse-switch.
- Recurrence rate: The estimated % share of total burden who experience recurrences based on the natural history.

[63] The wage losses for those who seek Rx is due to time lost in going for an appointment. Each appointment incurs 1 hour of work loss.

[64] Average annual hours actually worked per worker. (n.d.). © OECD. https://stats.oecd.org/index.aspx?DataSetCode=ANHRS

[65] For those who seek alternate treatments and do nothing, each episode incurs 30 minutes of work loss.

- Average wage per hour: Average wage per hour derived from the OECD data[66]. For those countries that do not have the data available, we applied the average wage per hour of OECD European countries.

3. Do nothing decision pathway

$$Productivity\ cost_{\ Do\ nothing} = Burden\ \times c\% \times Recurrence\ rate \times Average\ wage\ per\ hour\ \times 0.5\ hours$$[67]

Where:

- Burden: The number of individuals infected with any of the specified indications who exhibit symptoms and receive Non-prescription medicine (NPM)treatment.
- c%: The % of total burden who chose to do nothing as their decision pathways in case of reverse-switch.
- Recurrence rate: The estimated % share of total burden who experience recurrences based on the natural history.
- Average wage per hour: Average wage per hour derived from the OECD data[68]. For those countries that do not have the data available, we applied the average wage per hour of OECD European countries.

6. Volume impact

This section outlines the methodology for estimating the volume impact of reverse-switching on the consumption of antiviral or antifungal medicines. The methodology involves calculating the volume of medicines consumed before and after the reverse switch, taking into account surveyed patient behaviors, persona and model assumptions outlined above.

Formula for Volume Impact

1. **Volume Before Reverse Switch:** This represents the initial volume of medicines consumed, calculated as:

   $$Volume\ before\ reverse\ switch = Burden\ \times Number\ of\ Units\ Taken\ per\ Person$$

   Where:

   - Burden: The number of individuals infected with any of the specified indications who exhibit symptoms and receive NPM treatment.
   - Number of units taken per person: The average standard unit of drugs taken by each burden case before reverse-switch.

2. **Volume After Reverse Switch:** The volume after the reverse switch is calculated separately for each decision pathways based on their behavior and recurrence rates.

   a. For seeking prescription v:

[66] Average annual hours actually worked per worker. (n.d.). © OECD. https://stats.oecd.org/index.aspx?DataSetCode=ANHRS

[67] For those who seek alternate treatments and do nothing, each episode incurs 30 minutes of work loss.

[68] Average annual hours actually worked per worker. (n.d.). © OECD. https://stats.oecd.org/index.aspx?DataSetCode=ANHRS

$$Volume\ after_{Seek\ Rx} = (Burden \times Seeking\ Rx\ share) + (Burden \times Recurrence\ rate \times a\% \times Number\ of\ episodes_{lower\ bound})$$

Where:

- Burden: The number of individuals infected with any of the specified indications who exhibit symptoms and receive Non-prescription medicine (NPM) before reverse-switching.
- $a\%$: The % of total burden who chose to Seek Rx as their decision pathway in case of reverse-switch.
- Recurrence rate: The estimated % share of total burden who experience recurrences based on the natural history.
- $Number\ of\ episodes_{lower\ bound}$: The least number of bound episode range based on the natural history.

b. For seeking alternative treatment decision pathway:

$$Volume\ after_{Seek\ alternative\ treatment} = (Burden \times Recurrence\ rate \times b\% \times Number\ of\ episodes_{upper\ bound})$$

Where:

- Burden: The number of individuals infected with any of the specified indications who exhibit symptoms and receive Non-prescription medicine (NPM)treatment.
- b%: The % of total burden who chose to Seek alternative treatment as their decision pathways in case of reverse-switch.
- Recurrence rate: The estimated % share of total burden who experience recurrences based on the natural history.
- $Number\ of\ episodes_{upper\ bound}$: The greatest number of bound episode range based on the natural history[69].

c. For do nothing decision pathway:

$$Volume\ after_{Do\ nothing} = (Burden \times Recurrence\ rate \times c\%)$$

Where:

- Burden: The number of individuals infected with any of the specified indications who exhibit symptoms and receive Non-prescription medicine (NPM)) treatment.
- c%: The % of total burden who chose to do nothing as their decision pathways in case of reverse-switch.
- Recurrence rate: The estimated % share of total burden who experience recurrences based on the natural history.

[69] It is assumed that individuals who seek alternative and do nothing are more likely to experience higher episodes due to delayed or alternative treatments.

- $Number\ of\ episodes_{upper\ bound}$: The greatest number of bound episode range based on the natural history[70].

3. **Reverse-Switching Volume Impact:** The overall impact on volume due to reverse switching is calculated as:

$$Reverse\ switching\ volume\ impact = Volume\ before - (Volume\ after_{Seek\ Rx} + Volume\ after_{Seek\ alternative\ product} + Volume\ after_{Do\ nothing})$$

Assumptions

1. Standard Units per Doctor's Visit: Upon reverse-switching, it is assumed that individuals will receive one standard unit[71] of antiviral or antifungal medicine with each doctor's visit.
2. Standard Units per Prescription Refill: Individuals are also assumed to receive one standard unit[72] of antiviral or antifungal medicine with each prescription refill.
3. Number of Doctor's Visits and Refills: The number of doctor's visits and prescription refills are based on agreed assumptions used in estimating the cost impact. These assumptions include the frequency of visits and refills as dictated by the treatment protocols for the conditions in question.

This methodology provides a comprehensive approach to estimating the volume impact of reverse-switching on the consumption of antiviral or antifungal medicines. By considering the different behaviors of patient decision pathways, recurrence rates, and treatment protocols, we ensure an accurate assessment of how reverse-switching will affect medicines usage.

7. Extrapolation

G.1. Country selection

The scope of this project includes 28 countries, specifically all European Union (EU) member states plus the United Kingdom. The countries in scope are:

1. Austria (AT)
2. Belgium (BE)
3. Bulgaria (BG)
4. Croatia (HR)
5. Czech Republic (CZ)
6. Estonia (EE)

[70] It is assumed that individuals who seek alternative and do nothing are more likely to experience higher episodes due to delayed or alternative treatments.

[71] Standard unit: Total number of smallest SKU (stock keeping unit) consumed. For the topical products under consideration, we assumed one SKU would be consumed during each episode.

[72] Standard unit: Total number of smallest SKU (stock keeping unit) consumed. For the topical products under consideration, we assumed one SKU would be consumed during each episode.

7. Finland (FI)
8. France (FR)
9. Germany (DE)
10. Greece (GR)
11. Hungary (HU)
12. Ireland (IE)
13. Italy (IT)
14. Latvia (LV)
15. Lithuania (LT)
16. Netherlands (NL)
17. Poland (PL)
18. Portugal (PT)
19. Romania (RO)
20. Slovakia (SK)
21. Spain (ES)
22. United Kingdom (UK)
23. Slovenia (SI)
24. Sweden (SE)
25. Malta (MT)
26. Luxembourg (LU)
27. Republic of Cyprus (CY)
28. Denmark (DK)

Extrapolation of Burden and Cost Estimation

Within these 28 countries, we extrapolated the burden and cost estimations for six specific countries due to the unavailability of data for certain diseases. These countries are:

Herpes labialis extrapolated countries:

1. Slovenia (SI)
2. Sweden (SE)
3. Malta (MT)
4. Luxembourg (LU)
5. Republic of Cyprus (CY)
6. Denmark (DK)

Vaginal thrush, Dermatomycosis, and Athlete's foot extrapolated countries:

1. Sweden (SE)
2. Malta (MT)
3. Luxembourg (LU)
4. Republic of Cyprus (CY)
5. Denmark (DK)

The methodology for extrapolating data for these countries will be detailed in the subsequent section.

G.2. Burden disease extrapolation

1. Dermatomycosis

With burden estimates available for 23 out of the 28 countries, we extrapolated the burden estimates for the remaining five countries: Cyprus, Denmark, Luxembourg, Malta, and Sweden using a 3-step approach:

Step 1: Identification of Anchor Countries

To identify anchor countries for the extrapolated countries, we considered two key factors: Dermatomycosis prevalence rates and Non-prescription medicine (NPM)health spending per capita.

a. Dermatomycosis Prevalence:
   - Utilizing data from the Institute for Health Metrics and Evaluation (IHME), we obtained Dermatomycosis prevalence rates for the 28 in-scope countries, filtering specifically for fungal skin diseases.
   - We identified the nearest prevalence rates among the 23 countries for each of the five extrapolated countries.

b. NPM Health Spending per Capita:
   - IHME Global Burden of Disease (GBD) provided population data projected to 2023.
   - OTC health spending data for 2023 was sourced from multiple databases, including IQVIA OTC data and Statista.
   - By calculating NPM health spending per capita, we determined anchor countries with the nearest NPM health spend to the extrapolated countries.

Step 2: Calculation of Dermatomycosis Burden % for Anchor Countries

Once the anchor country was decided, we calculated the burden as a percentage of the total population.

$$Dermatomycosis\ burden\ \% = \left(\frac{Dermatomycosis\ Burden}{Total\ population}\right) \times 100\%$$

For instance, if the anchor country selected is France, with dermatomycosis burden of 1.5 million out of a population of 67 million, the "Dermatomycosis Burden %" would be 2.2%.

Step 3: Extrapolation of Burden Estimates

Next, we proceeded with extrapolation by multiplying the population of each of the five countries with the "Burden %" of their respective anchor countries. This extrapolation allowed us to derive the burden of dermatomycosis for Cyprus, Denmark, Luxembourg, Malta, and Sweden.

The table below summarizes the analysis, specifying the anchor countries and the calculated burden estimates for each of the five extrapolated countries.

Table 9 Dermatomycosis burden extrapolation

Country	DM prevalence % (IHME)	Prevalence rate top 3-4 closest countries	NPM spend per capita in USD	NPM spend per capita top 3-4 closest countries	Country anchor	DM Burden %	Extrapolated burden disease
Austria	10.7%		86			0.9%	
Belgium	10.8%		141			2.2%	
Bulgaria	7.9%		105			0.3%	
Croatia	8.0%		71			1.2%	
Cyprus	9.3%	Ireland, Latvia, Lithuania, Croatia	79	Romania, Latvia, Austria, Croatia	Latvia		14,144
Czechia	7.8%		109			1.6%	
Denmark	10.7%	Netherlands, Austria, Belgium, UK	31	Netherlands, UK, Estonia	Netherlands		51,488
Estonia	8.0%		69			0.3%	
Finland	11.4%		94			0.6%	
France	11.0%		147			2.2%	
Germany	11.4%		116			1.2%	
Greece	11.8%		111			1.3%	
Hungary	7.8%		108			1.8%	
Ireland	9.4%		67			1.6%	
Italy	12.1%		159			1.2%	
Latvia	8.1%		84			1.0%	
Lithuania	8.1%		101			0.0%	
Luxembourg	9.7%	Ireland, UK, Netherlands, Austria	51	Ireland, Estonia, Croatia	Ireland		11,002
Malta	11.2%	France, Finland, Germany	217	Italy, France, Belgium	France		9,684
Netherlands	10.7%		26			0.9%	
Poland	7.7%		105			2.1%	
Portugal	11.6%		131			1.6%	

Romania	7.7%		77		0.9%	
Slovak Republic	7.1%		126		2.3%	
Slovenia	8.1%		93		2.1%	
Spain	8.0%		119		0.1%	
Sweden	11.0%	France, Belgium, Austria, Netherlands, Finland, Germany	31	Netherlands, UK, Ireland	Netherlands	91,822
United Kingdom	10.5%		20		0.7%	

2. Athlete's foot (Tinea Pedis)

Athlete's foot, also known as Tinea Pedis, is classified under the broader category of Dermatomycosis in the Medical Subject Headings (MeSH). Due to this classification, we used the same anchor countries identified for dermatomycosis and methodology to extrapolate the burden of Athlete's Foot.

The table below summarizes the analysis, specifying the anchor countries and the calculated burden estimates for each of the five extrapolated countries for Athlete's foot indication.

Table 10 Athlete's foot extrapolation

Country	2023 Population	AF Burden disease	Country anchor	AF Burden %	Extrapolated burden disease
Austria	9,079,172	12,511		0.1%	
Belgium	11,545,599	36,804		0.3%	
Bulgaria	6,665,339	3,248		0.0%	
Croatia	4,171,250	7,448		0.2%	
Cyprus	1,398,478		Latvia		2,089
Czechia	10,645,359	25,756		0.2%	
Denmark	5,909,673		Netherlands		7,606
Estonia	1,309,237	521		0.0%	
Finland	5,546,701	4,884		0.1%	
France	66,732,724	214,455		0.3%	
Germany	86,134,855	155,150		0.2%	
Greece	10,046,434	19,385		0.2%	
Hungary	9,521,807	25,213		0.3%	
Ireland	4,983,996	12,062		0.2%	
Italy	59,459,557	101,462		0.2%	
Latvia	1,831,152	2,736		0.1%	
Lithuania	2,666,783	114		0.0%	
Luxembourg	671,575		Ireland		1,625
Malta	445,121		France		1,430
Netherlands	17,302,251	22,268		0.1%	
Poland	38,145,389	116,141		0.3%	
Portugal	10,560,882	25,348		0.2%	
Romania	18,652,554	25,947		0.1%	
Slovak Republic	5,429,950	18,332		0.3%	
Slovenia	2,069,354	6,391		0.3%	
Spain	45,145,713	8,645		0.02%	
Sweden	10,539,251		Netherlands		13,564
United Kingdom	68,593,669	69,733		0.1%	

3. Herpes Labialis

This section outlines the methodology used to extrapolate the burden estimates of Herpes Labialis for the remaining six countries—Slovenia, Cyprus, Denmark, Luxembourg, Malta, and Sweden—using data from 22 of the 28 countries with available burden estimates. The extrapolation was performed using a three-step approach to ensure accuracy and consistency.

Extrapolation Methodology

1. Calculate the Burden % for Each of the 22 Countries:

For each of the 22 countries with available burden estimates, we calculated the Herpes Labialis burden as a percentage of the total population. Formula:

$$Herpes\ Labialis\ burden\ \% = \left(\frac{Herpes\ Labialis\ Burden}{Total\ population}\right) \times 100\%$$

2. Calculate the average prevalence % across the 22 countries

$$Average\ burden\ \% = \frac{\sum Herpes\ Labialis\ burden\ \%\ of\ each\ 22\ countries}{22}$$

Using the above formula, we found that the average prevalence % for Herpes Labialis is 4.3%

3. Calculate the extrapolated burden for the 6 extrapolated countries

Using the average prevalence percentage calculated in step 2, we estimated the Herpes Labialis burden for the six extrapolated countries.

$$Herpes\ labialis\ burden\ estimate = population\ of\ the\ extrapolated\ country\ \times average\ prevalence\ \%$$

Table 11 Herpes Labialis burden extrapolation

Country	2023 Population	HL Burden disease	HL Burden %	Extrapolated burden disease
Austria	9,079,172	357,944	3.9%	
Belgium	11,545,599	341,969	3.0%	
Bulgaria	6,665,339	187,551	2.8%	
Croatia	4,171,250	122,850	2.9%	
Cyprus	1,398,478			60,321
Czechia	10,645,359	473,987	4.5%	
Denmark	5,909,673			254,903
Estonia	1,309,237	85,915	6.6%	
Finland	5,546,701	196,837	3.5%	
France	66,732,724	2,646,341	4.0%	
Germany	86,134,855	6,036,160	7.0%	
Greece	10,046,434	422,879	4.2%	
Hungary	9,521,807	494,091	5.2%	
Ireland	4,983,996	387,251	7.8%	
Italy	59,459,557	2,007,716	3.4%	
Latvia	1,831,152	89,644	4.9%	

Lithuania	2,666,783	192,184	7.2%	
Luxembourg	671,575			28,967
Malta	445,121			19,199
Netherlands	17,302,251	310,058	1.8%	
Poland	38,145,389	2,503,831	6.6%	
Portugal	10,560,882	706,411	6.7%	
Romania	18,652,554	127,440	0.7%	
Slovak Republic	5,429,950	214,487	4.0%	
Slovenia	2,069,354			89,258
Spain	45,145,713	1,430,859	3.2%	
Sweden	10,539,251			454,591
United Kingdom	68,593,669	821,915	1.2%	
		Average burden %	4.3%	

4. Vaginal thrush (Candidiasis, Vulvovaginal)

Vaginal thrush, also known as Candidiasis, Vulvovaginal (VVC), is classified under the broader category of Mycosis in the Medical Subject Headings (MeSH). As Dermatomycosis also falls under the same category of Mycosis, we used the same anchor countries identified for dermatomycosis and the same methodology to extrapolate the burden of VVC.

The table below summarizes the analysis, specifying the anchor countries and the calculated burden estimates for each of the five extrapolated countries for VVC indication.

Table 12 Vaginal thrush extrapolation

Country	2023 Population	VVC Burden disease	VVC Prevalence %	Country anchor	Extrapolated burden disease
Austria	9,079,172	283,943	3.1%		
Belgium	11,545,599	417,539	3.6%		
Bulgaria	6,665,339	57,363	0.9%		
Croatia	4,171,250	229,604	5.5%		
Cyprus	1,398,478			Latvia	45,602
Czechia	10,645,359	560,293	5.3%		
Denmark	5,909,673			Netherlands	202,774
Estonia	1,309,237	24,711	1.9%		
Finland	5,546,701	151,988	2.7%		
France	66,732,724	6,275,003	9.4%		
Germany	86,134,855	4,516,657	5.2%		
Greece	10,046,434	17,247	0.2%		
Hungary	9,521,807	327,216	3.4%		
Ireland	4,983,996	299,484	6.0%		
Italy	59,459,557	3,423,639	5.8%		
Latvia	1,831,152	59,711	3.3%		
Lithuania	2,666,783	109,441	4.1%		

Luxembourg	671,575			Ireland	40,354
Malta	445,121			France	41,856
Netherlands	17,302,251	593,680	3.4%		
Poland	38,145,389	1,364,306	3.6%		
Portugal	10,560,882	761,237	7.2%		
Romania	18,652,554	401,774	2.2%		
Slovak Republic	5,429,950	240,745	4.4%		
Slovenia	2,069,354	116,897			
Spain	45,145,713	1,172,809	2.6%		
Sweden	10,539,251			Netherlands	361,626
United Kingdom	68,593,669	1,451,875	2.1%		

G.3. Cost extrapolation

Following the burden extrapolation, we proceeded to cost extrapolation for a comprehensive economic assessment of the four indications across the 6 extrapolated countries in scope. The cost extrapolation process aims to provide an accurate estimation by adjusting for cost differences among countries.

To account for differences in healthcare costs between countries, we applied cost factors to the preliminary cost outputs. This adjustment is critical to reflect the true economic burden more accurately.

The process for determining the cost factor involved the following steps:

Step 1: Identifying Anchor Countries

We identified anchor countries by finding the closest percentage absolute difference in GDP per capita for the six extrapolated countries.

The five anchor countries used were:

- Italy
- Germany
- France
- United Kingdom
- Poland

The table below illustrates the calculation process for finding the anchor countries:

Table 13 Cost extrapolation: Anchor countries classification

Country Name	GDP per capita[73]	Italy	Germany	France	UK	Poland	Anchor countries
Austria	44,590	45%	7%	21%	2%	245%	United Kingdom

[73] World Bank Data (https://data.worldbank.org/indicator/NY.GDP.PCAP.CD)

Country Name	GDP per capita[73]	Italy	Germany	France	UK	Poland	Anchor countries
Belgium	41,318	35%	1%	12%	9%	219%	Germany
Bulgaria	7,344	76%	82%	80%	84%	43%	Poland
Croatia	12,617	59%	70%	66%	72%	2%	Poland
Cyprus	24,805	19%	40%	33%	45%	92%	Italy
Czechia	18,247	41%	56%	51%	60%	41%	Italy
Denmark	54,556	78%	31%	48%	20%	322%	United Kingdom
Estonia	17,946	42%	57%	51%	61%	39%	Poland
Finland	43,879	43%	5%	19%	4%	239%	United Kingdom
France	36,957	20%	11%	0%	19%	186%	France
Germany	41,682	36%	0%	13%	8%	222%	Germany
Greece	18,071	41%	57%	51%	60%	40%	Poland
Hungary	13,035	58%	69%	65%	71%	1%	Poland
Ireland	62,567	104%	50%	69%	38%	384%	United Kingdom
Italy	30,686	0%	26%	17%	33%	137%	Italy
Latvia	14,243	54%	66%	61%	69%	10%	Poland
Lithuania	14,810	52%	64%	60%	67%	14%	Poland
Luxembourg	108,351	253%	160%	193%	138%	738%	United Kingdom
Malta	25,181	18%	40%	32%	45%	95%	Italy
Netherlands	45,939	50%	10%	24%	1%	255%	United Kingdom
Poland	12,937	58%	69%	65%	72%	0%	Poland
Portugal	19,701	36%	53%	47%	57%	52%	Italy
Romania	9,287	70%	78%	75%	80%	28%	Poland
Slovak Republic	16,688	46%	60%	55%	63%	29%	Poland
Slovenia	21,541	30%	48%	42%	53%	67%	Italy
Spain	26,514	14%	36%	28%	42%	105%	Italy
Sweden	51,956	69%	25%	41%	14%	302%	United Kingdom
United Kingdom	45,482	48%	9%	23%	0%	252%	United Kingdom

Step 2: Calculating the Cost Factor

Once the anchor countries were identified, the next step was to determine the cost factor. This factor was calculated using the following formula:

$$Cost\ factor = \frac{Health\ spend\ of\ the\ extrapolated\ country}{Health\ spend\ of\ the\ anchor\ country}$$

The table below details the calculation of the cost factor:

Table 14 Cost extrapolation factor

Country	Health Spend per capita	Anchor country	Cost Factor
Austria	1,533	United Kingdom	**1.224**
Belgium	1,454	Germany	**0.882**
Bulgaria	412	Poland	**0.903**
Croatia	447	Poland	**0.980**
Cyprus	637	Italy	**0.639**
Czechia	689	Italy	**0.690**
Denmark	1,522	United Kingdom	**1.216**
Estonia	517	Poland	**1.134**
Finland	1,240	United Kingdom	**0.990**
France	1,384	France	**1.000**
Germany	1,648	Germany	**1.000**
Greece	638	Poland	**1.399**
Hungary	528	Poland	**1.158**
Ireland	1,597	United Kingdom	**1.275**
Italy	998	Italy	**1.000**
Latvia	449	Poland	**0.985**
Lithuania	509	Poland	**1.116**
Luxembourg	2,120	United Kingdom	**1.693**
Malta	1,053	Italy	**1.055**
Netherlands	1,677	United Kingdom	**1.339**
Poland	456	Poland	**1.000**
Portugal	764	Italy	**0.765**
Romania	291	Poland	**0.638**
Slovak Republic	592	Poland	**1.299**
Slovenia	744	Italy	**0.746**
Spain	976	Italy	**0.978**
Sweden	1,691	United Kingdom	**1.351**
United Kingdom	1,252	United Kingdom	**1.000**

This calculated factor is then used to adjust the preliminary cost output, providing a final cost estimation for the extrapolated countries. This method ensures that the cost differences due to varying healthcare spending levels are adequately accounted and lead to a more precise economic assessment.

8. Projection

The 5-year projection leverages historical growth rates to forecast future costs, ensuring that our estimates are grounded in recent trends and data.

The projection methodology involves the following steps:

1. **Historical Data Collection:**
    a. We collected data on the burden disease case numbers, prescription drug (Rx) prices, and annual wages for each country over the past five years (2018-2023).
    b. We assume constant rate for mean outpatient cost.

2. **Compound Annual Growth Rate (CAGR):**
    a. The Compound Annual Growth Rate (CAGR) was calculated for each of the three key components: burden disease case numbers, Rx prices, and productivity costs.
    b. CAGR is determined using the formula:

$$CAGR = \left(\frac{Ending\ value}{Beginning\ value}\right)^{\frac{1}{Number\ of\ years}} - 1$$

    c. This growth rate provides an annual rate of growth over the period which offers a reliable measure of historical trends.

3. **Projection of Future Costs:**
    a. The CAGR for each component is applied to the 2023 baseline data to project costs for the next five years.
    b. For burden disease case numbers, the projected cases for each year are calculated by applying the respective CAGR to the previous year's cases.
    c. Rx price projections are similarly calculated by applying the CAGR to the previous year's prices.
    d. Productivity costs are projected by applying the CAGR to the previous year's productivity costs, using the average wage per hour data to adjust for changes in labor costs.

4. **Integration and Final Estimation:**
    a. The projected figures for burden disease cases, Rx prices, and productivity costs are integrated to derive the final cost estimates for each year from 2023 to 2028.
    b. This integration ensures that all relevant economic factors are accounted for, providing a comprehensive estimate of the future financial burden.

Results

1. Summary of results

A.1. Survey result

Population parameters

The survey results provide insights on individuals' characteristics, barriers, choices and decision pathways in the event of a reverse switch. The survey respondent characteristics are as follows[74]:

Table 15 Survey respondent characteristics

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total respondent	378	90	83	79	66	60
Gender						
Male	152	37	33	34	27	21
Female	226	53	50	45	39	39
Others	-	-	-	-	-	-
Age						
Below 18 years	-	-	-	-	-	-
18-24 years	36	9	7	4	6	10
25-29 years	36	9	7	9	5	6
30-34 years	42	6	14	7	10	5
35-39 years	40	10	4	8	6	12
40-44 years	40	10	8	6	10	6
45-49 years	40	6	12	10	8	4
50-54 years	37	4	9	6	10	8
55-59 years	29	11	4	9	3	2
60 years and above	78	25	18	20	8	7
Household income						
Below threshold	34	9	7	10	5	3
Above threshold	344	81	76	69	61	57

[74] Value in the table represents the number of respondents

Prefer not to answer	0	-	-	-	-	-
Working status						
Self-employed	35	7	4	3	12	9
Full-time employee	199	32	49	47	35	36
Part-time employee	47	25	2	7	8	5
Unemployed	35	10	12	9	2	2
Retired	50	14	15	11	4	6
Student	12	2	1	2	5	2
Education level						
No formal education	-	-	-	-	-	-
Primary education	9	4	1	3	-	1
Lower secondary education	19	13	3	1	2	-
Upper secondary education	101	9	15	26	27	24
Post-secondary non-tertiary education	52	31	4	11	4	2
Short-cycle tertiary education	29	1	20	4	2	2
Tertiary education - Bachelors	76	12	19	21	12	12
Tertiary education - Masters	76	19	12	12	14	19
Tertiary education - PhD	16	1	9	1	5	-
None of the above	-	-	-	-	-	-

The main choices leading to decision pathways reflect the choices made by affected persons which include:

1. Choosing to obtain Rx for reverse switched medicine
2. Choosing an alternate treatment, other than antifungals and antivirals
3. Doing nothing

Total Population: This encompasses the entire population surveyed in each country. The population parameters of Total population are as follows:

Table 16 Share of population surveyed for each decision pathways (Total Population)

Country	Indication	Seek Prescription	Seek Alternative Treatment	Do nothing
France	Herpes Labialis	38%	50%	13%
France	Vaginal Thrush	80%	20%	0%
France	Athlete's Foot	72%	22%	6%

France	Dermatomycosis	72%	22%	6%
Germany	Herpes Labialis	68%	26%	5%
Germany	Vaginal Thrush	74%	21%	5%
Germany	Athlete's Foot	58%	37%	5%
Germany	Dermatomycosis	58%	37%	5%
Italy	Herpes Labialis	45%	55%	0%
Italy	Vaginal Thrush	52%	48%	0%
Italy	Athlete's Foot	59%	41%	0%
Italy	Dermatomycosis	59%	41%	0%
Poland	Herpes Labialis	53%	37%	10%
Poland	Vaginal Thrush	75%	20%	5%
Poland	Athlete's Foot	61%	39%	0%
Poland	Dermatomycosis	61%	39%	0%
UK	Herpes Labialis	67%	28%	6%
UK	Vaginal Thrush	68%	21%	10%
UK	Athlete's Foot	50%	45%	5%
UK	Dermatomycosis	50%	45%	5%

A.2. Total burden

Based on the approach and assumption elaborated in the methodology section, the following table details the estimated burden for the four indications across 27 European countries and the United Kingdom across the current and 5 years projection.

Table 17 Estimated burden

Country and indications	Year 1	Year 2	Year 3	Year 4	Year 5
Austria	**739,090**	**790,873**	**847,228**	**908,597**	**975,468**
Athlete's Foot	12,511	12,566	12,622	12,678	12,735
Dermatomycosis	84,692	85,068	85,447	85,826	86,208
Herpes Labialis	357,944	378,028	399,238	421,639	445,296
Vaginal Thrush	283,943	315,211	349,921	388,453	431,229
Belgium	**1,045,458**	**1,040,653**	**1,035,892**	**1,031,176**	**1,026,504**
Athlete's Foot	36,804	36,368	35,938	35,512	35,092
Dermatomycosis	249,146	246,196	243,282	240,402	237,556
Herpes Labialis	341,969	340,740	339,515	338,294	337,078
Vaginal Thrush	417,539	417,349	417,158	416,968	416,778
Bulgaria	**270,147**	**270,444**	**270,794**	**271,197**	**271,651**
Athlete's Foot	3,248	3,278	3,308	3,339	3,370
Dermatomycosis	21,986	22,190	22,397	22,605	22,815
Herpes Labialis	187,551	189,101	190,664	192,239	193,828
Vaginal Thrush	57,363	55,875	54,425	53,013	51,638
Croatia	**410,322**	**411,289**	**412,335**	**413,461**	**414,666**
Athlete's Foot	7,448	7,414	7,380	7,345	7,312
Dermatomycosis	50,420	50,187	49,956	49,725	49,496
Herpes Labialis	122,850	120,848	118,879	116,942	115,037
Vaginal Thrush	229,604	232,840	236,121	239,448	242,822
Cyprus	**122,157**	**112,856**	**116,634**	**120,538**	**124,614**
Athlete's Foot	2,089	1,882	1,909	1,935	1,961
Dermatomycosis	14,144	12,743	12,925	13,101	13,273

Herpes Labialis	60,321	55,029	55,725	56,390	57,063
Vaginal Thrush	45,602	43,202	46,075	49,111	52,318
Czech Republic	**1,234,394**	**1,232,129**	**1,229,966**	**1,227,904**	**1,225,942**
Athlete's Foot	25,756	25,234	24,722	24,221	23,729
Dermatomycosis	174,358	170,821	167,356	163,961	160,635
Herpes Labialis	473,987	472,690	471,396	470,105	468,818
Vaginal Thrush	560,293	563,384	566,492	569,617	572,759
Denmark	**516,771**	**531,480**	**552,464**	**574,636**	**598,261**
Athlete's Foot	7,606	7,752	8,080	8,422	8,778
Dermatomycosis	51,488	52,480	54,697	57,011	59,425
Herpes Labialis	254,903	258,281	260,975	263,565	266,234
Vaginal Thrush	202,774	212,967	228,712	245,638	263,824
Estonia	**114,672**	**110,719**	**106,920**	**103,269**	**99,758**
Athlete's Foot	521	492	464	438	414
Dermatomycosis	3,525	3,328	3,142	2,966	2,801
Herpes Labialis	85,915	82,479	79,181	76,014	72,974
Vaginal Thrush	24,711	24,421	24,134	23,850	23,570
Finland	**386,773**	**383,539**	**380,453**	**377,514**	**374,725**
Athlete's Foot	4,884	5,089	5,302	5,524	5,755
Dermatomycosis	33,064	34,448	35,891	37,393	38,959
Herpes Labialis	196,837	193,039	189,314	185,661	182,079
Vaginal Thrush	151,988	150,963	149,946	148,935	147,932
France	**10,587,556**	**10,563,255**	**10,544,618**	**10,531,656**	**10,524,383**
Athlete's Foot	214,455	219,473	224,609	229,865	235,244
Dermatomycosis	1,451,757	1,485,729	1,520,496	1,556,077	1,592,490
Herpes Labialis	2,646,341	2,717,060	2,789,668	2,864,217	2,940,758
Vaginal Thrush	6,275,003	6,140,993	6,009,845	5,881,497	5,755,890
Germany	**11,758,258**	**11,806,005**	**11,854,297**	**11,903,141**	**11,952,543**
Athlete's Foot	155,150	156,084	157,024	157,969	158,921
Dermatomycosis	1,050,292	1,056,615	1,062,977	1,069,377	1,075,815

Herpes Labialis	6,036,160	6,029,373	6,022,594	6,015,822	6,009,058
Vaginal Thrush	4,516,657	4,563,932	4,611,703	4,659,974	4,708,749
Greece	**590,737**	**577,031**	**563,661**	**550,620**	**537,900**
Athlete's Foot	19,385	18,999	18,622	18,251	17,889
Dermatomycosis	131,226	128,617	126,060	123,553	121,097
Herpes Labialis	422,879	412,061	401,519	391,247	381,238
Vaginal Thrush	17,247	17,353	17,461	17,568	17,677
Hungary	**1,017,199**	**987,442**	**958,563**	**930,536**	**903,335**
Athlete's Foot	25,213	24,391	23,597	22,828	22,084
Dermatomycosis	170,679	165,118	159,738	154,533	149,498
Herpes Labialis	494,091	480,996	468,248	455,838	443,757
Vaginal Thrush	327,216	316,937	306,980	297,337	287,997
Ireland	**780,449**	**816,720**	**855,107**	**895,748**	**938,792**
Athlete's Foot	12,062	12,779	13,538	14,343	15,195
Dermatomycosis	81,652	86,504	91,645	97,092	102,862
Herpes Labialis	387,251	396,225	405,407	414,802	424,414
Vaginal Thrush	299,484	321,212	344,517	369,512	396,320
Italy	**6,219,665**	**6,223,810**	**6,228,381**	**6,233,383**	**6,238,819**
Athlete's Foot	101,462	100,719	99,982	99,250	98,523
Dermatomycosis	686,848	681,820	676,829	671,874	666,956
Herpes Labialis	2,007,716	2,032,919	2,058,439	2,084,279	2,110,443
Vaginal Thrush	3,423,639	3,408,351	3,393,132	3,377,980	3,362,896
Latvia	**170,612**	**173,555**	**176,641**	**179,875**	**183,266**
Athlete's Foot	2,736	2,729	2,721	2,714	2,707
Dermatomycosis	18,520	18,471	18,422	18,373	18,324
Herpes Labialis	89,644	89,735	89,825	89,916	90,007
Vaginal Thrush	59,711	62,621	65,672	68,872	72,228
Lithuania	**302,508**	**313,417**	**324,853**	**336,867**	**349,527**
Athlete's Foot	114	152	204	273	365
Dermatomycosis	769	1,030	1,378	1,845	2,469

Herpes Labialis	192,184	197,050	202,039	207,154	212,399
Vaginal Thrush	109,441	115,186	121,232	127,596	134,294
Luxembourg	**81,949**	**82,878**	**87,279**	**91,933**	**96,890**
Athlete's Foot	1,625	1,640	1,743	1,853	1,969
Dermatomycosis	11,002	11,102	11,802	12,544	13,329
Herpes Labialis	28,967	28,912	29,365	29,798	30,234
Vaginal Thrush	40,354	41,225	44,368	47,738	51,357
Malta	**72,169**	**84,582**	**84,101**	**83,623**	**83,168**
Athlete's Foot	1,430	1,718	1,759	1,801	1,844
Dermatomycosis	9,684	11,630	11,908	12,192	12,481
Herpes Labialis	19,199	23,165	23,364	23,548	23,732
Vaginal Thrush	41,856	48,069	47,069	46,082	45,111
Netherlands	**1,076,751**	**1,102,650**	**1,133,761**	**1,170,175**	**1,212,012**
Athlete's Foot	22,268	23,169	24,106	25,082	26,096
Dermatomycosis	150,745	156,843	163,189	169,791	176,660
Herpes Labialis	310,058	286,156	264,097	243,738	224,949
Vaginal Thrush	593,680	636,481	682,368	731,564	784,306
Poland	**4,770,497**	**5,331,031**	**6,141,481**	**7,308,671**	**8,985,124**
Athlete's Foot	116,141	114,560	113,001	111,462	109,945
Dermatomycosis	786,219	775,516	764,959	754,546	744,274
Herpes Labialis	2,503,831	2,492,980	2,482,175	2,471,417	2,460,706
Vaginal Thrush	1,364,306	1,947,975	2,781,346	3,971,245	5,670,199
Portugal	**1,664,592**	**1,738,629**	**1,816,622**	**1,898,806**	**1,985,431**
Athlete's Foot	25,348	25,745	26,148	26,557	26,973
Dermatomycosis	171,596	174,281	177,009	179,779	182,593
Herpes Labialis	706,411	727,340	748,889	771,076	793,921
Vaginal Thrush	761,237	811,263	864,577	921,394	981,945
Romania	**730,807**	**736,906**	**744,334**	**753,079**	**763,131**
Athlete's Foot	25,947	25,709	25,474	25,241	25,010
Dermatomycosis	175,646	174,039	172,447	170,869	169,305

Herpes Labialis	127,440	118,607	110,386	102,735	95,614
Vaginal Thrush	401,774	418,550	436,028	454,234	473,201
Slovakia	**597,665**	**637,453**	**683,761**	**737,655**	**800,379**
Athlete's Foot	18,332	18,173	18,016	17,860	17,705
Dermatomycosis	124,100	123,025	121,960	120,903	119,856
Herpes Labialis	214,487	215,957	217,436	218,926	220,426
Vaginal Thrush	240,745	280,298	326,349	379,966	442,391
Slovenia	**255,809**	**262,336**	**267,310**	**272,453**	**277,839**
Athlete's Foot	6,391	6,308	6,227	6,146	6,066
Dermatomycosis	43,264	42,704	42,151	41,605	41,066
Herpes Labialis	89,258	91,534	92,046	92,505	92,976
Vaginal Thrush	116,897	121,789	126,887	132,198	137,731
Spain	**2,670,837**	**2,761,600**	**2,855,878**	**2,953,816**	**3,055,566**
Athlete's Foot	8,645	8,582	8,519	8,457	8,395
Dermatomycosis	58,524	58,097	57,672	57,251	56,833
Herpes Labialis	1,430,859	1,466,816	1,503,677	1,541,464	1,580,200
Vaginal Thrush	1,172,809	1,228,106	1,286,010	1,346,644	1,410,137
Sweden	**921,603**	**946,318**	**984,580**	**1,024,870**	**1,067,737**
Athlete's Foot	13,564	13,803	14,400	15,020	15,667
Dermatomycosis	91,822	93,442	97,478	101,680	106,057
Herpes Labialis	454,591	459,878	465,100	470,071	475,157
Vaginal Thrush	361,626	379,195	407,602	438,099	470,855
UK	**2,815,579**	**2,819,443**	**2,824,603**	**2,831,038**	**2,838,732**
Athlete's Foot	69,733	70,441	71,157	71,880	72,611
Dermatomycosis	472,057	476,854	481,699	486,595	491,539
Herpes Labialis	821,915	795,834	770,581	746,129	722,454
Vaginal Thrush	1,451,875	1,476,314	1,501,165	1,526,434	1,552,128

A.3. Excess appointments

The following chart and table detail the number of excess appointments per indication in each country for a single year for the total population. Overall, we estimate that ~59 million additional visits to doctor's practice will occur in a single year as people seek treatment. There will be a shift of self-care patients into the healthcare system as they seek treatment from doctors, either immediately (Scenario 1) or eventually as their symptoms worsen (Scenarios 2 & 3).

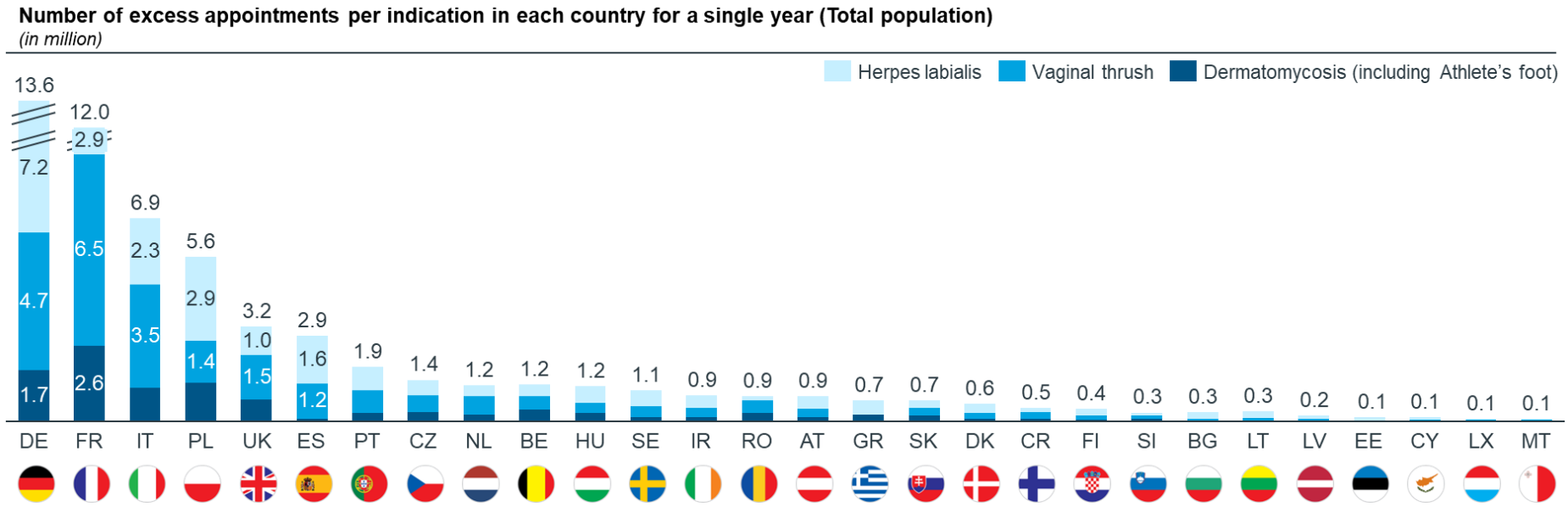


Figure 7 Excess appointments per indication in each country for a single year (Total Population)

Table 18 Number of excess appointments per indication in each country for a single year (Total Population)

Country and Indications	Excess appointments for Seeking Rx decision pathways	Excess appointments for Seeking Alternative decision pathways	Excess appointments for Do nothing decision pathways	Total excess appointments
Austria	**629,438**	**189,822**	**39,172**	**858,431**
Athlete's Foot	10,503	4,604	663	15,770
Dermatomycosis	88,266	31,167	4,489	123,921
Herpes Labialis	310,939	94,139	18,971	424,049
Vaginal Thrush	219,730	59,912	15,049	294,691
Belgium	**910,733**	**283,268**	**55,409**	**1,249,410**
Athlete's Foot	30,899	13,544	1,951	46,393
Dermatomycosis	259,660	91,686	13,205	364,550
Herpes Labialis	297,062	89,938	18,124	405,124
Vaginal Thrush	323,113	88,101	22,130	433,343
Bulgaria	**232,952**	**70,715**	**14,318**	**317,985**
Athlete's Foot	2,727	1,195	172	4,094
Dermatomycosis	22,914	8,091	1,165	32,170
Herpes Labialis	162,922	49,326	9,940	222,188
Vaginal Thrush	44,390	12,104	3,040	59,534
Croatia	**324,930**	**113,640**	**24,379**	**462,950**
Athlete's Foot	6,599	2,897	-	9,496
Dermatomycosis	55,452	19,613	-	75,065
Herpes Labialis	82,066	45,209	12,899	140,174
Vaginal Thrush	180,813	45,921	11,480	238,215
Cyprus	**76,316**	**61,571**	**-**	**137,887**
Athlete's Foot	1,781	861	-	2,642
Dermatomycosis	14,970	5,827	-	20,798
Herpes Labialis	34,473	33,176	-	67,650
Vaginal Thrush	25,090	21,707	-	46,797
Czech Republic	**949,943**	**393,478**	**70,455**	**1,413,875**

Athlete's Foot	26,964	5,718	1,442	34,125
Dermatomycosis	226,596	38,707	9,764	275,067
Herpes Labialis	225,736	236,994	59,248	521,978
Vaginal Thrush	470,646	112,059	-	582,705
Denmark	**413,411**	**140,240**	**38,521**	**592,172**
Athlete's Foot	5,514	3,423	380	9,317
Dermatomycosis	46,339	23,169	2,574	72,083
Herpes Labialis	215,926	70,863	14,275	301,063
Vaginal Thrush	145,633	42,785	21,291	209,709
Estonia	**81,191**	**38,133**	**10,257**	**129,580**
Athlete's Foot	461	203	-	664
Dermatomycosis	3,876	1,371	-	5,247
Herpes Labialis	57,393	31,617	9,021	98,031
Vaginal Thrush	19,460	4,942	1,236	25,638
Finland	**309,195**	**103,867**	**28,879**	**441,940**
Athlete's Foot	3,541	2,198	244	5,983
Dermatomycosis	29,757	14,879	1,653	46,289
Herpes Labialis	166,739	54,721	11,023	232,482
Vaginal Thrush	109,158	32,069	15,959	157,186
France	**8,642,539**	**2,948,070**	**424,100**	**12,014,709**
Athlete's Foot	224,513	47,609	12,009	284,131
Dermatomycosis	1,886,703	322,290	81,298	2,290,291
Herpes Labialis	1,260,320	1,323,171	330,793	2,914,283
Vaginal Thrush	5,271,003	1,255,001	-	6,526,004
Germany	**9,963,577**	**2,984,127**	**623,188**	**13,570,892**
Athlete's Foot	130,256	57,095	8,223	195,575
Dermatomycosis	1,094,614	386,507	55,665	1,536,787
Herpes Labialis	5,243,492	1,587,510	319,916	7,150,918
Vaginal Thrush	3,495,215	953,015	239,383	4,687,612
Greece	**406,582**	**302,845**	**-**	**709,427**
Athlete's Foot	16,528	7,987	-	24,514
Dermatomycosis	138,890	54,065	-	192,955

Herpes Labialis	241,675	232,583	-	474,259
Vaginal Thrush	9,489	8,210	-	17,699
Hungary	**797,795**	**323,471**	**68,240**	**1,189,506**
Athlete's Foot	22,337	9,808	-	32,145
Dermatomycosis	187,713	66,394	-	254,107
Herpes Labialis	330,063	181,825	51,880	563,768
Vaginal Thrush	257,682	65,443	16,361	339,486
Ireland	**554,737**	**274,327**	**53,654**	**882,718**
Athlete's Foot	12,627	2,678	675	15,980
Dermatomycosis	106,114	18,127	4,572	128,814
Herpes Labialis	184,428	193,626	48,406	426,460
Vaginal Thrush	251,567	59,897	-	311,464
Italy	**3,844,562**	**3,058,680**	**-**	**6,903,242**
Athlete's Foot	86,506	41,802	-	128,309
Dermatomycosis	726,960	282,981	-	1,009,941
Herpes Labialis	1,147,410	1,104,244	-	2,251,653
Vaginal Thrush	1,883,686	1,629,652	-	3,513,338
Latvia	**129,699**	**53,200**	**12,398**	**195,297**
Athlete's Foot	2,424	1,064	-	3,488
Dermatomycosis	20,369	7,204	-	27,573
Herpes Labialis	59,884	32,989	9,413	102,286
Vaginal Thrush	47,023	11,942	2,986	61,950
Lithuania	**215,514**	**92,955**	**25,651**	**334,121**
Athlete's Foot	101	44	-	145
Dermatomycosis	846	299	-	1,145
Herpes Labialis	128,383	70,724	20,179	219,286
Vaginal Thrush	86,185	21,888	5,472	113,545
Luxembourg	**63,693**	**25,358**	**4,328**	**93,379**
Athlete's Foot	1,701	361	91	2,153
Dermatomycosis	14,299	2,443	616	17,357
Herpes Labialis	13,796	14,484	3,621	31,900
Vaginal Thrush	33,898	8,071	-	41,969

Malta	**45,470**	**35,062**	**-**	**80,532**
Athlete's Foot	1,220	589	-	1,809
Dermatomycosis	10,249	3,990	-	14,239
Herpes Labialis	10,972	10,560	-	21,532
Vaginal Thrush	23,029	19,923	-	42,952
Netherlands	**840,842**	**289,318**	**88,350**	**1,218,511**
Athlete's Foot	16,144	10,021	1,113	27,278
Dermatomycosis	135,670	67,835	7,537	211,042
Herpes Labialis	262,647	86,196	17,363	366,206
Vaginal Thrush	426,381	125,266	62,336	613,984
Poland	**3,714,580**	**1,545,289**	**331,118**	**5,590,986**
Athlete's Foot	102,895	45,179	-	148,074
Dermatomycosis	864,684	305,839	-	1,170,523
Herpes Labialis	1,672,609	921,410	262,902	2,856,921
Vaginal Thrush	1,074,391	272,861	68,215	1,415,468
Portugal	**1,025,775**	**832,016**	**-**	**1,857,791**
Athlete's Foot	21,612	10,444	-	32,055
Dermatomycosis	181,617	70,697	-	252,314
Herpes Labialis	403,714	388,526	-	792,240
Vaginal Thrush	418,832	362,349	-	781,181
Romania	**617,693**	**205,672**	**33,470**	**856,835**
Athlete's Foot	22,987	10,093	-	33,081
Dermatomycosis	193,176	68,326	-	261,502
Herpes Labialis	85,132	46,898	13,381	145,412
Vaginal Thrush	316,397	80,355	20,089	416,840
Slovakia	**485,595**	**182,486**	**34,558**	**702,640**
Athlete's Foot	16,241	7,131	-	23,373
Dermatomycosis	136,485	48,275	-	184,760
Herpes Labialis	143,282	78,931	22,521	244,734
Vaginal Thrush	189,587	48,149	12,037	249,773
Slovenia	**203,619**	**79,032**	**13,938**	**296,589**
Athlete's Foot	6,691	1,419	358	8,467

Dermatomycosis	56,226	9,605	2,423	68,254
Herpes Labialis	42,509	44,629	11,157	98,295
Vaginal Thrush	98,193	23,379	-	121,572
Spain	**1,532,328**	**1,372,903**	**-**	**2,905,231**
Athlete's Foot	7,371	3,562	-	10,933
Dermatomycosis	61,942	24,112	-	86,054
Herpes Labialis	817,736	786,972	-	1,604,708
Vaginal Thrush	645,279	558,257	-	1,203,536
Sweden	**737,273**	**250,103**	**68,697**	**1,056,074**
Athlete's Foot	9,834	6,104	678	16,616
Dermatomycosis	82,640	41,320	4,591	128,551
Herpes Labialis	385,079	126,376	25,457	536,913
Vaginal Thrush	259,720	76,303	37,971	373,994
UK	**2,214,380**	**778,643**	**225,564**	**3,218,586**
Athlete's Foot	50,556	31,380	3,487	85,423
Dermatomycosis	424,851	212,425	23,603	660,879
Herpes Labialis	696,236	228,492	46,027	970,756
Vaginal Thrush	1,042,736	306,346	152,447	1,501,529
Grand Total	**39,964,361**	**17,028,292**	**2,288,644**	**59,281,297**

A.4. Emergency visits

In accordance with the approach and assumption elaborated in the methodology section, the following chart and table detail the number of emergency visits across the 28 in-scope countries for a single year. The additional healthcare visits include ~11 million visits to the emergency department with Germany and France having the highest estimates for the additional emergency visits across all countries.

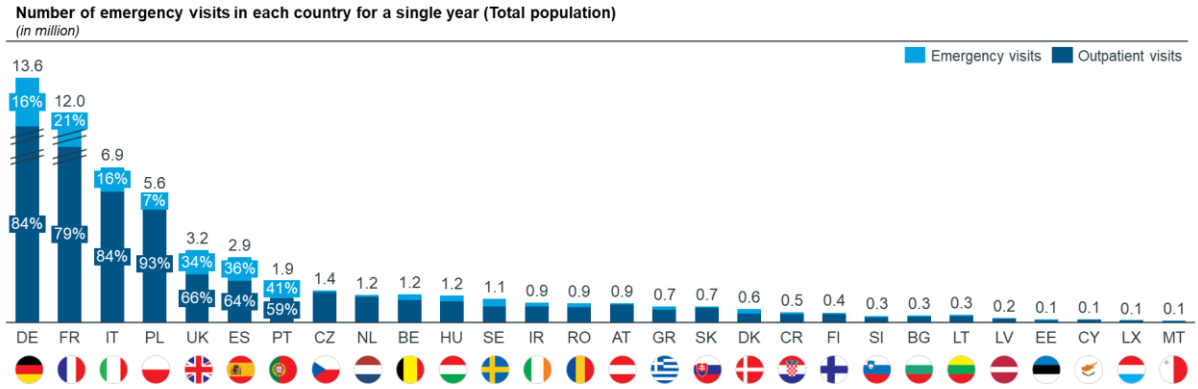


Figure 8 Number of emergency visits in each country for a single year in millions (Total Population)

Table 19 Detailed number of emergency visits in each country for a single year in millions (Total Population)

Country	Emergency visits	Outpatient visits	Total excess appointments
Austria	55,570	802,862	858,431
Belgium	241,459	1,007,951	1,249,410
Bulgaria	68,557	249,429	317,985
Croatia	95,889	367,061	462,950
Cyprus	22,395	115,492	137,887
Czech Republic	68,962	1,344,913	1,413,875
Denmark	199,083	393,090	592,172
Estonia	30,908	98,672	129,580
Finland	72,515	369,426	441,940
France	2,527,414	9,487,295	12,014,709
Germany	2,162,424	11,408,468	13,570,892
Greece	137,425	572,001	709,427
Hungary	245,389	944,117	1,189,506
Ireland	165,829	716,889	882,718
Italy	1,095,000	5,808,242	6,903,242
Latvia	29,035	166,263	195,297
Lithuania	57,763	276,358	334,121
Luxembourg	19,055	74,324	93,379
Malta	12,930	67,602	80,532
Netherlands	91,519	1,126,992	1,218,511
Poland	388,476	5,202,510	5,590,986
Portugal	762,333	1,095,458	1,857,791
Romania	185,719	671,115	856,835

Slovakia	50,204	652,436	702,640
Slovenia	61,252	235,336	296,589
Spain	1,060,027	1,845,204	2,905,231
Sweden	355,042	701,032	1,056,074
UK	1,084,375	2,134,211	3,218,586
Grand Total	**11,346,547**	**47,934,750**	**59,281,297**

A.5. Unresolved cases

Unresolved cases represent the number of cases that are expected to exacerbate due to patients delaying appropriate care as they seek an alternative treatment which is available for self-purchase (Non-prescription medicines), or they do nothing at all in the hope that their symptom will self-resolve. Overall, the total number of unresolved cases is 19,209,160. The following chart and tables detail the unresolved cases for each country across the indications.

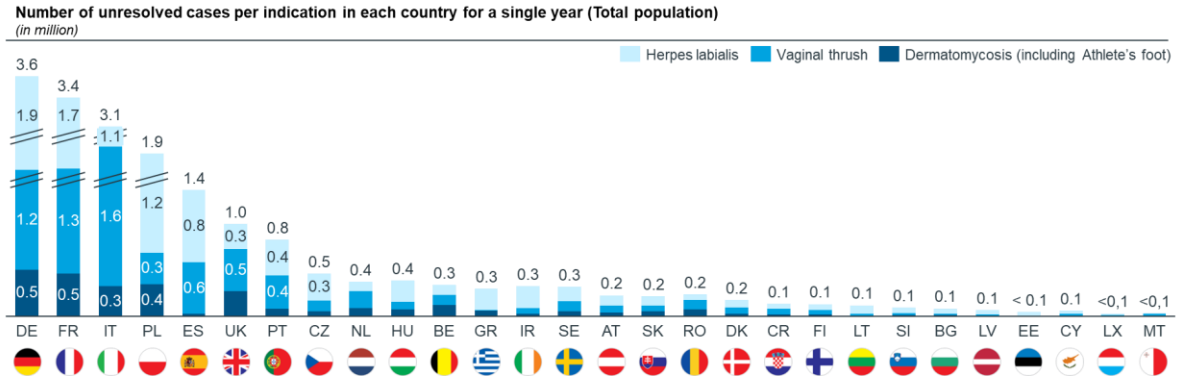


Figure 9 Number of unresolved cases per indication in each country for a single year in millions (Total population)

Table 20 Detailed number of unresolved cases per indication in each country for a single year (Total population)

Country and indications	Seek alternative treatment cases	Do nothing cases	Total unresolved cases
Austria	**189,822**	**39,172**	**228,994**
Athlete's Foot	4,604	663	5,267
Dermatomycosis	31,167	4,489	35,655
Herpes Labialis	94,139	18,971	113,110
Vaginal Thrush	59,912	15,049	74,961
Belgium	**283,268**	**55,409**	**338,677**
Athlete's Foot	13,544	1,951	15,495
Dermatomycosis	91,686	13,205	104,890
Herpes Labialis	89,938	18,124	108,062
Vaginal Thrush	88,101	22,130	110,230
Bulgaria	**70,715**	**14,318**	**85,033**

Athlete's Foot	1,195	172	1,367
Dermatomycosis	8,091	1,165	9,256
Herpes Labialis	49,326	9,940	59,266
Vaginal Thrush	12,104	3,040	15,144
Croatia	**113,640**	**24,379**	**138,020**
Athlete's Foot	2,897	-	2,897
Dermatomycosis	19,613	-	19,613
Herpes Labialis	45,209	12,899	58,108
Vaginal Thrush	45,921	11,480	57,401
Cyprus	**61,571**	**-**	**61,571**
Athlete's Foot	861	-	861
Dermatomycosis	5,827	-	5,827
Herpes Labialis	33,176	-	33,176
Vaginal Thrush	21,707	-	21,707
Czech Republic	**393,478**	**70,455**	**463,932**
Athlete's Foot	5,718	1,442	7,160
Dermatomycosis	38,707	9,764	48,472
Herpes Labialis	236,994	59,248	296,242
Vaginal Thrush	112,059	-	112,059
Denmark	**140,240**	**38,521**	**178,761**
Athlete's Foot	3,423	380	3,803
Dermatomycosis	23,169	2,574	25,744
Herpes Labialis	70,863	14,275	85,138
Vaginal Thrush	42,785	21,291	64,077
Estonia	**38,133**	**10,257**	**48,389**
Athlete's Foot	203	-	203
Dermatomycosis	1,371	-	1,371
Herpes Labialis	31,617	9,021	40,638
Vaginal Thrush	4,942	1,236	6,178
Finland	**103,867**	**28,879**	**132,746**
Athlete's Foot	2,198	244	2,442
Dermatomycosis	14,879	1,653	16,532
Herpes Labialis	54,721	11,023	65,744
Vaginal Thrush	32,069	15,959	48,028
France	**2,948,070**	**424,100**	**3,372,171**
Athlete's Foot	47,609	12,009	59,619
Dermatomycosis	322,290	81,298	403,588
Herpes Labialis	1,323,171	330,793	1,653,963
Vaginal Thrush	1,255,001	-	1,255,001
Germany	**2,984,127**	**623,188**	**3,607,315**
Athlete's Foot	57,095	8,223	65,318
Dermatomycosis	386,507	55,665	442,173
Herpes Labialis	1,587,510	319,916	1,907,427
Vaginal Thrush	953,015	239,383	1,192,397
Greece	**302,845**	**-**	**302,845**
Athlete's Foot	7,987	-	7,987

Dermatomycosis	54,065	-	54,065
Herpes Labialis	232,583	-	232,583
Vaginal Thrush	8,210	-	8,210
Hungary	**323,471**	**68,240**	**391,711**
Athlete's Foot	9,808	-	9,808
Dermatomycosis	66,394	-	66,394
Herpes Labialis	181,825	51,880	233,705
Vaginal Thrush	65,443	16,361	81,804
Ireland	**274,327**	**53,654**	**327,981**
Athlete's Foot	2,678	675	3,353
Dermatomycosis	18,127	4,572	22,699
Herpes Labialis	193,626	48,406	242,032
Vaginal Thrush	59,897	-	59,897
Italy	**3,058,680**	**-**	**3,058,680**
Athlete's Foot	41,802	-	41,802
Dermatomycosis	282,981	-	282,981
Herpes Labialis	1,104,244	-	1,104,244
Vaginal Thrush	1,629,652	-	1,629,652
Latvia	**53,200**	**12,398**	**65,598**
Athlete's Foot	1,064	-	1,064
Dermatomycosis	7,204	-	7,204
Herpes Labialis	32,989	9,413	42,402
Vaginal Thrush	11,942	2,986	14,928
Lithuania	**92,955**	**25,651**	**118,607**
Athlete's Foot	44	-	44
Dermatomycosis	299	-	299
Herpes Labialis	70,724	20,179	90,903
Vaginal Thrush	21,888	5,472	27,360
Luxembourg	**25,358**	**4,328**	**29,686**
Athlete's Foot	361	91	452
Dermatomycosis	2,443	616	3,059
Herpes Labialis	14,484	3,621	18,104
Vaginal Thrush	8,071	-	8,071
Malta	**35,062**	**-**	**35,062**
Athlete's Foot	589	-	589
Dermatomycosis	3,990	-	3,990
Herpes Labialis	10,560	-	10,560
Vaginal Thrush	19,923	-	19,923
Netherlands	**289,318**	**88,350**	**377,669**
Athlete's Foot	10,021	1,113	11,134
Dermatomycosis	67,835	7,537	75,372
Herpes Labialis	86,196	17,363	103,559
Vaginal Thrush	125,266	62,336	187,603
Poland	**1,545,289**	**331,118**	**1,876,407**
Athlete's Foot	45,179	-	45,179
Dermatomycosis	305,839	-	305,839

Herpes Labialis	921,410	262,902	1,184,312
Vaginal Thrush	272,861	68,215	341,077
Portugal	**832,016**	**-**	**832,016**
Athlete's Foot	10,444	-	10,444
Dermatomycosis	70,697	-	70,697
Herpes Labialis	388,526	-	388,526
Vaginal Thrush	362,349	-	362,349
Romania	**205,672**	**33,470**	**239,142**
Athlete's Foot	10,093	-	10,093
Dermatomycosis	68,326	-	68,326
Herpes Labialis	46,898	13,381	60,279
Vaginal Thrush	80,355	20,089	100,443
Slovakia	**182,486**	**34,558**	**217,045**
Athlete's Foot	7,131	-	7,131
Dermatomycosis	48,275	-	48,275
Herpes Labialis	78,931	22,521	101,452
Vaginal Thrush	48,149	12,037	60,186
Slovenia	**79,032**	**13,938**	**92,970**
Athlete's Foot	1,419	358	1,777
Dermatomycosis	9,605	2,423	12,027
Herpes Labialis	44,629	11,157	55,786
Vaginal Thrush	23,379	-	23,379
Spain	**1,372,903**	**-**	**1,372,903**
Athlete's Foot	3,562	-	3,562
Dermatomycosis	24,112	-	24,112
Herpes Labialis	786,972	-	786,972
Vaginal Thrush	558,257	-	558,257
Sweden	**250,103**	**68,697**	**318,800**
Athlete's Foot	6,104	678	6,782
Dermatomycosis	41,320	4,591	45,911
Herpes Labialis	126,376	25,457	151,833
Vaginal Thrush	76,303	37,971	114,274
UK	**778,643**	**225,564**	**1,004,207**
Athlete's Foot	31,380	3,487	34,866
Dermatomycosis	212,425	23,603	236,028
Herpes Labialis	228,492	46,027	274,520
Vaginal Thrush	306,346	152,447	458,792
Grand Total	**17,028,292**	**2,288,644**	**19,316,936**

A.6. Total costs

Cumulatively, the total costs of reverse-switching for five years amount to €50.1 billion, increasing by 1.98% year-on-year. Approximately 81% of these costs, equivalent to €40.7 billion, are healthcare-related expenditures. Of these healthcare costs, 81% are borne by public payers, followed by 14% by individuals, and 5% by private health insurance. The remaining 19% of the total costs, equivalent to €9.4 billion, are attributed to productivity losses due to disability and individuals seeking care at doctors' practices. The largest costs are attributed to vaginal thrush (€20,4 billion), followed by herpes labialis (€19 billion), and dermatomycosis (€10.7 billion).

A.6.1. Projected total costs

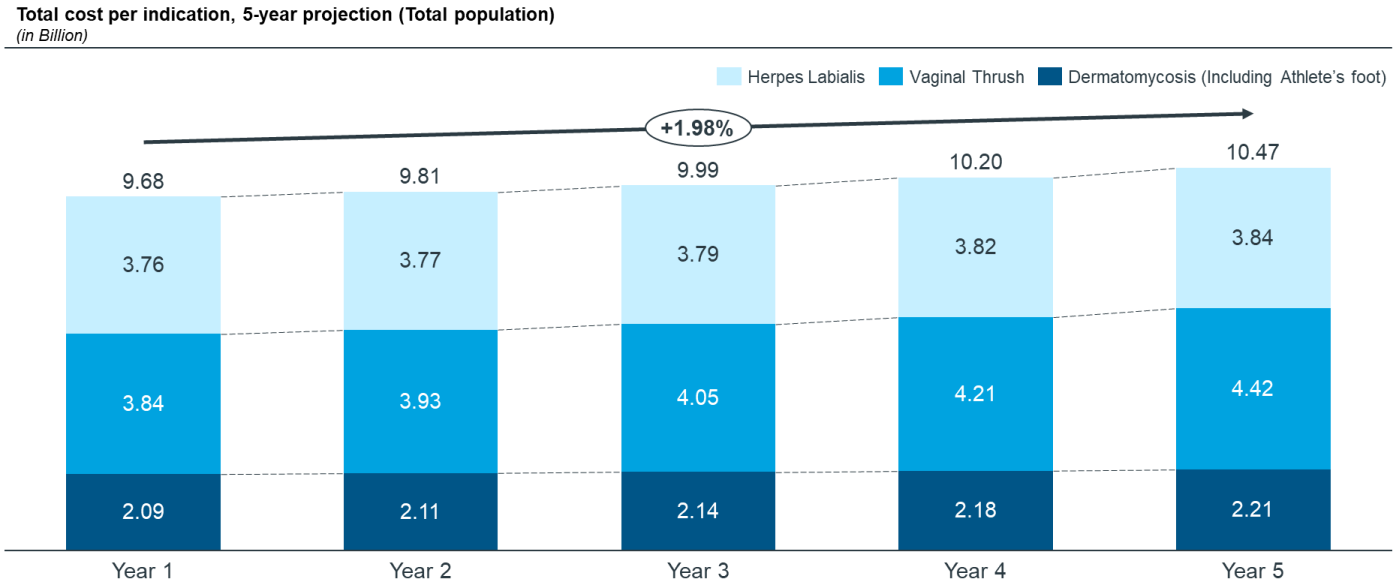


Figure 10 5-year projection of the total cost per indication (Total Population)

Table 21 Total cost by indication for 5 years (Total Population)

Indications	Year 1	Year 2	Year 3	Year 4	Year 5
Athlete's Foot	206,044,729	208,390,100	211,285,251	214,301,999	217,446,280
Dermatomycosis	1,884,441,310	1,906,091,286	1,932,887,715	1,960,821,441	1,989,949,294
Herpes Labialis	3,756,680,912	3,770,424,183	3,791,751,075	3,815,492,004	3,841,874,504
Vaginal Thrush	3,835,087,879	3,925,286,684	4,049,525,090	4,210,227,337	4,421,249,398

A.6.2. Total costs by country and indications for a single year

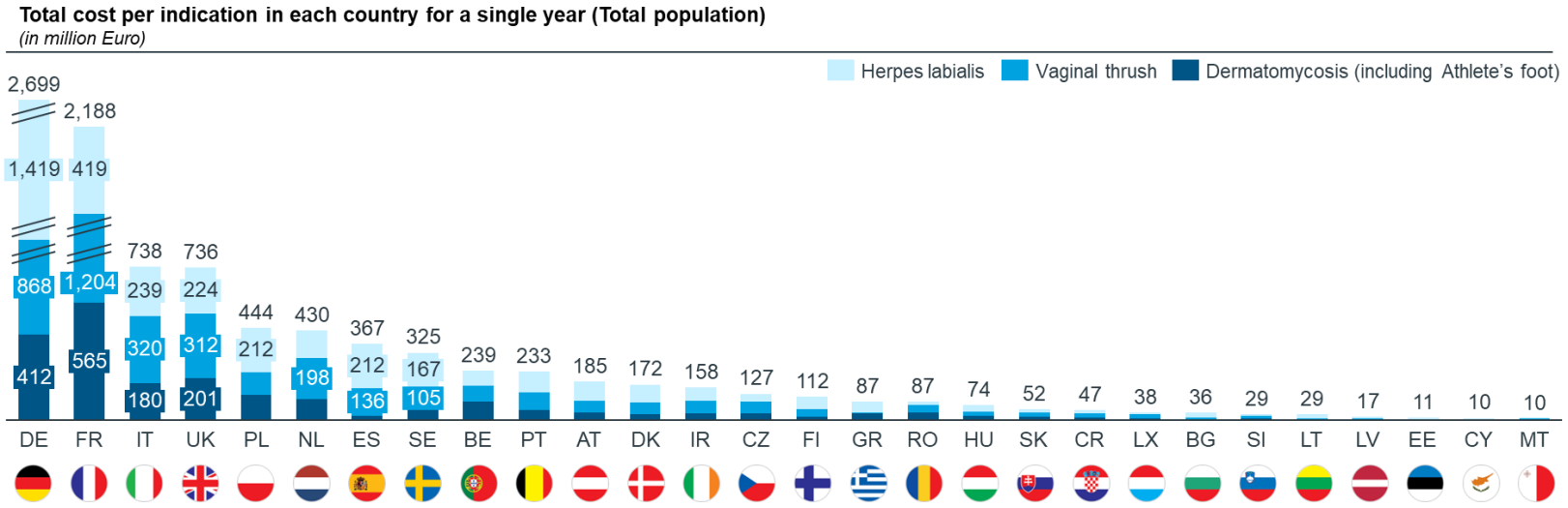


Figure 11 Total cost per indication in each country for a single year (Total Population)

Table 22 Total costs by country and indication for a single year (Total Population)

Country and indications	Total Rx cost	Total Outpatient cost	Productivity cost	Total overall cost
Austria	**5,913,670**	**143,303,624**	**35,930,247**	**185,147,541**
Athlete's Foot	124,762	2,655,881	678,525	3,459,168
Dermatomycosis	1,321,938	24,094,342	6,468,181	31,884,461
Herpes Labialis	2,756,097	70,448,795	17,918,574	91,123,466
Vaginal Thrush	1,710,874	46,104,605	10,864,966	58,680,445
Belgium	**10,519,932**	**175,378,985**	**52,983,538**	**238,882,455**
Athlete's Foot	423,583	6,409,154	1,954,167	8,786,904
Dermatomycosis	4,488,140	58,144,301	18,628,513	81,260,954
Herpes Labialis	2,908,197	55,210,891	16,759,403	74,878,491
Vaginal Thrush	2,700,012	55,614,639	15,641,454	73,956,105
Bulgaria	**1,687,870**	**25,128,814**	**9,318,273**	**36,134,957**
Athlete's Foot	25,097	325,842	122,134	473,073
Dermatomycosis	265,919	2,956,059	1,164,273	4,386,252
Herpes Labialis	1,230,585	17,445,057	6,509,936	25,185,579
Vaginal Thrush	166,269	4,401,856	1,521,929	6,090,053
Croatia	**2,153,598**	**31,834,312**	**13,105,889**	**47,093,799**
Athlete's Foot	48,934	697,861	284,134	1,030,930
Dermatomycosis	515,212	6,282,581	2,679,962	9,477,755
Herpes Labialis	467,480	8,632,782	3,985,508	13,085,771
Vaginal Thrush	1,121,971	16,221,088	6,156,285	23,499,345
Cyprus	**806,935**	**6,827,194**	**2,371,550**	**10,005,679**
Athlete's Foot	24,359	161,987	50,374	236,721
Dermatomycosis	257,638	1,466,327	478,763	2,202,728
Herpes Labialis	300,095	3,243,828	1,208,936	4,752,858
Vaginal Thrush	224,843	1,955,052	633,477	2,813,372
Czech Republic	**11,958,242**	**90,165,716**	**25,159,008**	**127,282,966**
Athlete's Foot	270,763	2,525,946	641,468	3,438,178

Dermatomycosis	2,790,075	22,205,914	5,839,901	30,835,890
Herpes Labialis	5,626,026	25,582,217	8,941,624	40,149,867
Vaginal Thrush	3,271,377	39,851,639	9,736,015	52,859,031
Denmark	**4,059,252**	**136,313,983**	**31,264,947**	**171,638,182**
Athlete's Foot	50,042	2,132,322	510,047	2,692,412
Dermatomycosis	538,754	19,752,867	4,995,499	25,287,119
Herpes Labialis	1,638,915	70,505,613	16,259,237	88,403,765
Vaginal Thrush	1,831,541	43,923,180	9,500,164	55,254,886
Estonia	**814,601**	**7,915,314**	**2,398,830**	**11,128,745**
Athlete's Foot	6,149	46,686	13,029	65,864
Dermatomycosis	64,745	420,297	122,889	607,931
Herpes Labialis	570,639	5,777,624	1,828,299	8,176,562
Vaginal Thrush	173,067	1,670,707	434,614	2,278,388
Finland	**4,167,442**	**93,451,210**	**14,270,305**	**111,888,956**
Athlete's Foot	66,214	1,261,704	201,365	1,529,283
Dermatomycosis	712,858	11,687,858	1,972,208	14,372,924
Herpes Labialis	2,071,499	50,166,451	7,718,960	59,956,911
Vaginal Thrush	1,316,870	30,335,196	4,377,772	36,029,838
France	**48,968,321**	**1,752,341,436**	**386,991,435**	**2,188,301,192**
Athlete's Foot	1,117,899	46,354,061	9,707,295	57,179,255
Dermatomycosis	11,519,369	407,504,468	88,374,793	507,398,629
Herpes Labialis	13,835,348	314,796,170	90,733,339	419,364,857
Vaginal Thrush	22,495,705	983,686,738	198,176,008	1,204,358,451
Germany	**78,697,594**	**2,059,694,300**	**560,583,105**	**2,698,974,999**
Athlete's Foot	1,788,576	30,108,898	8,369,213	40,266,687
Dermatomycosis	18,951,132	273,150,063	79,781,300	371,882,494
Herpes Labialis	32,675,340	1,086,016,058	300,537,593	1,419,228,991
Vaginal Thrush	25,282,546	670,419,281	171,895,000	867,596,827
Greece	**4,862,796**	**72,823,017**	**9,379,627**	**87,065,441**
Athlete's Foot	159,224	2,836,247	321,757	3,317,228

Dermatomycosis	1,684,058	25,674,012	3,058,014	30,416,084
Herpes Labialis	2,894,619	42,917,327	5,834,912	51,646,859
Vaginal Thrush	124,896	1,395,431	164,944	1,685,271
Hungary	**10,667,777**	**43,726,708**	**19,511,311**	**73,905,796**
Athlete's Foot	321,732	1,267,978	538,705	2,128,415
Dermatomycosis	3,387,395	11,415,129	5,081,083	19,883,607
Herpes Labialis	4,130,821	18,635,722	8,977,679	31,744,222
Vaginal Thrush	2,827,830	12,407,880	4,913,843	20,149,553
Ireland	**5,982,608**	**126,507,526**	**25,834,815**	**158,324,949**
Athlete's Foot	86,507	2,782,338	499,256	3,368,102
Dermatomycosis	891,413	24,459,892	4,545,203	29,896,508
Herpes Labialis	2,625,702	49,161,769	12,141,369	63,928,841
Vaginal Thrush	2,378,985	50,103,527	8,648,987	61,131,499
Italy	**63,526,071**	**522,799,132**	**152,168,692**	**738,493,896**
Athlete's Foot	1,852,537	12,319,339	3,279,802	17,451,679
Dermatomycosis	19,593,712	111,515,972	31,171,576	162,281,260
Herpes Labialis	15,643,084	169,091,458	53,950,970	238,685,513
Vaginal Thrush	26,436,738	229,872,363	63,766,343	320,075,444
Latvia	**1,349,031**	**11,374,224**	**4,152,928**	**16,876,183**
Athlete's Foot	11,461	222,879	77,427	311,767
Dermatomycosis	120,671	2,006,495	730,294	2,857,460
Herpes Labialis	668,886	5,477,047	2,157,488	8,303,420
Vaginal Thrush	548,013	3,667,803	1,187,719	5,403,536
Lithuania	**2,786,351**	**17,868,186**	**8,343,879**	**28,998,416**
Athlete's Foot	1,072	8,915	3,926	13,913
Dermatomycosis	11,289	80,256	37,029	128,574
Herpes Labialis	1,931,349	11,306,105	5,645,774	18,883,229
Vaginal Thrush	842,641	6,472,910	2,657,149	9,972,700
Luxembourg	**978,744**	**29,447,739**	**7,892,743**	**38,319,227**
Athlete's Foot	15,772	783,027	192,845	991,644

Dermatomycosis	162,523	6,883,687	1,755,651	8,801,861
Herpes Labialis	263,031	7,680,515	2,603,448	10,546,994
Vaginal Thrush	537,418	14,100,511	3,340,799	17,978,728
Malta	**818,137**	**6,515,495**	**2,195,944**	**9,529,575**
Athlete's Foot	27,566	183,315	57,007	267,888
Dermatomycosis	291,560	1,659,388	541,798	2,492,745
Herpes Labialis	157,887	1,706,660	636,052	2,500,599
Vaginal Thrush	341,123	2,966,132	961,088	4,268,343
Netherlands	**8,461,523**	**373,024,833**	**49,009,010**	**430,495,366**
Athlete's Foot	203,048	8,363,868	1,148,714	9,715,630
Dermatomycosis	2,186,008	77,479,083	11,250,724	90,915,814
Herpes Labialis	2,083,808	114,896,627	15,213,566	132,194,002
Vaginal Thrush	3,988,659	172,285,254	21,396,007	197,669,920
Poland	**28,422,496**	**304,942,996**	**110,808,809**	**444,174,301**
Athlete's Foot	291,969	8,705,597	2,993,061	11,990,626
Dermatomycosis	3,074,031	78,373,225	28,230,636	109,677,892
Herpes Labialis	16,868,841	140,756,283	54,873,559	212,498,683
Vaginal Thrush	8,187,655	77,107,892	24,711,553	110,007,100
Portugal	**14,069,641**	**187,559,029**	**31,711,396**	**233,340,065**
Athlete's Foot	239,521	4,078,311	622,110	4,939,941
Dermatomycosis	2,533,336	36,917,305	5,912,596	45,363,237
Herpes Labialis	7,310,790	78,835,862	14,412,122	100,558,774
Vaginal Thrush	3,985,994	67,727,551	10,764,568	82,478,114
Romania	**5,269,225**	**56,714,232**	**25,232,959**	**87,216,417**
Athlete's Foot	211,037	2,236,213	989,831	3,437,081
Dermatomycosis	2,221,932	20,131,785	9,336,115	31,689,832
Herpes Labialis	801,998	8,237,359	4,134,417	13,173,773
Vaginal Thrush	2,034,259	26,108,876	10,772,596	38,915,730
Slovakia	**6,299,002**	**34,427,585**	**11,079,595**	**51,806,182**
Athlete's Foot	168,287	1,200,433	374,161	1,742,882

Dermatomycosis	1,771,836	10,807,052	3,529,096	16,107,984
Herpes Labialis	2,724,920	10,533,551	3,722,832	16,981,303
Vaginal Thrush	1,633,959	11,886,548	3,453,506	16,974,013
Slovenia	**1,464,464**	**21,841,690**	**6,091,957**	**29,398,111**
Athlete's Foot	37,024	710,468	182,152	929,644
Dermatomycosis	381,509	6,245,816	1,658,307	8,285,631
Herpes Labialis	520,666	5,460,736	1,926,941	7,908,343
Vaginal Thrush	525,265	9,424,670	2,324,557	12,274,493
Spain	**19,262,676**	**285,365,482**	**62,405,770**	**367,033,929**
Athlete's Foot	139,050	1,427,732	275,822	1,842,604
Dermatomycosis	1,470,688	12,923,984	2,621,441	17,016,113
Herpes Labialis	10,023,724	163,908,444	37,949,051	211,881,219
Vaginal Thrush	7,629,214	107,105,322	21,559,456	136,293,993
Sweden	**8,043,548**	**270,110,862**	**46,455,069**	**324,609,479**
Athlete's Foot	99,160	4,225,270	757,854	5,082,285
Dermatomycosis	1,067,559	39,140,988	7,422,569	47,631,116
Herpes Labialis	3,247,567	139,709,306	24,158,812	167,115,685
Vaginal Thrush	3,629,262	87,035,298	14,115,833	104,780,393
UK	**19,576,318**	**610,800,985**	**105,810,723**	**736,188,026**
Athlete's Foot	377,434	16,082,644	2,894,847	19,354,925
Dermatomycosis	4,063,449	148,982,320	28,352,685	181,398,453
Herpes Labialis	4,347,322	187,020,416	32,454,599	223,822,338
Vaginal Thrush	10,788,113	258,715,606	42,108,592	311,612,311
Grand Total	**371,587,867**	**7,498,204,608**	**1,812,462,354**	**9,682,254,829**

A.7. Healthcare system related costs

Healthcare system related cost is the sum of prescription (Rx) and outpatient costs. Overall, out of an estimated 9.7 billion Euros in total costs, approximately 7.9 billion Euros is attributed to healthcare-related spending. These figures are subject to the assumptions in our methodology. The table below details the healthcare system-related costs for each country, with a specific breakdown of Rx and outpatient expenses.

Table 23 Health system related costs country breakdown in a single year (Total Population)

Country	Total Rx cost	Total Outpatient cost	Total health system related cost
Austria	5,913,670	143,303,624	149,217,294
Belgium	10,519,932	175,378,985	185,898,917
Bulgaria	1,687,870	25,128,814	26,816,684
Croatia	2,153,598	31,834,312	33,987,910
Cyprus	806,935	6,827,194	7,634,129
Czech Republic	11,958,242	90,165,716	102,123,958
Denmark	4,059,252	136,313,983	140,373,235
Estonia	814,601	7,915,314	8,729,915
Finland	4,167,442	93,451,210	97,618,651
France	48,968,321	1,752,341,436	1,801,309,757
Germany	78,697,594	2,059,694,300	2,138,391,894
Greece	4,862,796	72,823,017	77,685,814
Hungary	10,667,777	43,726,708	54,394,485
Ireland	5,982,608	126,507,526	132,490,134
Italy	63,526,071	522,799,132	586,325,204
Latvia	1,349,031	11,374,224	12,723,255
Lithuania	2,786,351	17,868,186	20,654,537
Luxembourg	978,744	29,447,739	30,426,484
Malta	818,137	6,515,495	7,333,632
Netherlands	8,461,523	373,024,833	381,486,355
Poland	28,422,496	304,942,996	333,365,492
Portugal	14,069,641	187,559,029	201,628,670
Romania	5,269,225	56,714,232	61,983,457
Slovakia	6,299,002	34,427,585	40,726,586
Slovenia	1,464,464	21,841,690	23,306,153
Spain	19,262,676	285,365,482	304,628,158
Sweden	8,043,548	270,110,862	278,154,410
UK	19,576,318	610,800,985	630,377,303
Grand Total	**371,587,867**	**7,498,204,608**	**7,869,792,475**

A.8. Costs to payers

This section details the distribution of healthcare costs among three primary stakeholders: public payers, individuals, and private insurance providers. On average, across all countries, public payers bear the majority of healthcare costs, accounting for approximately 81% of the total expenses. Individuals cover about 14% of healthcare costs through out-of-pocket expenses, co-payments, and deductibles. Private health insurance providers contribute the remaining 5%, offering supplementary coverage to alleviate financial pressure on both public payers and individuals.

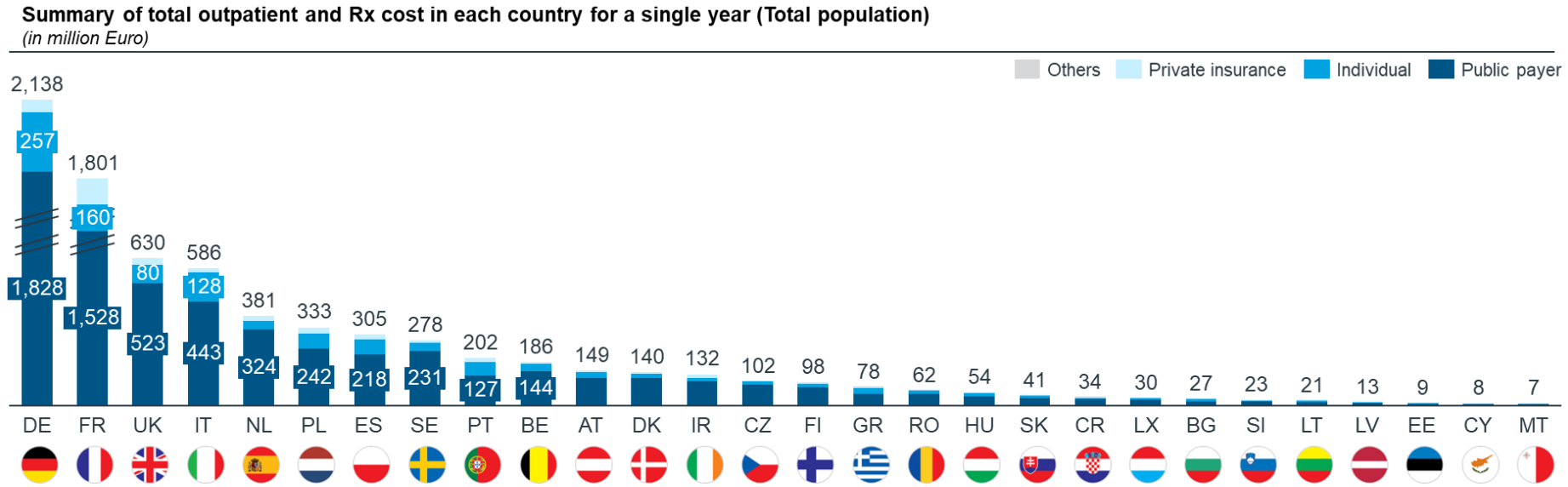


Figure 12 Total health system related cost in each country for a single year (Total Population)

Table 24 Healthcare cost payers breakdown for each country in a single year (Total Population)

Country	Public Payer Share	Individual share	Private Insurance share	Others	Total health system related cost
Austria	116,837,140	23,576,333	8,803,820	-	149,217,294
Belgium	144,257,561	33,275,904	8,365,452	-	185,898,917
Bulgaria	17,350,395	9,117,673	348,617	-	26,816,684
Croatia	28,889,725	3,058,912	1,733,383	305,890	33,987,910
Cyprus	5,763,768	1,671,874	198,487	-	7,634,129
Czech Republic	88,235,099	12,969,743	919,116	-	102,123,958
Denmark	116,509,784	17,827,401	6,036,049	-	140,373,235
Estonia	6,652,195	1,929,311	148,409	-	8,729,915
Finland	77,899,684	15,716,603	4,002,364	-	97,618,651
France	1,527,510,683	160,316,558	113,482,517	-	1,801,309,757
Germany	1,828,325,076	256,607,021	53,459,797	-	2,138,391,894
Greece	48,242,890	25,869,376	3,418,176	155,372	77,685,814
Hungary	39,436,001	13,381,044	1,577,440	-	54,394,485
Ireland	102,547,364	14,176,444	15,766,325	-	132,490,134
Italy	442,675,531	128,405,218	15,244,455	-	586,325,204
Latvia	8,829,939	3,435,279	458,037	-	12,723,255
Lithuania	14,148,357	6,237,670	268,509	-	20,654,537
Luxembourg	25,253,981	3,864,164	1,308,339	-	30,426,484
Malta	5,536,892	1,606,065	190,674	-	7,333,632
Netherlands	323,881,918	35,859,716	21,744,721	-	381,486,355
Poland	241,689,982	66,006,367	25,669,143	-	333,365,492
Portugal	127,429,321	58,472,313	15,727,037	-	201,628,670
Romania	48,347,095	13,016,526	433,884	185,953	61,983,457
Slovakia	32,459,090	7,900,957	366,539	-	40,726,586
Slovenia	17,176,635	3,006,494	3,123,025	-	23,306,153
Spain	218,113,763	63,971,911	22,542,484	-	304,628,158
Sweden	230,868,159	35,325,611	11,960,640	-	278,154,410
UK	523,213,159	80,057,920	27,106,225	-	630,377,303

Grand Total	**6,408,081,187**	**1,096,660,409**	**364,403,664**	**647,215**	**7,869,792,475**

A.9. Productivity costs

The Productivity cost represents wage losses due to lost time from work either due to physician consultations or due to the severity of the disease. Based on our methodology and assumptions made, the total productivity cost is estimated at 1.8 billion Euros. The following figure and table highlight the detailed breakdown per country and indications.

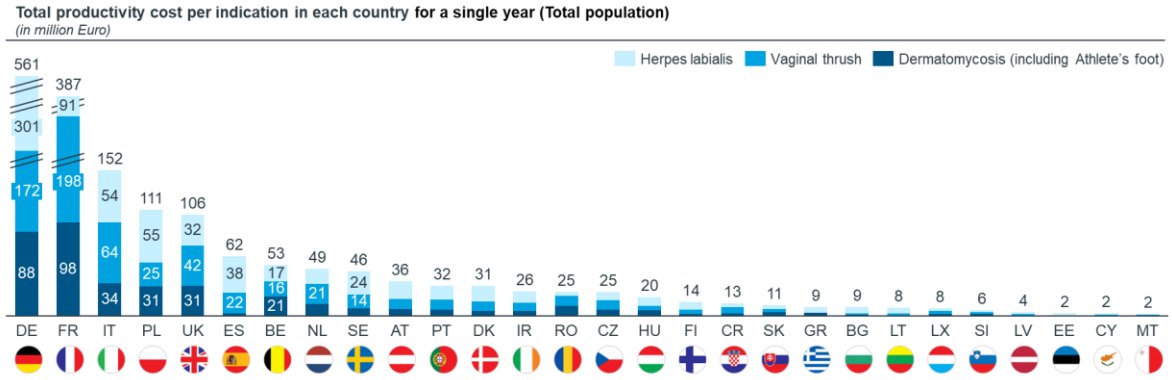


Figure 13 Total cost per indication in each country for a single year (Total Population)

Table 25 Productivity cost breakdown per country and indications in a single year (Total Population)

Country and indications	Total Productivity cost
Austria	**35,930,247**
Athlete's Foot	678,525
Dermatomycosis	6,468,181
Herpes Labialis	17,918,574
Vaginal Thrush	10,864,966
Belgium	**52,983,538**
Athlete's Foot	1,954,167
Dermatomycosis	18,628,513
Herpes Labialis	16,759,403
Vaginal Thrush	15,641,454
Bulgaria	**9,318,273**
Athlete's Foot	122,134
Dermatomycosis	1,164,273
Herpes Labialis	6,509,936
Vaginal Thrush	1,521,929
Croatia	**13,105,889**
Athlete's Foot	284,134
Dermatomycosis	2,679,962
Herpes Labialis	3,985,508
Vaginal Thrush	6,156,285
Cyprus	**2,371,550**
Athlete's Foot	50,374
Dermatomycosis	478,763

Herpes Labialis	1,208,936
Vaginal Thrush	633,477
Czech Republic	**25,159,008**
Athlete's Foot	641,468
Dermatomycosis	5,839,901
Herpes Labialis	8,941,624
Vaginal Thrush	9,736,015
Denmark	**31,264,947**
Athlete's Foot	510,047
Dermatomycosis	4,995,499
Herpes Labialis	16,259,237
Vaginal Thrush	9,500,164
Estonia	**2,398,830**
Athlete's Foot	13,029
Dermatomycosis	122,889
Herpes Labialis	1,828,299
Vaginal Thrush	434,614
Finland	**14,270,305**
Athlete's Foot	201,365
Dermatomycosis	1,972,208
Herpes Labialis	7,718,960
Vaginal Thrush	4,377,772
France	**386,991,435**
Athlete's Foot	9,707,295
Dermatomycosis	88,374,793
Herpes Labialis	90,733,339
Vaginal Thrush	198,176,008
Germany	**560,583,105**
Athlete's Foot	8,369,213
Dermatomycosis	79,781,300
Herpes Labialis	300,537,593
Vaginal Thrush	171,895,000
Greece	**9,379,627**
Athlete's Foot	321,757
Dermatomycosis	3,058,014
Herpes Labialis	5,834,912
Vaginal Thrush	164,944
Hungary	**19,511,311**
Athlete's Foot	538,705
Dermatomycosis	5,081,083
Herpes Labialis	8,977,679
Vaginal Thrush	4,913,843
Ireland	**25,834,815**
Athlete's Foot	499,256
Dermatomycosis	4,545,203
Herpes Labialis	12,141,369

Vaginal Thrush	8,648,987
Italy	**152,168,692**
Athlete's Foot	3,279,802
Dermatomycosis	31,171,576
Herpes Labialis	53,950,970
Vaginal Thrush	63,766,343
Latvia	**4,152,928**
Athlete's Foot	77,427
Dermatomycosis	730,294
Herpes Labialis	2,157,488
Vaginal Thrush	1,187,719
Lithuania	**8,343,879**
Athlete's Foot	3,926
Dermatomycosis	37,029
Herpes Labialis	5,645,774
Vaginal Thrush	2,657,149
Luxembourg	**7,892,743**
Athlete's Foot	192,845
Dermatomycosis	1,755,651
Herpes Labialis	2,603,448
Vaginal Thrush	3,340,799
Malta	**2,195,944**
Athlete's Foot	57,007
Dermatomycosis	541,798
Herpes Labialis	636,052
Vaginal Thrush	961,088
Netherlands	**49,009,010**
Athlete's Foot	1,148,714
Dermatomycosis	11,250,724
Herpes Labialis	15,213,566
Vaginal Thrush	21,396,007
Poland	**110,808,809**
Athlete's Foot	2,993,061
Dermatomycosis	28,230,636
Herpes Labialis	54,873,559
Vaginal Thrush	24,711,553
Portugal	**31,711,396**
Athlete's Foot	622,110
Dermatomycosis	5,912,596
Herpes Labialis	14,412,122
Vaginal Thrush	10,764,568
Romania	**25,232,959**
Athlete's Foot	989,831
Dermatomycosis	9,336,115
Herpes Labialis	4,134,417
Vaginal Thrush	10,772,596

Slovakia	**11,079,595**
Athlete's Foot	374,161
Dermatomycosis	3,529,096
Herpes Labialis	3,722,832
Vaginal Thrush	3,453,506
Slovenia	**6,091,957**
Athlete's Foot	182,152
Dermatomycosis	1,658,307
Herpes Labialis	1,926,941
Vaginal Thrush	2,324,557
Spain	**62,405,770**
Athlete's Foot	275,822
Dermatomycosis	2,621,441
Herpes Labialis	37,949,051
Vaginal Thrush	21,559,456
Sweden	**46,455,069**
Athlete's Foot	757,854
Dermatomycosis	7,422,569
Herpes Labialis	24,158,812
Vaginal Thrush	14,115,833
UK	**105,810,723**
Athlete's Foot	2,894,847
Dermatomycosis	28,352,685
Herpes Labialis	32,454,599
Vaginal Thrush	42,108,592
Grand Total	**1,812,462,354**

A.10. Volume impact

The volume impact results reveal that reverse-switching may not reduce the use of antifungal and antiviral medicines. The volume is estimated based on IQVIA OTC sales data and the following factors:

- Share of patient population who seek Rx, seek alternative treatment or do nothing
    - Share of patient population who develop recurrences
    - Severity and chronicity of conditions
    - Number of doctor's visits and refills
- We assumed that the delay in appropriate treatment for patients who seek alternative treatment or do nothing, causes worsening of conditions, which increases the use of antiviral and antifungal medicines.
- We did not account for potential changes in treatment regime, for example from topical to oral formulation, in the event of worsening of conditions.
- We have not included impact of secondary infections resulting from delayed treatment in estimating volume upon reverse-switching.

Based on these assumptions and factors, the volume impact of herpes labialis shows a potential 58% increase, with consumption rising from 21.1 million units to 33.2 million units. Dermatomycosis, including Athlete's foot, potentially experiences the most significant increase of 177%, with consumption jumping from 8.4 million units to 23.2 million units. These potential increases are attributed to those who seek alternative treatment or do nothing as they will delay appropriate treatment, resulting in worsening of symptoms and eventual need for a doctor's appointment as well as prescription for a more severe condition. Reverse-switch could also lead to a shift in prescribing practices, for instance, from prescribing topical/external treatment to oral/systemic treatment.

Conversely, the volume impact for Vaginal Thrush shows a potential of 13% decrease, with consumption dropping from 27.1 million units to 23.6 million units. This decline is attributed to several factors. First, most patients with vaginal thrush are women, and a majority of them seek prescription treatments rather than alternative treatments or doing nothing. Second, those who seek prescriptions are assumed to do so immediately[75], leading to better-managed conditions and fewer recurrences. Consequently, the lower recurrence rate results in a negative volume impact for vaginal thrush.

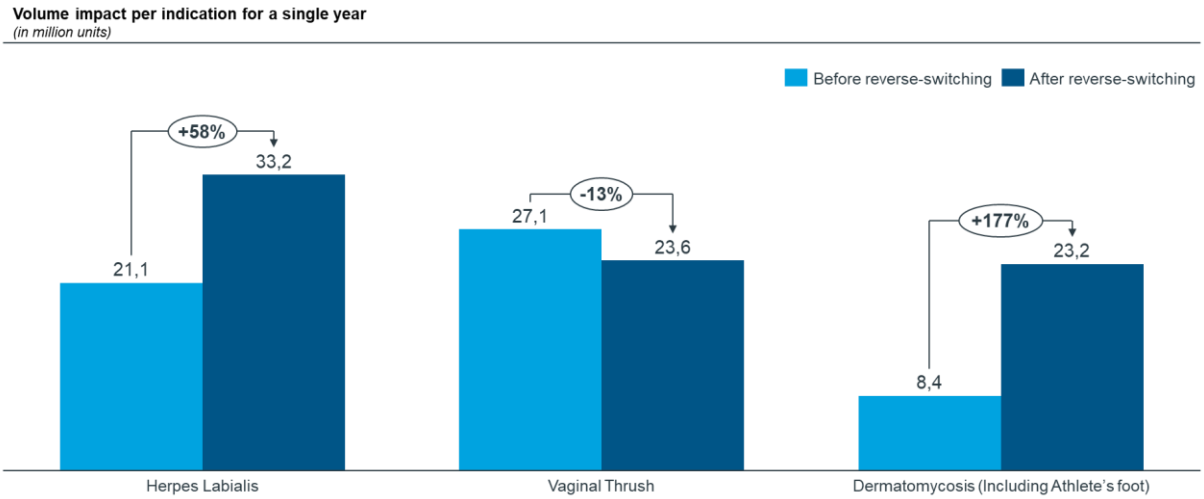


Figure 14 Volume impact per indication for a single year in million units (Total Population)

Table 26 Volume impact per indication for a single year details (Total Population)

	Herpes Labialis	Vaginal Thrush	Dermatomycosis (Including Athlete's foot)
Before reverse-switching	21,065,559	27,081,781	8,368,568
After reverse-switching	33,198,414	23,581,154	23,180,044

These numbers show that, contrary to expectations, reverse-switching may not reduce the volume of antiviral and antifungal medicines use.

[75] We did not factor in the potential increase in waiting time to see a doctor due to increased doctor visits upon reverse-switching.

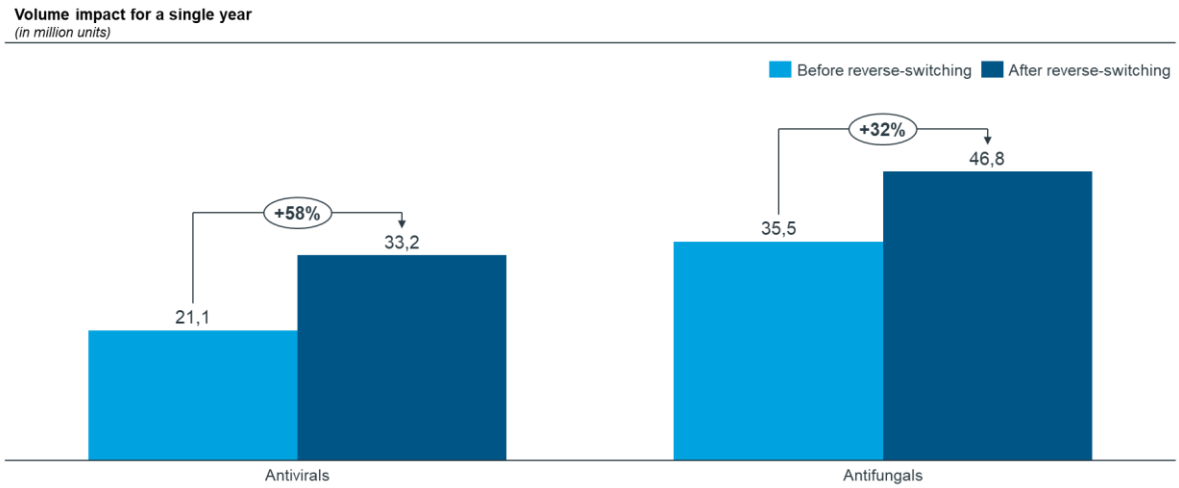


Figure 15 Volume impact in a single year for Antiviral and Antifungal medicines (Total Population)

Table 27 Volume impact in a single year for Antiviral and Antifungal medicines details (Total Population)

	Antiviral	Antifungal
Before reverse-switching	28,463,923	57,803,041
After reverse-switching	44,670,850	75,385,858

2. Country results

B.1. Austria

In Austria, the total economic burden of Herpes Labialis, Vaginal Thrush, and Dermatomycosis (including Athlete's foot) is 165 million Euro, with Herpes Labialis contributing the largest share across all cost breakdown – productivity, outpatient, and Rx cost. The accompanying chart and table provide a detailed breakdown of costs, illustrating the impact of these conditions on productivity, outpatient expenses, and prescription costs.

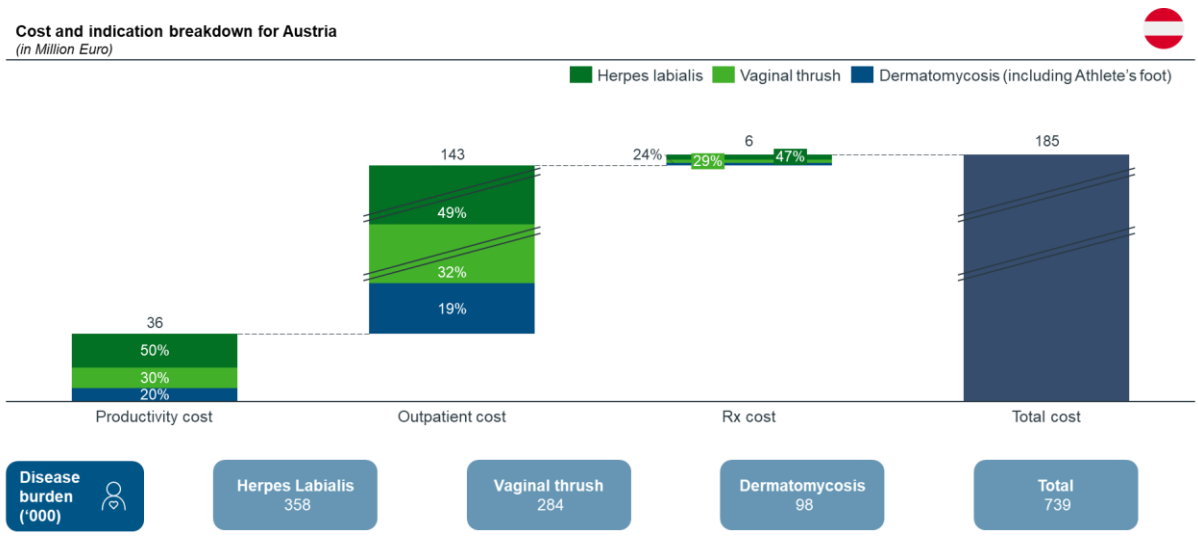


Figure 16 Overall burden and cost breakdown for Austria

Table 28 Cost and Indication breakdown for Austria

Indications	Productivity cost	Outpatient cost	Rx cost	Total cost
Herpes labialis	17,918,574	70,448,795	2,756,097	91,123,466
Vaginal thrush	10,864,966	46,104,605	1,710,874	58,680,445
Dermatomycosis (including Athlete's foot)	7,146,706	26,750,223	1,446,700	35,343,629
Total cost	35,930,247	143,303,624	5,913,670	185,147,541

B.2. Belgium

In Belgium, the total economic burden of Herpes Labialis, Vaginal Thrush, and Dermatomycosis (including Athlete's foot) is 239 million Euro, with Dermatomycosis contributing the largest share across all cost breakdown – productivity, outpatient, and Rx cost. The accompanying chart and table provide a detailed breakdown of costs, illustrating the impact of these conditions on productivity, outpatient expenses, and prescription costs.

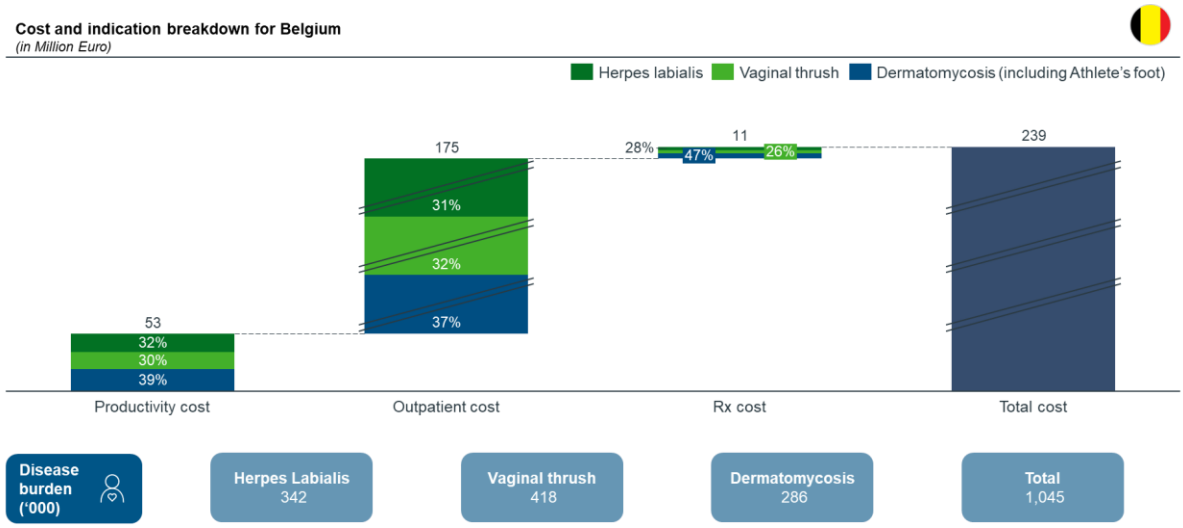


Figure 17 Overall burden and cost breakdown for Belgium

Table 29 Cost and Indication breakdown for Belgium

Indications	Productivity cost	Outpatient cost	Rx cost	Total cost
Herpes labialis	16,759,403	55,210,891	2,908,197	**74,878,491**
Vaginal thrush	15,641,454	55,614,639	2,700,012	**73,956,105**
Dermatomycosis (including Athlete's foot)	20,582,681	64,553,455	4,911,724	**90,047,859**
Total cost	**52,983,538**	**175,378,985**	**10,519,932**	**238,882,455**

B.3. Bulgaria

In Bulgaria, the total economic burden of Herpes Labialis, Vaginal Thrush, and Dermatomycosis (including Athlete's foot) is 36 million Euro, with Herpes Labialis contributing the largest share across all cost breakdown – productivity, outpatient, and Rx cost. The accompanying chart and table provide a detailed breakdown of costs, illustrating the impact of these conditions on productivity, outpatient expenses, and prescription costs.

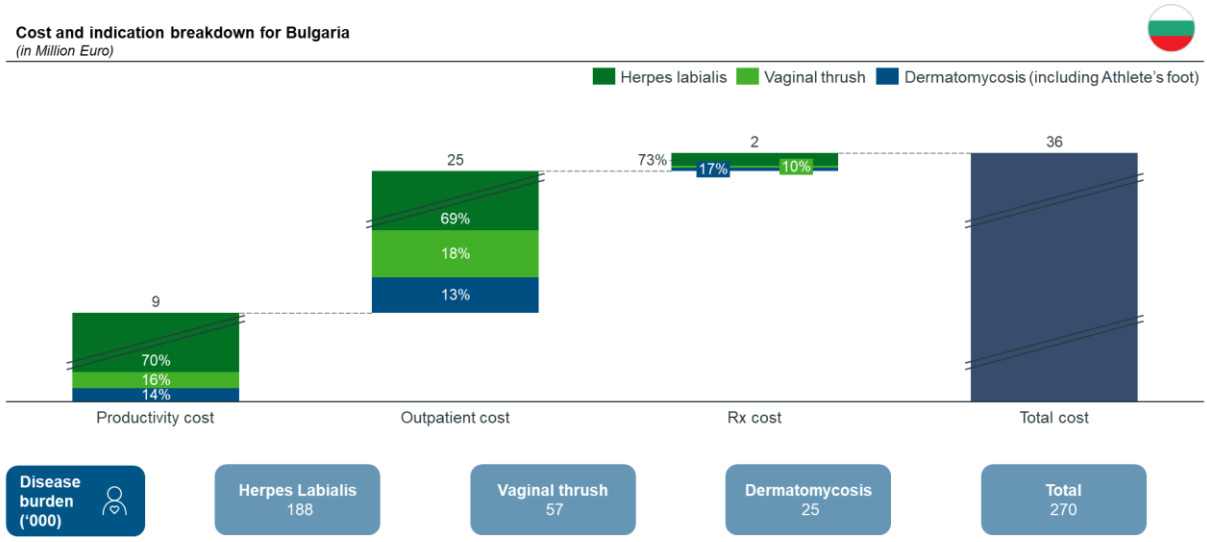


Figure 18 Overall burden and cost breakdown for Bulgaria

Table 30 Cost and Indication breakdown for Bulgaria

Indications	Productivity cost	Outpatient cost	Rx cost	Total cost
Herpes labialis	6,509,936	17,445,057	1,230,585	**25,185,579**
Vaginal thrush	1,521,929	4,401,856	166,269	**6,090,053**
Dermatomycosis (including Athlete's foot)	1,286,407	3,281,901	291,016	**4,859,325**
Total cost	**9,318,273**	**25,128,814**	**1,687,870**	**36,134,957**

B.4. Croatia

In Croatia, the total economic burden of Herpes Labialis, Vaginal Thrush, and Dermatomycosis (including Athlete's foot) is 47 million Euro, with Vaginal Thrush contributing the largest share across all cost breakdown – productivity, outpatient, and Rx cost. The accompanying chart and table provide a detailed breakdown of costs, illustrating the impact of these conditions on productivity, outpatient expenses, and prescription costs.

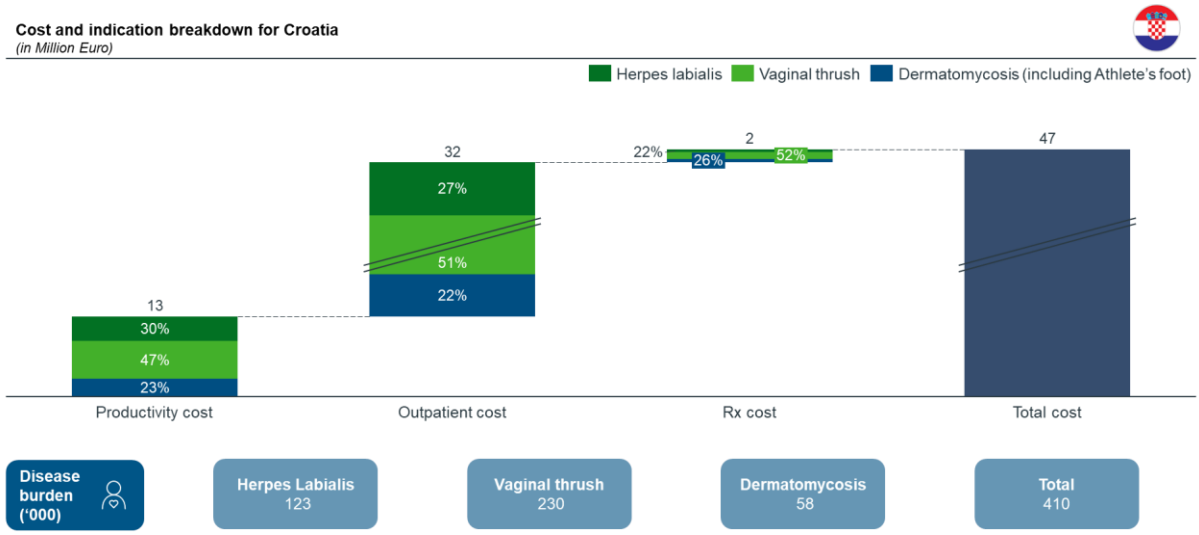


Figure 19 Overall burden and cost breakdown for Croatia

Table 31 Cost and Indication breakdown for Croatia

Indications	Productivity cost	Outpatient cost	Rx cost	Total cost
Herpes labialis	3,985,508	8,632,782	467,480	**13,085,771**
Vaginal thrush	6,156,285	16,221,088	1,121,971	**23,499,345**
Dermatomycosis (including Athlete's foot)	2,964,096	6,980,442	564,147	**10,508,684**
Total cost	**13,105,889**	**31,834,312**	**2,153,598**	**47,093,799**

B.5. Cyprus

In Cyprus, the total economic burden of Herpes Labialis, Vaginal Thrush, and Dermatomycosis (including Athlete's foot) is 10 million Euro, with Herpes Labialis contributing the largest share across all cost breakdown – productivity, outpatient, and Rx cost. The accompanying chart and table provide a detailed breakdown of costs, illustrating the impact of these conditions on productivity, outpatient expenses, and prescription costs.

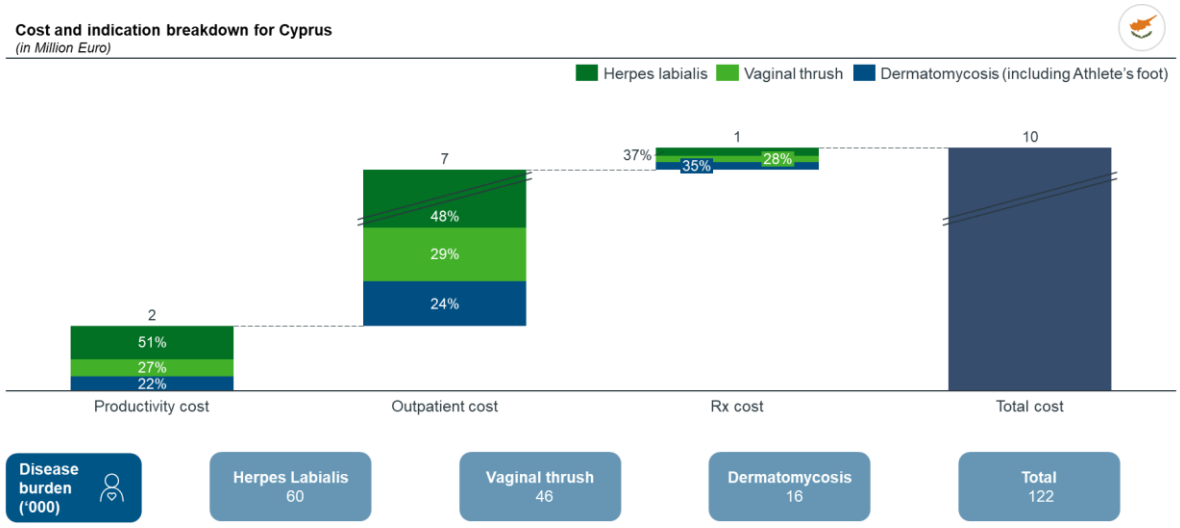


Figure 20 Overall burden and cost breakdown for Cyprus

Table 32 Cost and Indication breakdown for Cyprus

Indications	Productivity cost	Outpatient cost	Rx cost	Total cost
Herpes labialis	1,208,936	3,243,828	300,095	**4,752,858**
Vaginal thrush	633,477	1,955,052	224,843	**2,813,372**
Dermatomycosis (including Athlete's foot)	529,137	1,628,315	281,997	**2,439,449**
Total cost	**2,371,550**	**6,827,194**	**806,935**	**10,005,679**

B.6. Czech Republic

In Czech Republic, the total economic burden of Herpes Labialis, Vaginal Thrush, and Dermatomycosis (including Athlete's foot) is 127 million Euro, with Vaginal Thrush contributing the largest share of the total cost consisting of productivity, outpatient, and Rx cost. The accompanying chart and table provide a detailed breakdown of costs, illustrating the impact of these conditions on productivity, outpatient expenses, and prescription costs.

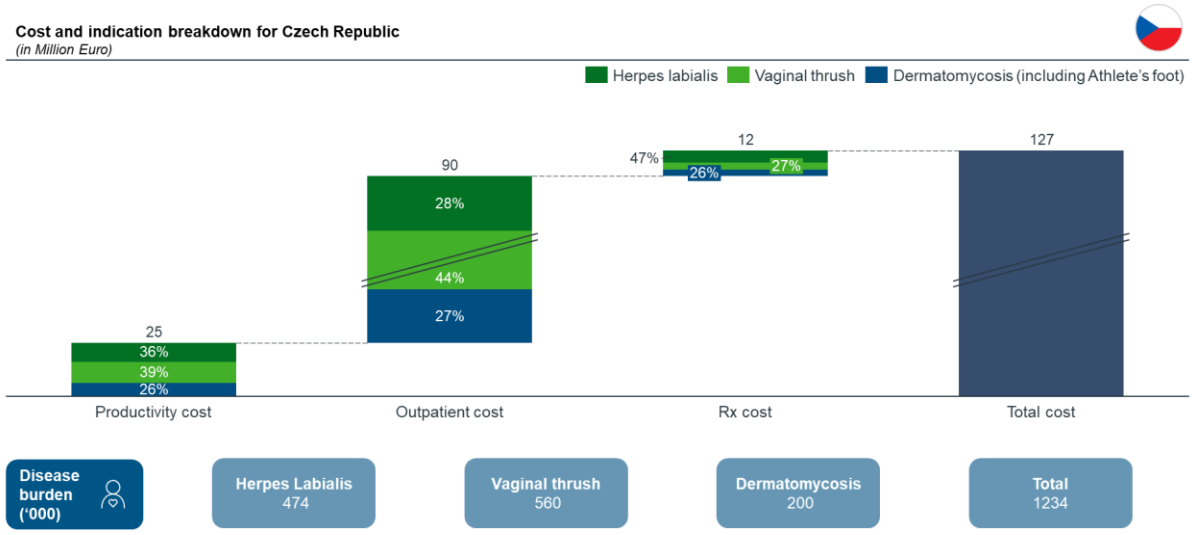


Figure 21 Overall burden and cost breakdown for Czech Republic

Table 33 Cost and Indication breakdown for Czech Republic

Indications	Productivity cost	Outpatient cost	Rx cost	Total cost
Herpes labialis	8,941,624	25,582,217	5,626,026	**40,149,867**
Vaginal thrush	9,736,015	39,851,639	3,271,377	**52,859,031**
Dermatomycosis (including Athlete's foot)	6,481,369	24,731,860	3,060,839	**34,274,068**
Total cost	**25,159,008**	**90,165,716**	**11,958,242**	**127,282,966**

B.7. Denmark

In Denmark, the total economic burden of Herpes Labialis, Vaginal Thrush, and Dermatomycosis (including Athlete's foot) is 172 million Euro, with Herpes Labialis contributing the largest share of the total cost consisting of productivity, outpatient, and Rx cost. The accompanying chart and table provide a detailed breakdown of costs, illustrating the impact of these conditions on productivity, outpatient expenses, and prescription costs.

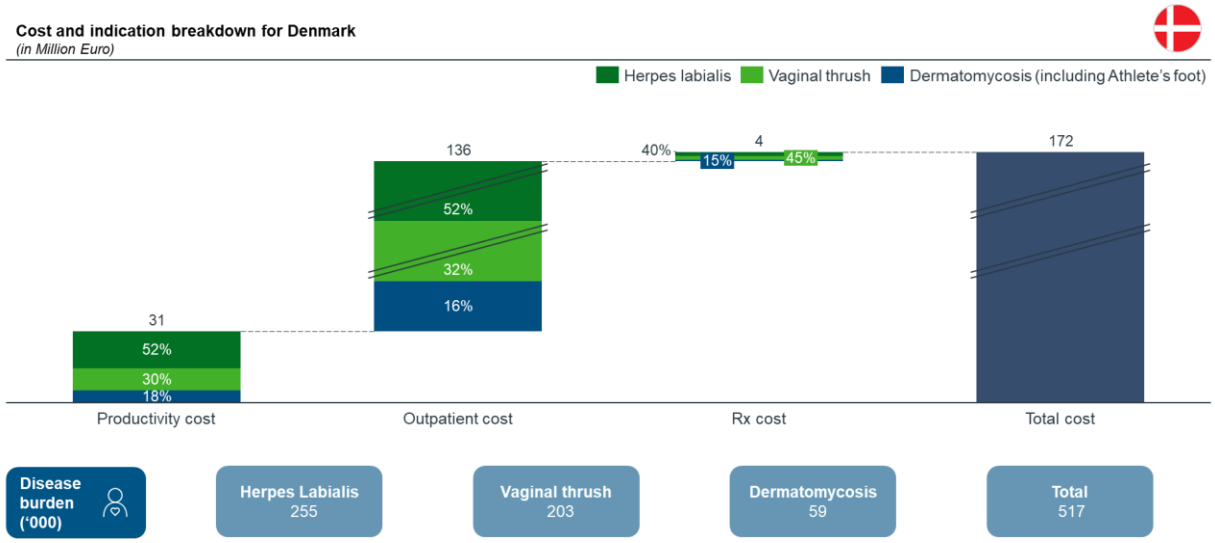


Figure 22 Overall burden and cost breakdown for Denmark

Table 34 Cost and Indication breakdown for Denmark

Indications	Productivity cost	Outpatient cost	Rx cost	Total cost
Herpes labialis	16,259,237	70,505,613	1,638,915	**88,403,765**
Vaginal thrush	9,500,164	43,923,180	1,831,541	**55,254,886**
Dermatomycosis (including Athlete's foot)	5,505,546	21,885,189	588,796	**27,979,531**
Total cost	**31,264,947**	**136,313,983**	**4,059,252**	**171,638,182**

B.8. Estonia

In Estonia, the total economic burden of Herpes Labialis, Vaginal Thrush, and Dermatomycosis (including Athlete's foot) is 11 million Euro, with Herpes Labialis contributing the largest share across all cost breakdown – productivity, outpatient, and Rx cost. The accompanying chart and table provide a detailed breakdown of costs, illustrating the impact of these conditions on productivity, outpatient expenses, and prescription costs.

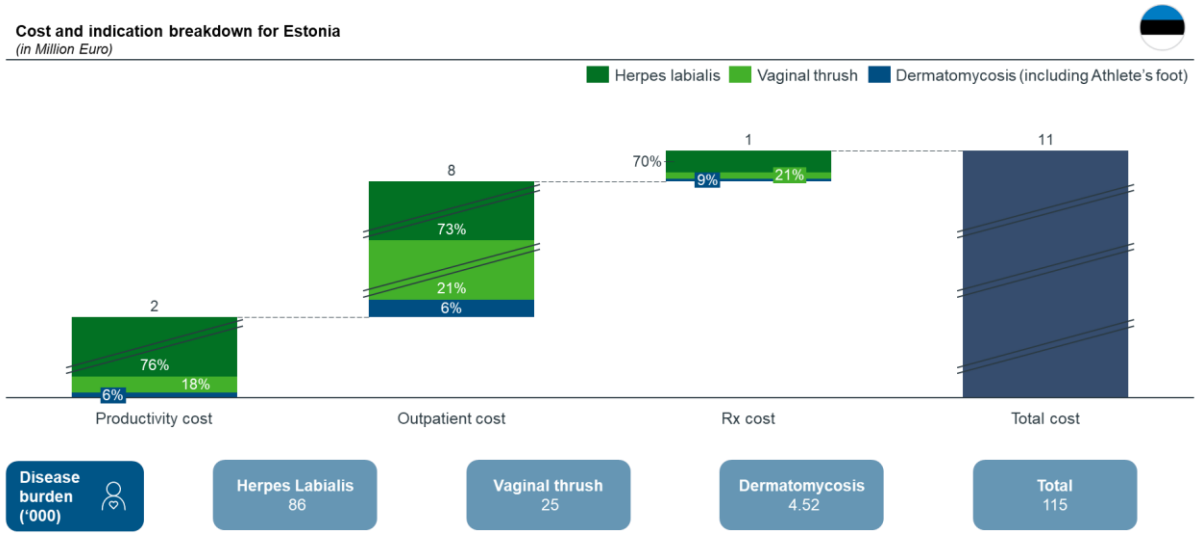


Figure 23 Overall burden and cost breakdown for Estonia

Table 35 Cost and Indication breakdown for Estonia

Indications	Productivity cost	Outpatient cost	Rx cost	Total cost
Herpes labialis	1,828,299	5,777,624	570,639	**8,176,562**
Vaginal thrush	434,614	1,670,707	173,067	**2,278,388**
Dermatomycosis (including Athlete's foot)	135,918	466,983	70,894	**673,795**
Total cost	**2,398,830**	**7,915,314**	**814,601**	**11,128,745**

B.9. Finland

In Finland, the total economic burden of Herpes Labialis, Vaginal Thrush, and Dermatomycosis (including Athlete's foot) is 112 million Euro, with Herpes Labialis contributing the largest share across all cost breakdown – productivity, outpatient, and Rx cost. The accompanying chart and table provide a detailed breakdown of costs, illustrating the impact of these conditions on productivity, outpatient expenses, and prescription costs.

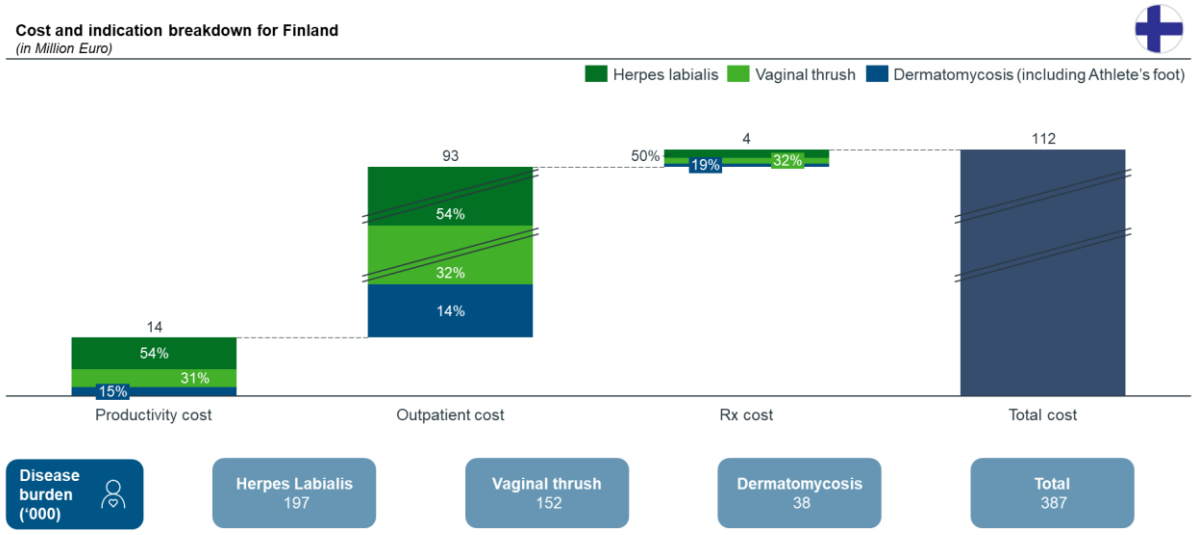


Figure 24 Overall burden and cost breakdown for Finland

Table 36 Cost and Indication breakdown for Finland

Indications	Productivity cost	Outpatient cost	Rx cost	Total cost
Herpes labialis	7,718,961	50,166,451	2,071,499	**59,956,911**
Vaginal thrush	4,377,772	30,335,196	1,316,870	**36,029,838**
Dermatomycosis (including Athlete's foot)	2,173,573	12,949,563	779,072	**15,902,208**
Total cost	**14,270,305**	**93,451,210**	**4,167,442**	**111,888,956**

B.10. France

In France, the total economic burden of Herpes Labialis, Vaginal Thrush, and Dermatomycosis (including Athlete's foot) is 2,188 million Euro, with Vaginal Thrush contributing the largest share across all cost breakdown – productivity, outpatient, and Rx cost. The accompanying chart and table provide a detailed breakdown of costs, illustrating the impact of these conditions on productivity, outpatient expenses, and prescription costs.

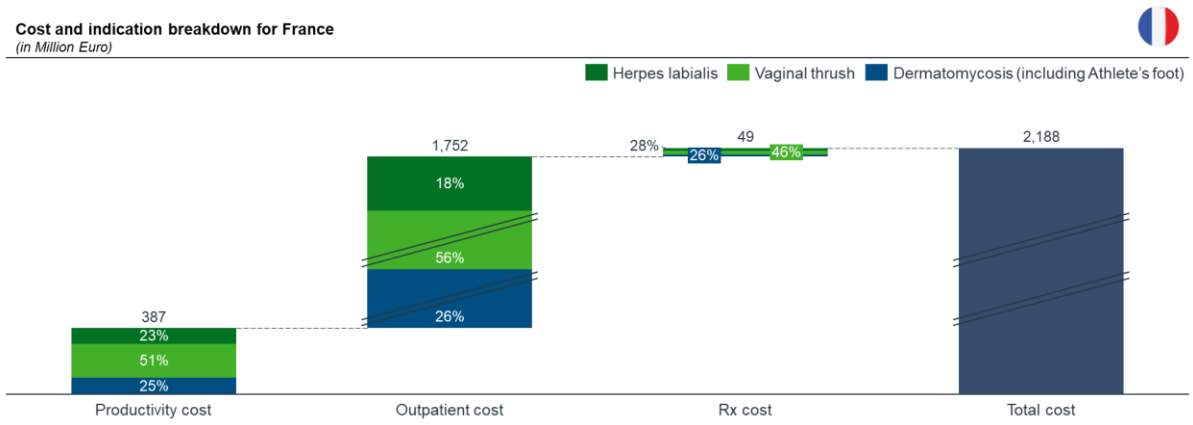


Figure 25 Overall burden and cost breakdown for France

Table 37 Cost and Indication breakdown for France

Indications	Productivity cost	Outpatient cost	Rx cost	Total cost
Herpes labialis	90,733,339	314,796,170	13,835,348	**419,364,857**
Vaginal thrush	198,176,008	983,686,738	22,495,705	**1,204,358,451**
Dermatomycosis (including Athlete's foot)	98,082,088	453,858,529	12,637,268	**564,577,885**
Total cost	**386,991,435**	**1,752,341,436**	**48,968,321**	**2,188,301,192**

B.11. Germany

In Germany, the total economic burden of Herpes Labialis, Vaginal Thrush, and Dermatomycosis (including Athlete's foot) is 2,699 million Euro, with Herpes Labialis contributing the largest share across all cost breakdown – productivity, outpatient, and Rx cost. The accompanying chart and table provide a detailed breakdown of costs, illustrating the impact of these conditions on productivity, outpatient expenses, and prescription costs.

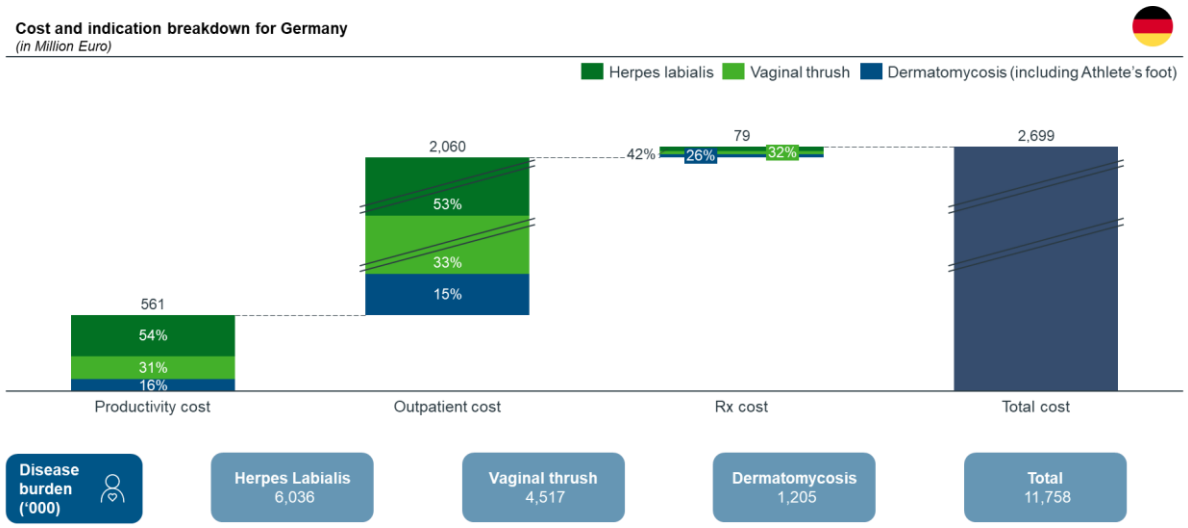


Figure 26 Overall burden and cost breakdown for Germany

Table 38 Cost and Indication breakdown for Germany

Indications	Productivity cost	Outpatient cost	Rx cost	Total cost
Herpes labialis	300,537,593	1,086,016,058	32,675,340	**1,419,228,991**
Vaginal thrush	171,895,000	670,419,281	25,282,546	**867,596,827**
Dermatomycosis (including Athlete's foot)	88,150,512	303,258,961	20,739,709	**412,149,182**
Total cost	**560,583,105**	**2,059,694,300**	**78,697,594**	**2,698,974,999**

B.12. Greece

In Greece, the total economic burden of Herpes Labialis, Vaginal Thrush, and Dermatomycosis (including Athlete's foot) is 87 million Euro, with Herpes Labialis contributing the largest share across all cost breakdown – productivity, outpatient, and Rx cost. The accompanying chart and table provide a detailed breakdown of costs, illustrating the impact of these conditions on productivity, outpatient expenses, and prescription costs.

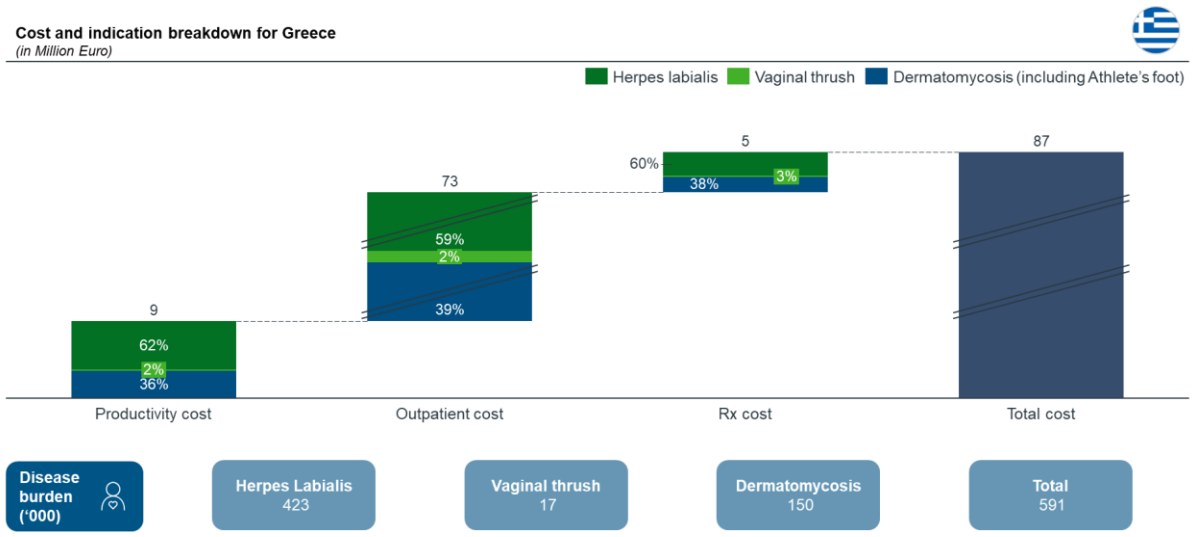


Figure 27 Overall burden and cost breakdown for Greece

Table 39 Cost and Indication breakdown for Greece

Indications	Productivity cost	Outpatient cost	Rx cost	Total cost
Herpes labialis	5,834,912	42,917,327	2,894,619	**51,646,859**
Vaginal thrush	164,944	1,395,431	124,896	**1,685,271**
Dermatomycosis (including Athlete's foot)	3,379,771	28,510,259	1,843,281	**33,733,311**
Total cost	**9,379,627**	**72,823,017**	**4,862,796**	**87,065,441**

B.13. Hungary

In Hungary, the total economic burden of Herpes Labialis, Vaginal Thrush, and Dermatomycosis (including Athlete's foot) is 74 million Euro, with Herpes Labialis contributing the largest share across all cost breakdown – productivity, outpatient, and Rx cost. The accompanying chart and table provide a detailed breakdown of costs, illustrating the impact of these conditions on productivity, outpatient expenses, and prescription costs.

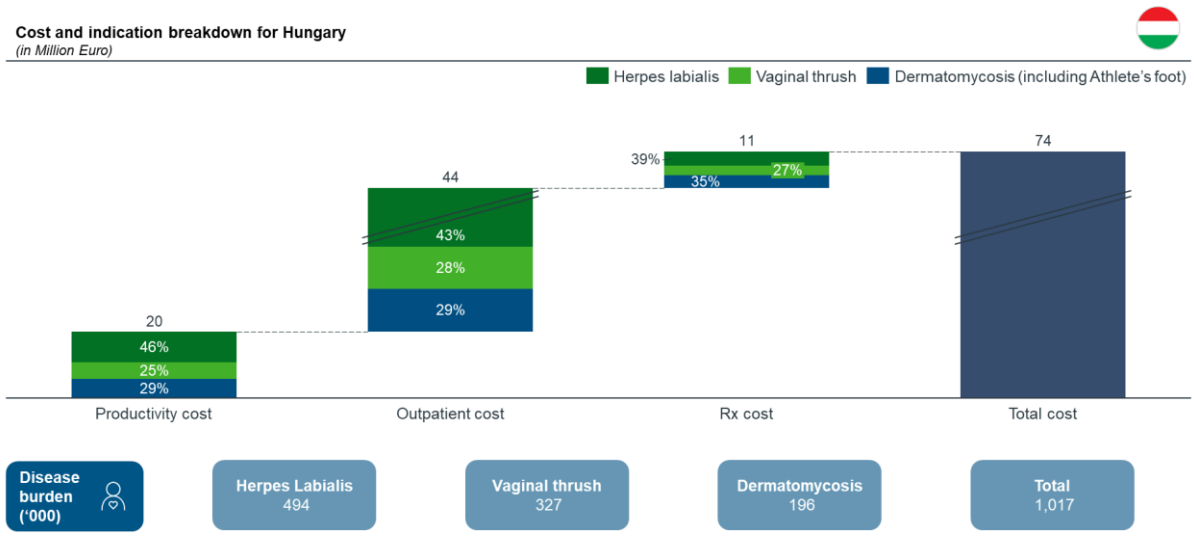


Figure 28 Overall burden and cost breakdown for Hungary

Table 40 Cost and Indication breakdown for Hungary

Indications	Productivity cost	Outpatient cost	Rx cost	Total cost
Herpes labialis	8,977,679	18,635,722	4,130,821	**31,744,222**
Vaginal thrush	4,913,843	12,407,880	2,827,830	**20,149,553**
Dermatomycosis (including Athlete's foot)	5,619,788	12,683,107	3,709,127	**22,012,022**
Total cost	**19,511,311**	**43,726,708**	**10,667,777**	**73,905,796**

B.14. Ireland

In Ireland, the total economic burden of Herpes Labialis, Vaginal Thrush, and Dermatomycosis (including Athlete's foot) is 158 million Euro, with Herpes Labialis contributing the largest share across all cost breakdown – productivity, outpatient, and Rx cost. The accompanying chart and table provide a detailed breakdown of costs, illustrating the impact of these conditions on productivity, outpatient expenses, and prescription costs.

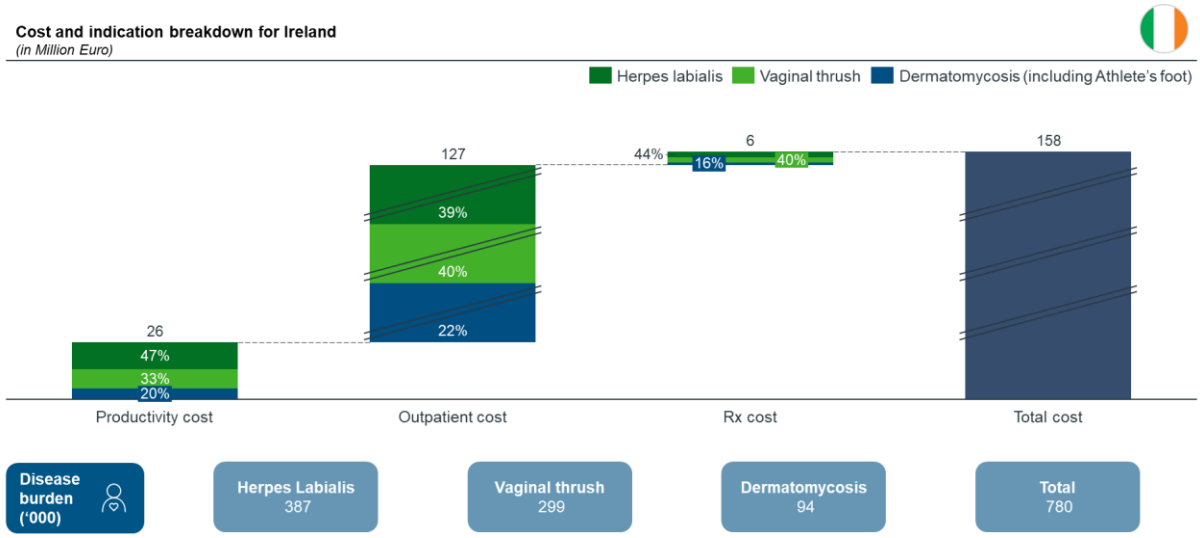


Figure 29 Overall burden and cost breakdown for Ireland

Table 41 Cost and Indication breakdown for Ireland

Indications	Productivity cost	Outpatient cost	Rx cost	Total cost
Herpes labialis	12,141,369	49,161,769	2,625,702	**63,928,841**
Vaginal thrush	8,648,987	50,103,527	2,378,985	**61,131,499**
Dermatomycosis (including Athlete's foot)	5,044,459	27,242,230	977,921	**33,264,610**
Total cost	**25,834,815**	**126,507,526**	**5,982,608**	**158,324,949**

B.15. Italy

In Italy, the total economic burden of Herpes Labialis, Vaginal Thrush, and Dermatomycosis (including Athlete's foot) is 738 million Euro, with Vaginal Thrush contributing the largest share across all cost breakdown – productivity, outpatient, and Rx cost. The accompanying chart and table provide a detailed breakdown of costs, illustrating the impact of these conditions on productivity, outpatient expenses, and prescription costs.

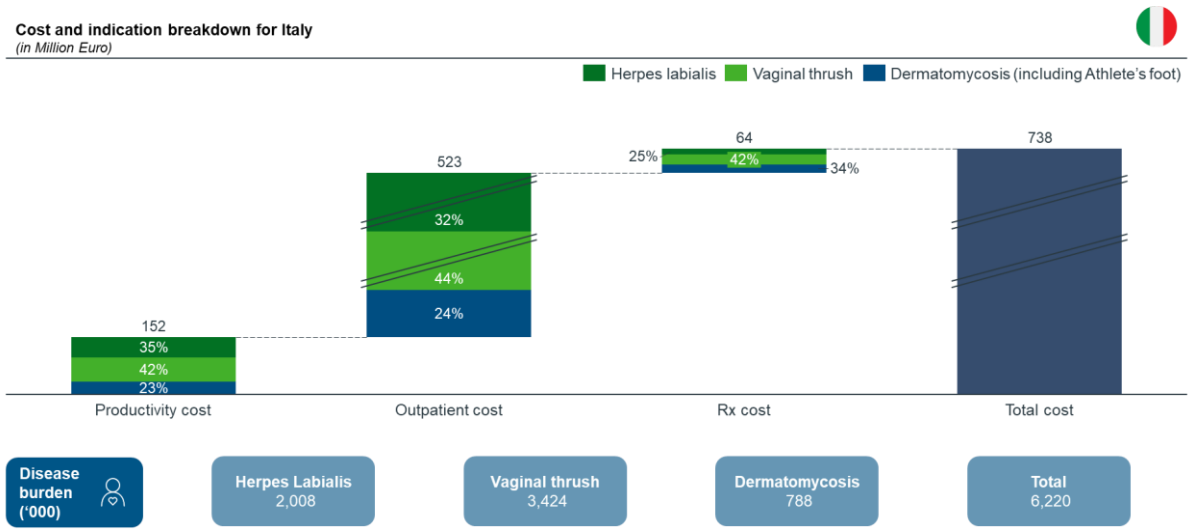


Figure 30 Overall burden and cost breakdown for Italy

Table 42 Cost and Indication breakdown for Italy

Indications	Productivity cost	Outpatient cost	Rx cost	Total cost
Herpes labialis	53,950,971	169,091,458	15,643,084	**238,685,513**
Vaginal thrush	63,766,343	229,872,363	26,436,738	**320,075,444**
Dermatomycosis (including Athlete's foot)	34,451,379	123,835,311	21,446,250	**179,732,939**
Total cost	**152,168,692**	**522,799,132**	**63,526,071**	**738,493,896**

B.16. Latvia

In Latvia, the total economic burden of Herpes Labialis, Vaginal Thrush, and Dermatomycosis (including Athlete's foot) is 17 million Euro, with Herpes Labialis contributing the largest share across all cost breakdown – productivity, outpatient, and Rx cost. The accompanying chart and table provide a detailed breakdown of costs, illustrating the impact of these conditions on productivity, outpatient expenses, and prescription costs.

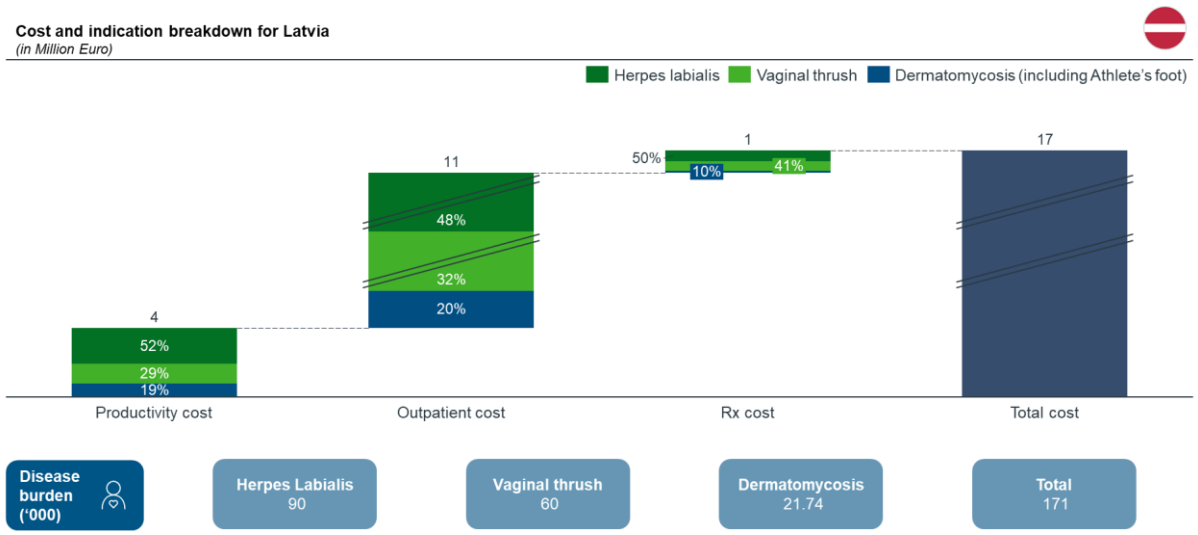


Figure 31 Overall burden and cost breakdown for Latvia

Table 43 Cost and Indication breakdown for Latvia

Indications	Productivity cost	Outpatient cost	Rx cost	Total cost
Herpes labialis	2,157,488	5,477,047	668,886	**8,303,420**
Vaginal thrush	1,187,719	3,667,803	548,013	**5,403,536**
Dermatomycosis (including Athlete's foot)	807,721	2,229,374	132,132	**3,169,227**
Total cost	**4,152,928**	**11,374,224**	**1,349,031**	**16,876,183**

B.17. Lithuania

In Lithuania, the total economic burden of Herpes Labialis, Vaginal Thrush, and Dermatomycosis (including Athlete's foot) is 29 million Euro, with Herpes Labialis contributing the largest share across all cost breakdown – productivity, outpatient, and Rx cost. The accompanying chart and table provide a detailed breakdown of costs, illustrating the impact of these conditions on productivity, outpatient expenses, and prescription costs.

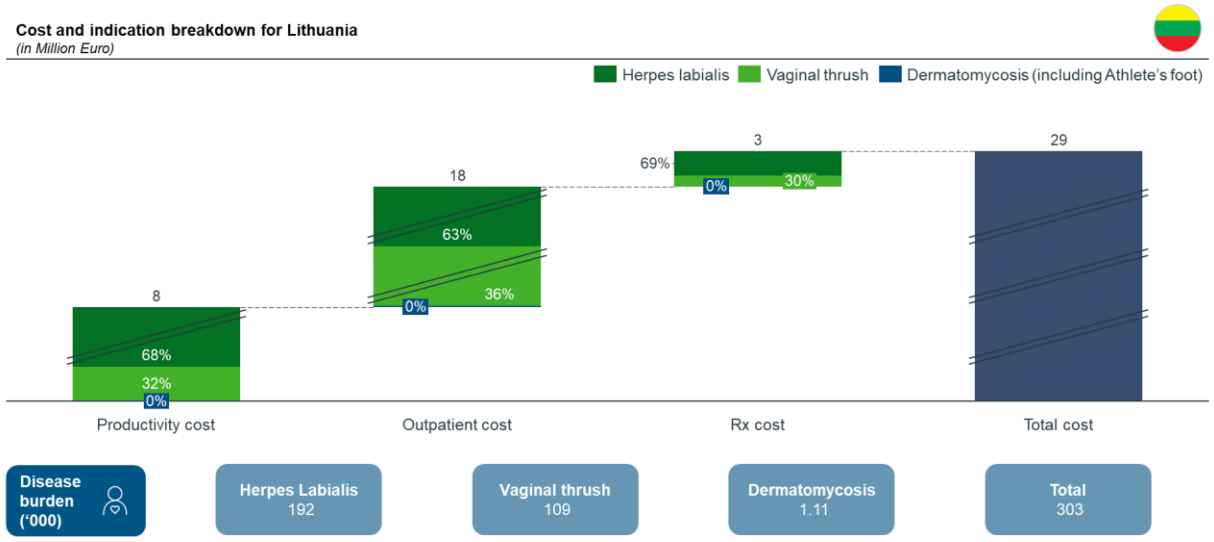


Figure 32 Overall burden and cost breakdown for Lithuania

Table 44 Cost and Indication breakdown for Lithuania

Indications	Productivity cost	Outpatient cost	Rx cost	Total cost
Herpes labialis	5,645,774	11,306,105	1,931,349	**18,883,229**
Vaginal thrush	2,657,149	6,472,910	842,641	**9,972,700**
Dermatomycosis (including Athlete's foot)	40,955	89,171	12,361	**142,487**
Total cost	**8,343,879**	**17,868,186**	**2,786,351**	**28,998,416**

B.18. Luxembourg

In Luxembourg, the total economic burden of Herpes Labialis, Vaginal Thrush, and Dermatomycosis (including Athlete's foot) is 38 million Euro, with Vaginal Thrush contributing the largest share across all cost breakdown – productivity, outpatient, and Rx cost. The accompanying chart and table provide a detailed breakdown of costs, illustrating the impact of these conditions on productivity, outpatient expenses, and prescription costs.

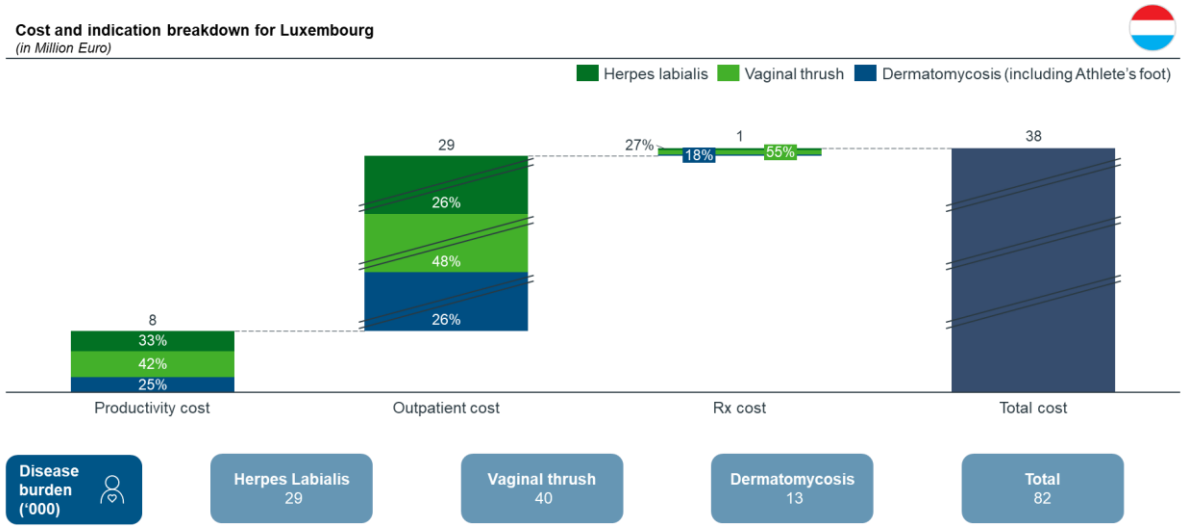


Figure 33 Overall burden and cost breakdown for Luxembourg

Table 45 Cost and Indication breakdown for Luxembourg

Indications	Productivity cost	Outpatient cost	Rx cost	Total cost
Herpes labialis	2,603,448	7,680,515	263,031	**10,546,994**
Vaginal thrush	3,340,799	14,100,511	537,418	**17,978,728**
Dermatomycosis (including Athlete's foot)	1,948,496	7,666,713	178,295	**9,793,504**
Total cost	**7,892,743**	**29,447,739**	**978,744**	**38,319,227**

B.19. Malta

In Malta, the total economic burden of Herpes Labialis, Vaginal Thrush, and Dermatomycosis (including Athlete's foot) is 10 million Euro, with Vaginal Thrush contributing the largest share across all cost breakdown – productivity, outpatient, and Rx cost. The accompanying chart and table provide a detailed breakdown of costs, illustrating the impact of these conditions on productivity, outpatient expenses, and prescription costs.

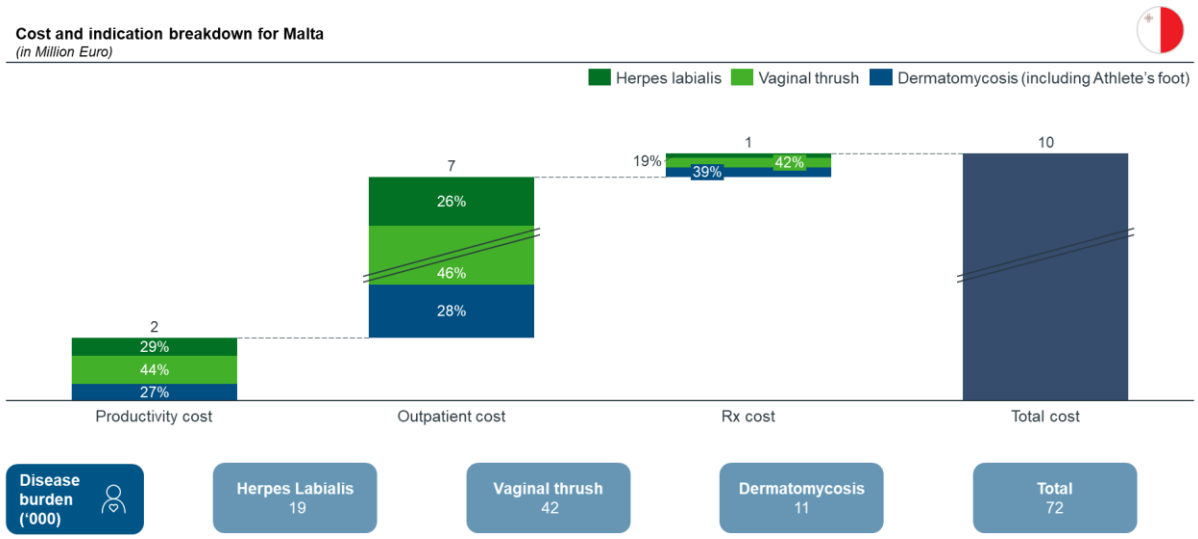


Figure 34 Overall burden and cost breakdown for Malta

Table 46 Cost and Indication breakdown for Malta

Indications	Productivity cost	Outpatient cost	Rx cost	Total cost
Herpes labialis	636,052	1,706,660	157,887	**2,500,599**
Vaginal thrush	961,088	2,966,132	341,123	**4,268,343**
Dermatomycosis (including Athlete's foot)	598,805	1,842,703	319,126	**2,760,633**
Total cost	**2,195,944**	**6,515,495**	**818,137**	**9,529,575**

B.20. Netherlands

In Netherlands, the total economic burden of Herpes Labialis, Vaginal Thrush, and Dermatomycosis (including Athlete's foot) is 430 million Euro, with Vaginal Thrush contributing the largest share across all cost breakdown – productivity, outpatient, and Rx cost. The accompanying chart and table provide a detailed breakdown of costs, illustrating the impact of these conditions on productivity, outpatient expenses, and prescription costs.

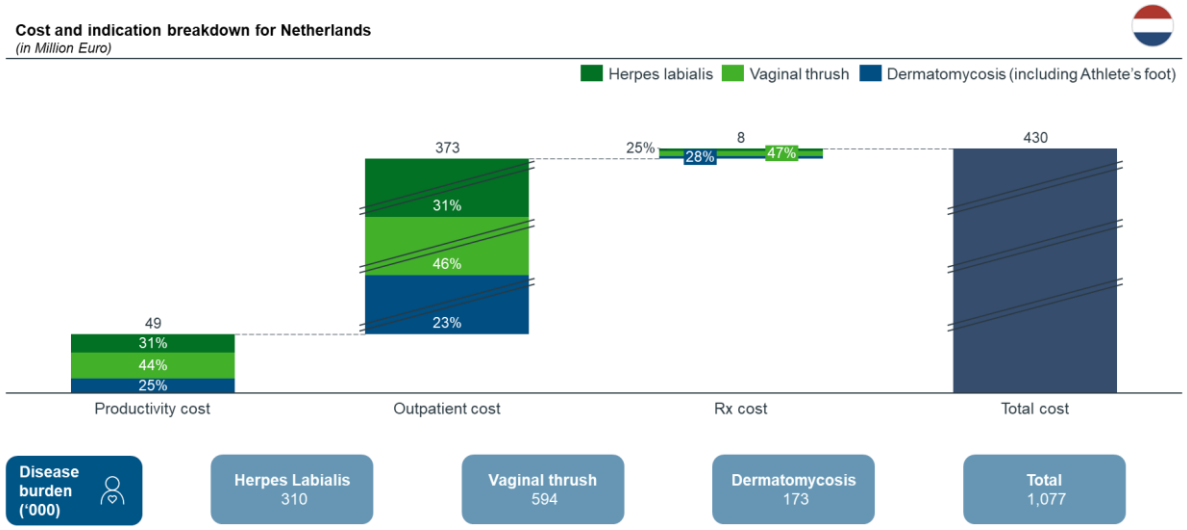


Figure 35 Overall burden and cost breakdown for Netherlands

Table 47 Cost and Indication breakdown for Netherlands

Indications	Productivity cost	Outpatient cost	Rx cost	Total cost
Herpes labialis	15,213,566	114,896,627	2,083,808	**132,194,002**
Vaginal thrush	21,396,007	172,285,254	3,988,659	**197,669,920**
Dermatomycosis (including Athlete's foot)	12,399,438	85,842,951	2,389,055	**100,631,444**
Total cost	**49,009,010**	**373,024,833**	**8,461,523**	**430,495,366**

B.21. Poland

In Poland, the total economic burden of Herpes Labialis, Vaginal Thrush, and Dermatomycosis (including Athlete's foot) is 444 million Euro, with Herpes Labialis contributing the largest share across all cost breakdown – productivity, outpatient, and Rx cost. The accompanying chart and table provide a detailed breakdown of costs, illustrating the impact of these conditions on productivity, outpatient expenses, and prescription costs.

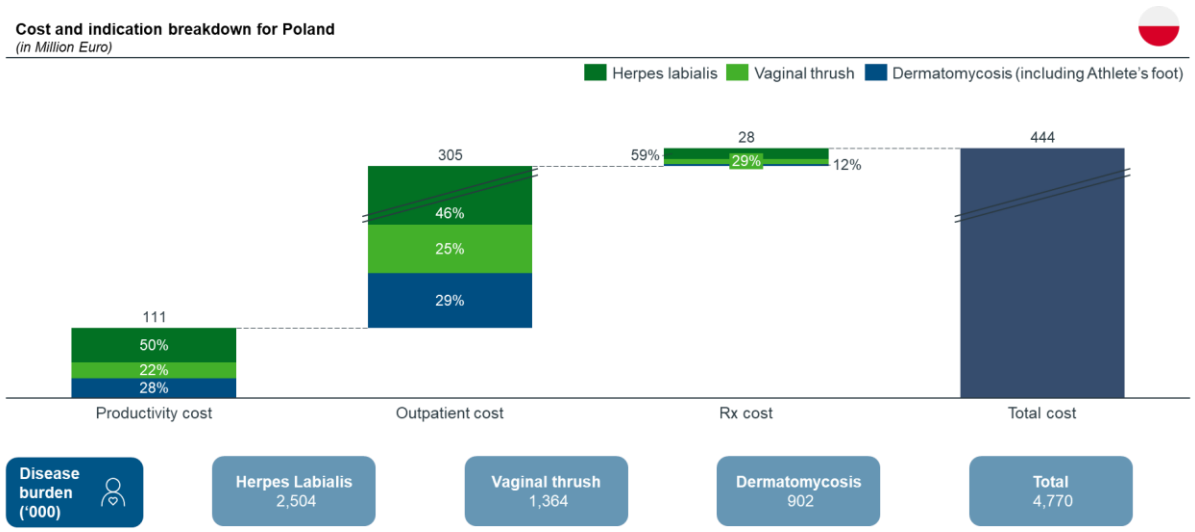


Figure 36 Overall burden and cost breakdown for Poland

Table 48 Cost and Indication breakdown for Poland

Indications	Productivity cost	Outpatient cost	Rx cost	Total cost
Herpes labialis	54,873,559	140,756,283	16,868,841	**212,498,683**
Vaginal thrush	24,711,553	77,107,892	8,187,655	**110,007,100**
Dermatomycosis (including Athlete's foot)	31,223,697	87,078,821	3,366,000	**121,668,518**
Total cost	**110,808,809**	**304,942,996**	**28,422,496**	**444,174,301**

B.22. Portugal

In Portugal, the total economic burden of Herpes Labialis, Vaginal Thrush, and Dermatomycosis (including Athlete's foot) is 233 million Euro, with Herpes Labialis contributing the largest share across all cost breakdown – productivity, outpatient, and Rx cost. The accompanying chart and table provide a detailed breakdown of costs, illustrating the impact of these conditions on productivity, outpatient expenses, and prescription costs.

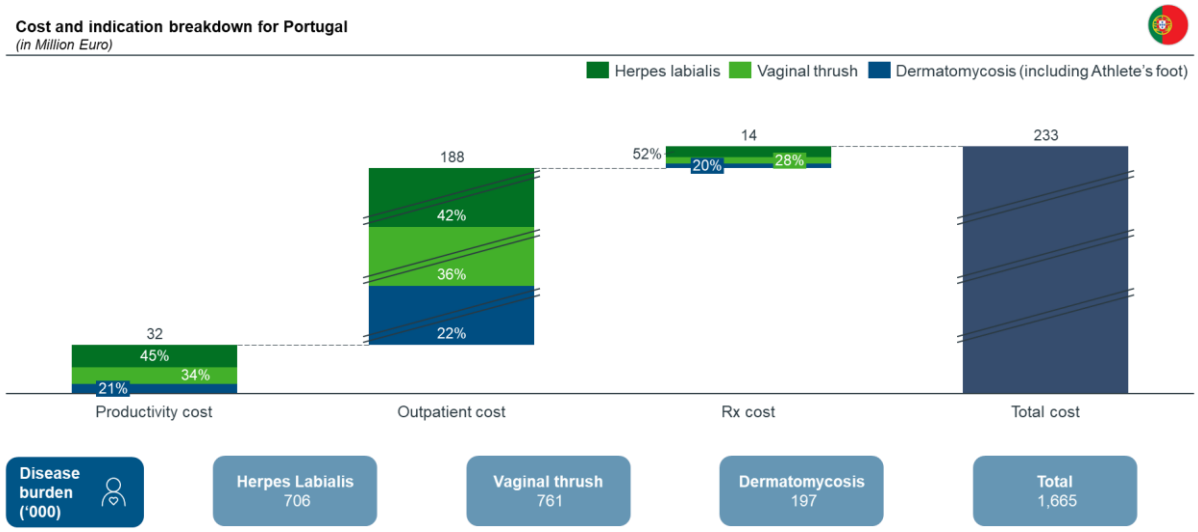


Figure 37 Overall burden and cost breakdown for Portugal

Table 49 Cost and Indication breakdown for Portugal

Indications	Productivity cost	Outpatient cost	Rx cost	Total cost
Herpes labialis	14,412,122	78,835,862	7,310,790	**100,558,774**
Vaginal thrush	10,764,568	67,727,551	3,985,994	**82,478,114**
Dermatomycosis (including Athlete's foot)	6,534,706	40,995,616	2,772,857	**50,303,178**
Total cost	**31,711,396**	**187,559,029**	**14,069,641**	**233,340,065**

B.23. Romania

In Romania, the total economic burden of Herpes Labialis, Vaginal Thrush, and Dermatomycosis (including Athlete's foot) is 87 million Euro, with Vaginal Thrush contributing the largest share of total cost breakdown which includes productivity, outpatient, and Rx cost. The accompanying chart and table provide a detailed breakdown of costs, illustrating the impact of these conditions on productivity, outpatient expenses, and prescription costs.

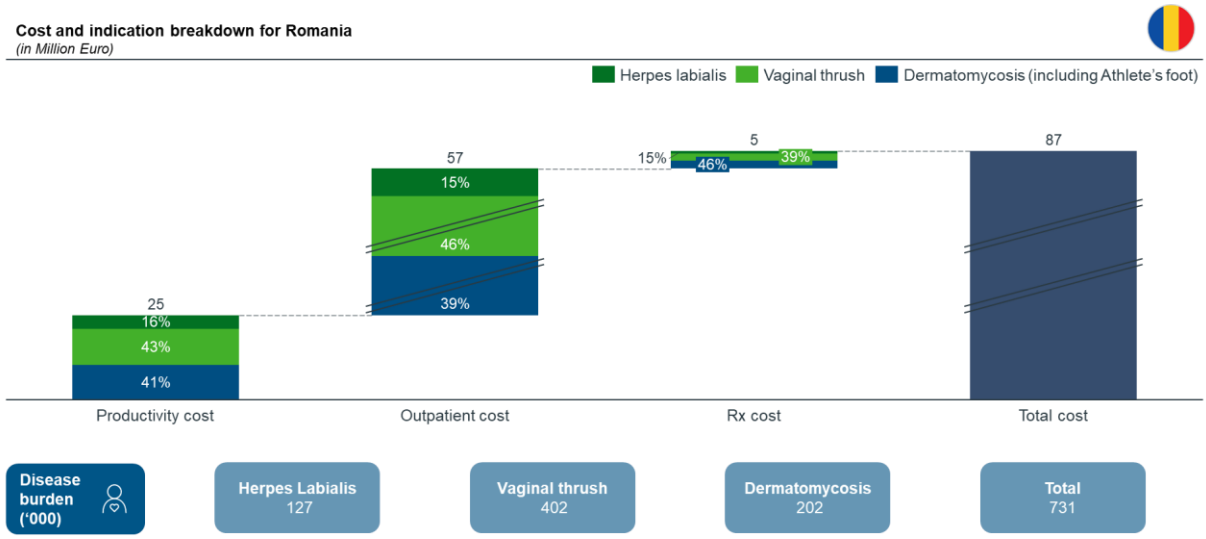


Figure 38 Overall burden and cost breakdown for Romania

Table 50 Cost and Indication breakdown for Portugal

Indications	Productivity cost	Outpatient cost	Rx cost	Total cost
Herpes labialis	4,134,417	8,237,359	801,998	**13,173,773**
Vaginal thrush	10,772,596	26,108,876	2,034,259	**38,915,730**
Dermatomycosis (including Athlete's foot)	10,325,947	22,367,997	2,432,969	**35,126,913**
Total cost	**25,232,959**	**56,714,232**	**5,269,225**	**87,216,417**

B.24. Slovakia

In Slovakia, the total economic burden of Herpes Labialis, Vaginal Thrush, and Dermatomycosis (including Athlete's foot) is 52 million Euro, with Dermatomycosis contributing the largest share of total cost breakdown which includes productivity, outpatient, and Rx cost. The accompanying chart and table provide a detailed breakdown of costs, illustrating the impact of these conditions on productivity, outpatient expenses, and prescription costs.

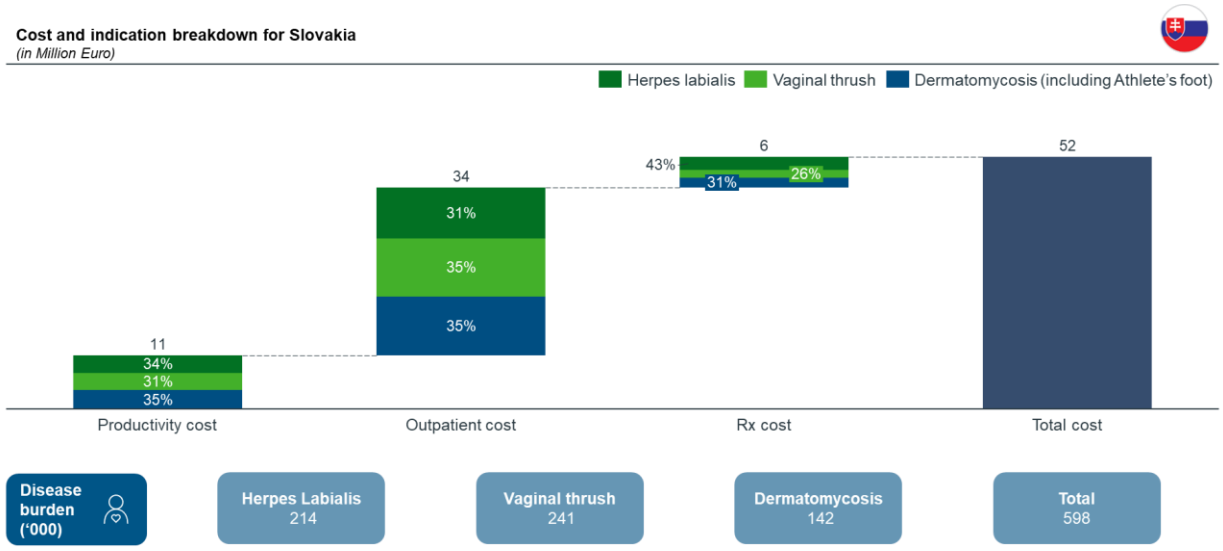


Figure 39 Overall burden and cost breakdown for Slovakia

Table 51 Cost and Indication breakdown for Slovakia

Indications	Productivity cost	Outpatient cost	Rx cost	Total cost
Herpes labialis	3,722,832	10,533,551	2,724,920	**16,981,303**
Vaginal thrush	3,453,506	11,886,548	1,633,959	**16,974,013**
Dermatomycosis (including Athlete's foot)	3,903,257	12,007,486	1,940,123	**17,850,866**
Total cost	**11,079,595**	**34,427,585**	**6,299,002**	**51,806,182**

B.25. Slovenia

In Slovenia, the total economic burden of Herpes Labialis, Vaginal Thrush, and Dermatomycosis (including Athlete's foot) is 29 million Euro, with Vaginal Thrush contributing the largest share across all cost breakdown – productivity, outpatient, and Rx cost. The accompanying chart and table provide a detailed breakdown of costs, illustrating the impact of these conditions on productivity, outpatient expenses, and prescription costs.

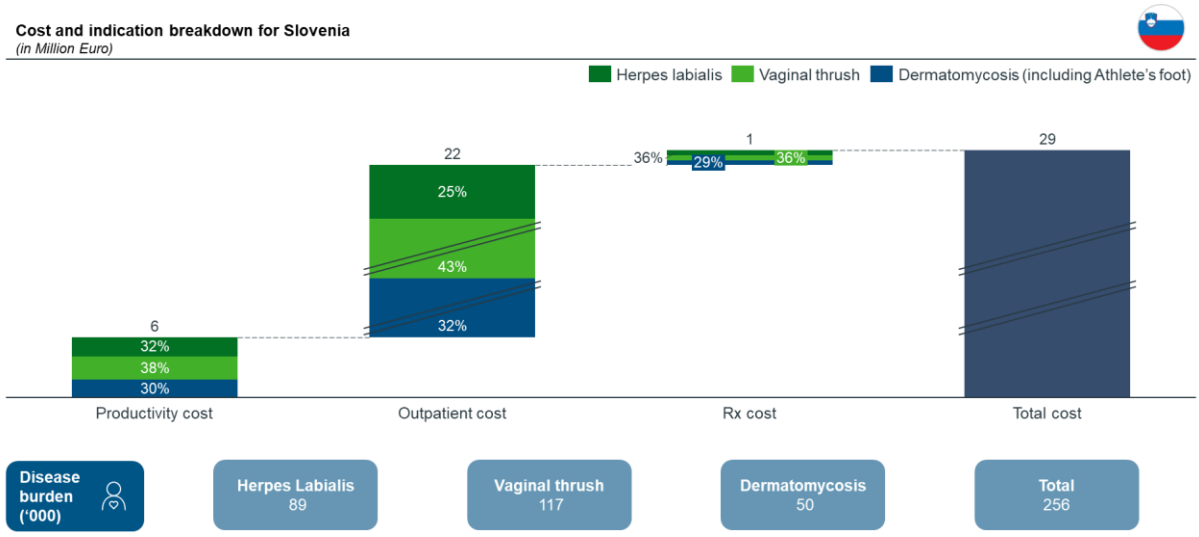


Figure 40 Overall burden and cost breakdown for Slovenia

Table 52 Cost and Indication breakdown for Slovenia

Indications	Productivity cost	Outpatient cost	Rx cost	Total cost
Herpes labialis	1,926,941	5,460,736	520,666	**7,908,343**
Vaginal thrush	2,324,557	9,424,670	525,265	**12,274,493**
Dermatomycosis (including Athlete's foot)	1,840,459	6,956,284	418,532	**9,215,275**
Total cost	**6,091,957**	**21,841,690**	**1,464,464**	**29,398,111**

B.26. Spain

In Spain, the total economic burden of Herpes Labialis, Vaginal Thrush, and Dermatomycosis (including Athlete's foot) is 367 million Euro, with Herpes Labialis contributing the largest share across all cost breakdown – productivity, outpatient, and Rx cost. The accompanying chart and table provide a detailed breakdown of costs, illustrating the impact of these conditions on productivity, outpatient expenses, and prescription costs.

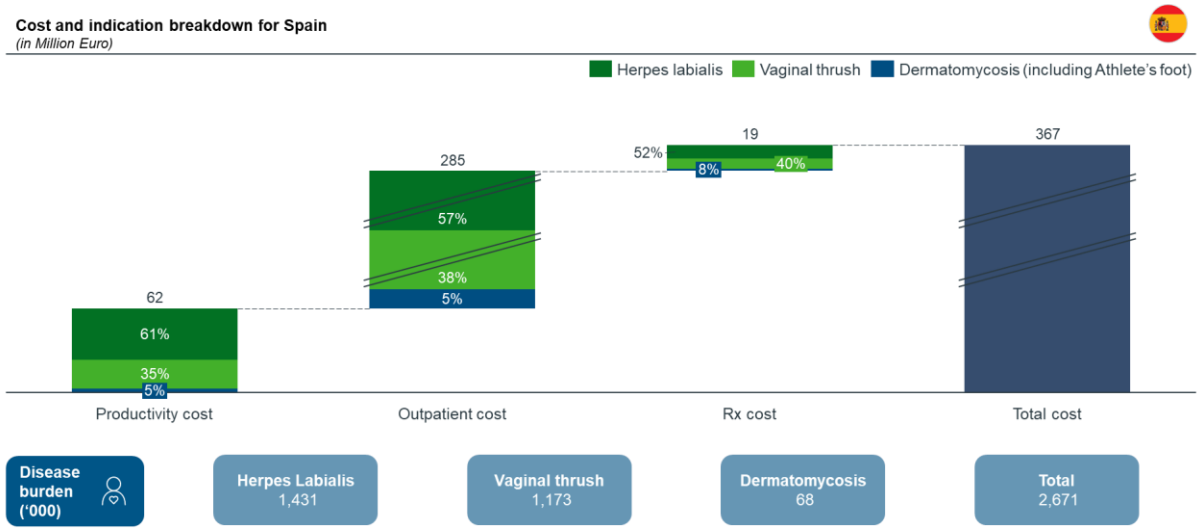


Figure 41 Overall burden and cost breakdown for Spain

Table 53 Cost and Indication breakdown for Spain

Indications	Productivity cost	Outpatient cost	Rx cost	Total cost
Herpes labialis	37,949,051	163,908,444	10,023,724	**211,881,219**
Vaginal thrush	21,559,456	107,105,323	7,629,214	**136,293,993**
Dermatomycosis (including Athlete's foot)	2,897,263	14,351,716	1,609,738	**18,858,717**
Total cost	**62,405,770**	**285,365,482**	**19,262,676**	**367,033,929**

B.27. Sweden

In Sweden, the total economic burden of Herpes Labialis, Vaginal Thrush, and Dermatomycosis (including Athlete's foot) is 325 million Euro, with Herpes Labialis contributing the largest share of total cost breakdown which includes productivity, outpatient, and Rx cost. The accompanying chart and table provide a detailed breakdown of costs, illustrating the impact of these conditions on productivity, outpatient expenses, and prescription costs.

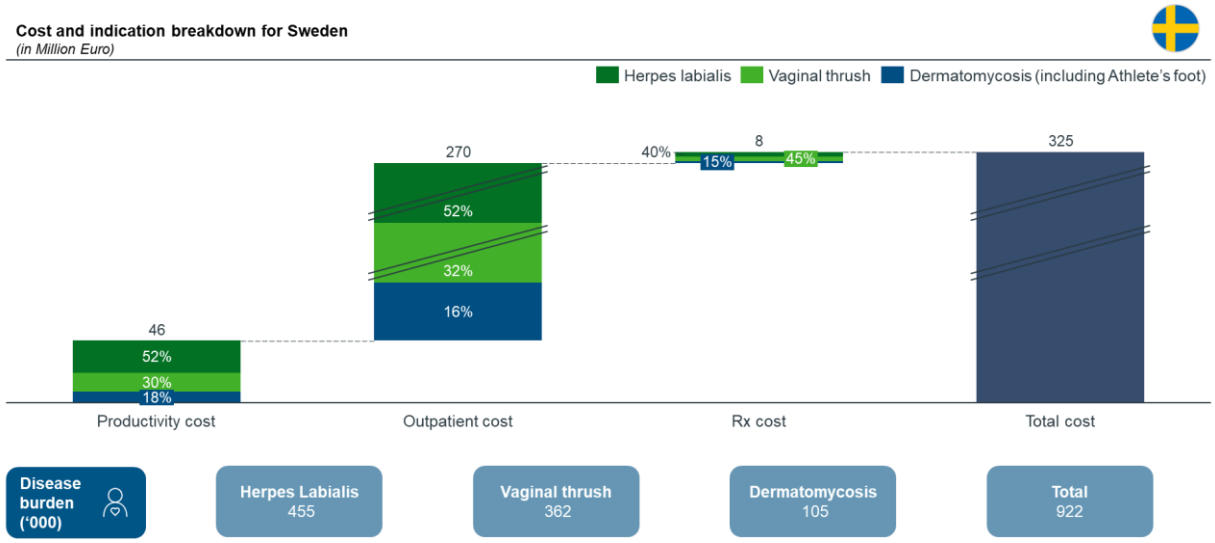


Figure 42 Overall burden and cost breakdown for Sweden

Table 54 Cost and Indication breakdown for Sweden

Indications	Productivity cost	Outpatient cost	Rx cost	Total cost
Herpes labialis	24,158,812	139,709,306	3,247,567	**167,115,685**
Vaginal thrush	14,115,833	87,035,298	3,629,262	**104,780,393**
Dermatomycosis (including Athlete's foot)	8,180,424	43,366,258	1,166,719	**52,713,401**
Total cost	**46,455,069**	**270,110,862**	**8,043,548**	**324,609,479**

B.28. United Kingdom

In United Kingdom, the total economic burden of Herpes Labialis, Vaginal Thrush, and Dermatomycosis (including Athlete's foot) is 736 million Euro, with Vaginal Thrush contributing the largest share across all cost breakdown – productivity, outpatient, and Rx cost. The accompanying chart and table provide a detailed breakdown of costs, illustrating the impact of these conditions on productivity, outpatient expenses, and prescription costs.

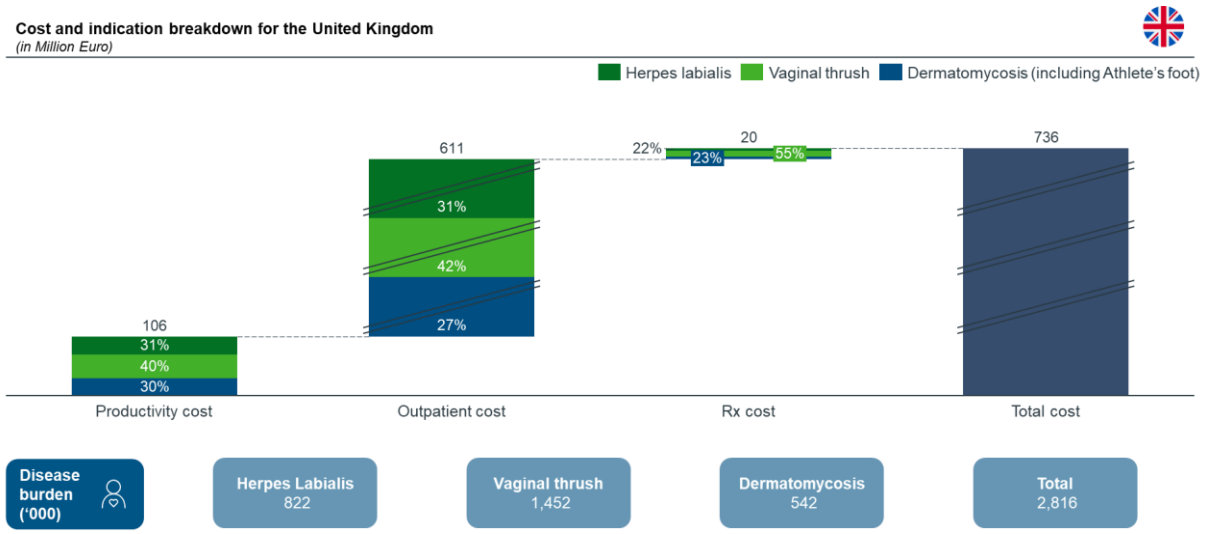


Figure 43 Overall burden and cost breakdown for United Kingdom

Table 55 Cost and Indication breakdown for United Kingdom

Indications	Productivity cost	Outpatient cost	Rx cost	Total cost
Herpes labialis	32,454,599	187,020,416	4,347,322	**223,822,338**
Vaginal thrush	42,108,592	258,715,606	10,788,113	**311,612,311**
Dermatomycosis (including Athlete's foot)	31,247,532	165,064,963	4,440,883	**200,753,378**
Total cost	**105,810,723**	**610,800,985**	**19,576,318**	**736,188,026**

Implication of study results

The reclassification of antifungal and antiviral NPMs to prescription-only status carries significant socio-economic and healthcare implications in four key areas:

1. **Delay in Seeking Care**
   Reverse-switching may cause individuals to delay seeking appropriate treatment, opting instead to either use an alternative treatment or do nothing due to existing physical and social barriers in accessing healthcare. This delay can lead to the exacerbation of conditions, resulting in an estimated 19.2 million unresolved cases and increased severity of illnesses over time. The longer conditions remain untreated, the more complex and costly they become to manage, increasing the risk of complications and long-term health issues.

2. **Additional Burden and Costs to the Healthcare System**
   The shift of patients to the healthcare system will create substantial additional burdens and costs. It is anticipated that there will be a major increase of 59 million excess visits to doctors, including 11 million emergency care visits. This surge in healthcare utilization will strain resources, reduce the availability of consultation time for each patient, and necessitate an additional €7.8 billion in healthcare-related spending expected to happen in a single year, with 81% of these costs borne by the public payer. The increased demand for healthcare services could also lead to longer wait times and reduced quality of care.

3. **Productivity Loss to Individuals**
   The economic impact on individuals includes €1.8 billion in productivity losses due to time spent seeking outpatient care and dealing with the disabilities caused by worsening conditions. These productivity losses highlight the broader socio-economic implications of reverse-switching outside of the healthcare system-related costs. As individuals spend more time managing their health conditions, their ability to contribute effectively to the workforce diminishes, potentially affecting overall economic productivity.

4. **Unintended Consequences**

   Contrary to the intended outcome, reverse-switching may not have the desired impact in reducing the volume of antiviral and antifungal medicines use. There is a potential increase of 58% and 32% respectively. Patients who choose to visit a doctor will receive a prescription, whereas patients who explore alternative options or take no action, may experience delay in appropriate treatment, which could lead to worsened symptoms. Eventually, they may require a doctor's appointment and a prescription for a more severe condition. Additionally, this unintended consequence could shift prescribing practices, such as moving from topical/external treatment to oral/systemic treatment. Therefore, the proposal for reverse-switching may not only fall short of its aim in reducing consumption of antifungals and antivirals but could also introduce new complexities in managing public health.

In summary, we believe the reverse-switching of antifungal and antiviral NPMs to prescription-only status will negatively impact health systems and individuals, including delayed care, increased healthcare system burdens, productivity losses, and unintended increases in antifungal and antiviral use and severity of conditions. These factors underscore the need for careful consideration and strategic planning to mitigate the negative impacts on both the healthcare system and society at large.

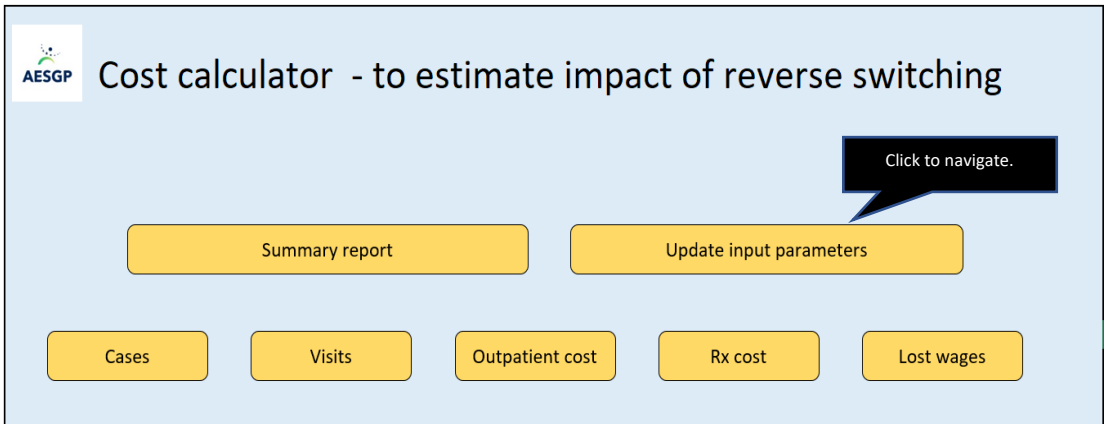
Design and operations of cost calculator

We took a modular approach designing the structure of the cost calculator. This design is crucial to enable future updates and modifications. Due to this approach, we will also save a considerable amount of time in making the required modifications to the calculator in future iterations.

Please find the description of each module mentioned below.

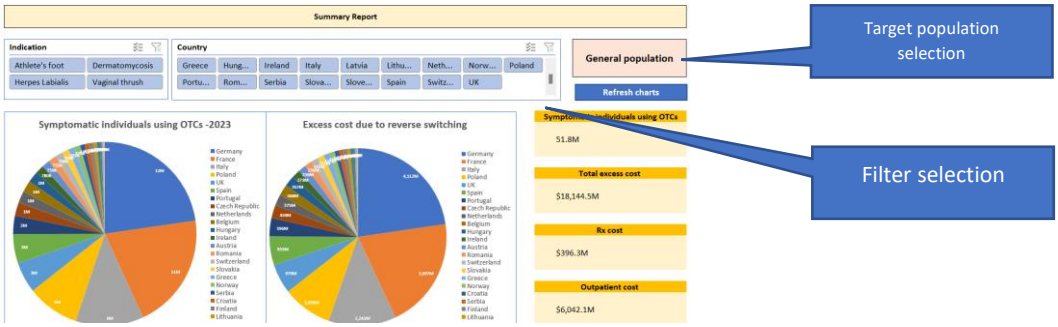
A. Introduction

- This is the default view when the user opens the report.
- The main functionality of this view is to allow users to navigate to each module through click functions easily.



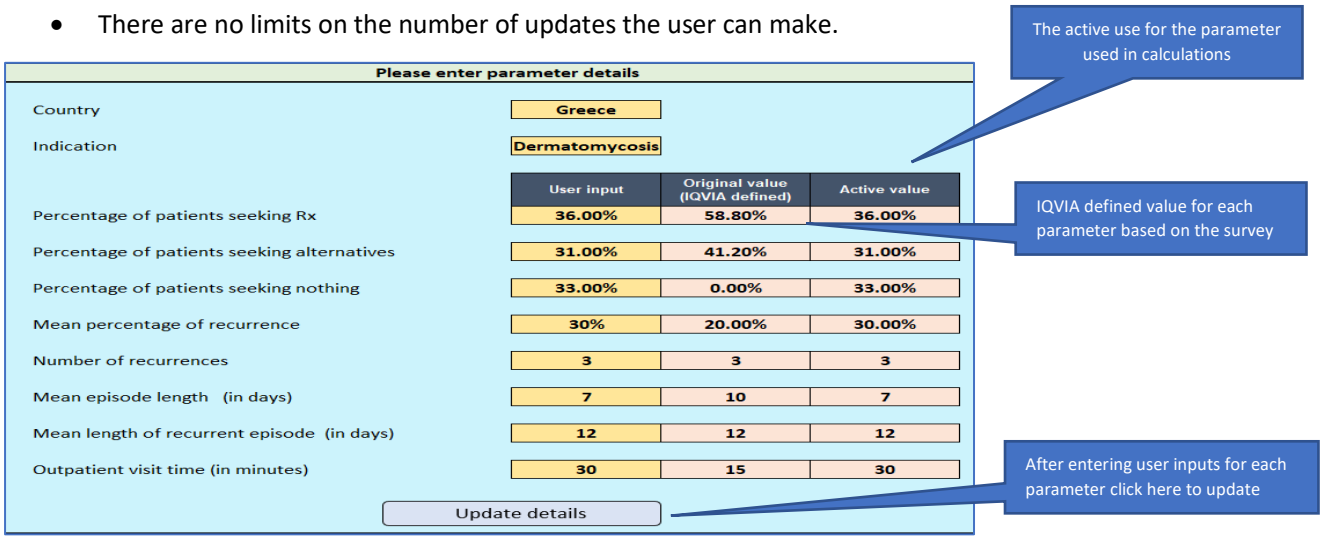
B. Summary report

- This view consolidates data from all different modules and presents it in visual charts.
- The view also provides functionality for the users to interact with the data. For example, the user is able to filter and view a specific cross section of the market by the use of slicers on top of the page.
- This view also provides the functionality to distinguish between vulnerable and general population.

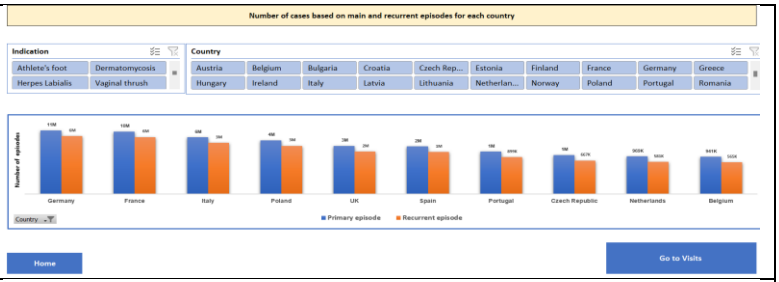
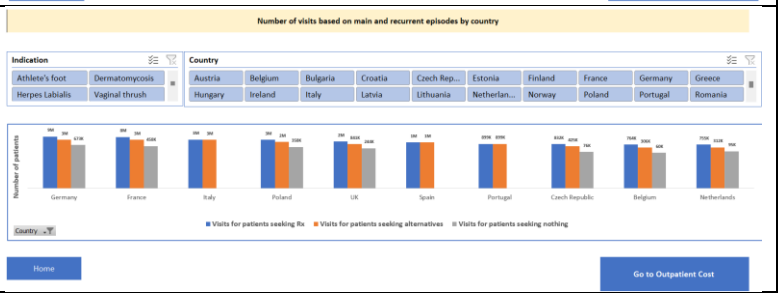


C. Update input parameters

- This view provides a user interactive space that allows users to look at the values of current parameters and update them if necessary.
- This view is designed in a way that the data entered for the new parameters are stored in a proper way so that the original value that was provided by IQVIA is still retained as part of the document.
- There are no limits on the number of updates the user can make.

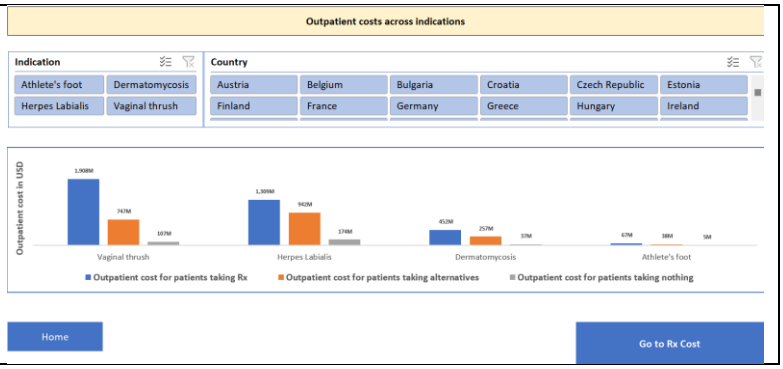


D. Metric level module

Cases This module gives the breakdown of number of primary episodes versus secondary episodes	
Visits This module gives the breakdown of number of visits by patients seeking Rx Vs alternatives Vs nothing for each indication?	

Outpatient cost Vs Rx cost Vs Lost wages

This module gives the breakdown of cost by patients seeking Rx Vs alternatives Vs nothing for each indication.



Annex I: General population summary results

A.1. Survey results

Population type distribution

This section elaborates on the distribution of the general and vulnerable populations surveyed within each country. Vulnerable population is defined as individuals who meet any of the following criteria:

1. Age 60 years and above
2. Household income below the defined threshold
3. Unemployed working status
4. Education level of no formal education or primary education

The survey results indicate the percentage of the total surveyed population that falls under each category:

Table 56 Population type parameters

Country	General population	Vulnerable Population
France	60%	40%
Germany	53%	47%
Italy	77%	23%
Poland	80%	20%
UK	59%	41%

Population parameters

The survey results provide insights on individuals' characteristics, barriers, choices and decision pathways in the event of a reverse switch. The main choices leading to decision pathways reflect the choices made by affected persons, which include:

1. Choosing to obtain Rx for the reverse-switched NPMs
2. Choosing an alternate treatment, other than antifungals or antiviral
3. Doing nothing

General Population: This subset excludes the vulnerable population and represents the average consumer behaviour. The distribution of decision pathways within this group is as follows:

Table 57 General population parameters

Country	Indication	Seek Prescription	Seek Alternative treatment	Do nothing
France	Herpes Labialis	44%	56%	0%
France	Vaginal Thrush	25%	75%	0%
France	Athlete's Foot	29%	71%	0%
France	Dermatomycosis	29%	71%	0%
Germany	Herpes Labialis	27%	73%	0%

Germany	Vaginal Thrush	0%	89%	11%
Germany	Athlete's Foot	38%	50%	13%
Germany	Dermatomycosis	38%	50%	13%
Italy	Herpes Labialis	36%	64%	0%
Italy	Vaginal Thrush	42%	58%	0%
Italy	Athlete's Foot	42%	58%	0%
Italy	Dermatomycosis	42%	58%	0%
Poland	Herpes Labialis	29%	59%	12%
Poland	Vaginal Thrush	19%	81%	0%
Poland	Athlete's Foot	29%	71%	0%
Poland	Dermatomycosis	29%	71%	0%
UK	Herpes Labialis	40%	60%	0%
UK	Vaginal Thrush	23%	69%	8%
UK	Athlete's Foot	38%	54%	8%
UK	Dermatomycosis	38%	54%	8%

A.2. Total burden

Based on the approach and assumption elaborated in the methodology section, the following table details the estimated burden for the four indications across 27 European countries and the United Kingdom across the current and 5 years projection.

Table 58 Estimated burden

Country and indications	Year 1	Year 2	Year 3	Year 4	Year 5
Austria	**739,090**	**790,873**	**847,228**	**908,597**	**975,468**
Athlete's Foot	12,511	12,566	12,622	12,678	12,735
Dermatomycosis	84,692	85,068	85,447	85,826	86,208
Herpes Labialis	357,944	378,028	399,238	421,639	445,296
Vaginal Thrush	283,943	315,211	349,921	388,453	431,229
Belgium	**1,045,458**	**1,040,653**	**1,035,892**	**1,031,176**	**1,026,504**
Athlete's Foot	36,804	36,368	35,938	35,512	35,092
Dermatomycosis	249,146	246,196	243,282	240,402	237,556
Herpes Labialis	341,969	340,740	339,515	338,294	337,078
Vaginal Thrush	417,539	417,349	417,158	416,968	416,778
Bulgaria	**270,147**	**270,444**	**270,794**	**271,197**	**271,651**
Athlete's Foot	3,248	3,278	3,308	3,339	3,370
Dermatomycosis	21,986	22,190	22,397	22,605	22,815
Herpes Labialis	187,551	189,101	190,664	192,239	193,828
Vaginal Thrush	57,363	55,875	54,425	53,013	51,638
Croatia	**410,322**	**411,289**	**412,335**	**413,461**	**414,666**
Athlete's Foot	7,448	7,414	7,380	7,345	7,312
Dermatomycosis	50,420	50,187	49,956	49,725	49,496
Herpes Labialis	122,850	120,848	118,879	116,942	115,037
Vaginal Thrush	229,604	232,840	236,121	239,448	242,822
Cyprus	**122,157**	**112,856**	**116,634**	**120,538**	**124,614**

Athlete's Foot	2,089	1,882	1,909	1,935	1,961
Dermatomycosis	14,144	12,743	12,925	13,101	13,273
Herpes Labialis	60,321	55,029	55,725	56,390	57,063
Vaginal Thrush	45,602	43,202	46,075	49,111	52,318
Czech Republic	**1,234,394**	**1,232,129**	**1,229,966**	**1,227,904**	**1,225,942**
Athlete's Foot	25,756	25,234	24,722	24,221	23,729
Dermatomycosis	174,358	170,821	167,356	163,961	160,635
Herpes Labialis	473,987	472,690	471,396	470,105	468,818
Vaginal Thrush	560,293	563,384	566,492	569,617	572,759
Denmark	**516,771**	**531,480**	**552,464**	**574,636**	**598,261**
Athlete's Foot	7,606	7,752	8,080	8,422	8,778
Dermatomycosis	51,488	52,480	54,697	57,011	59,425
Herpes Labialis	254,903	258,281	260,975	263,565	266,234
Vaginal Thrush	202,774	212,967	228,712	245,638	263,824
Estonia	**114,672**	**110,719**	**106,920**	**103,269**	**99,758**
Athlete's Foot	521	492	464	438	414
Dermatomycosis	3,525	3,328	3,142	2,966	2,801
Herpes Labialis	85,915	82,479	79,181	76,014	72,974
Vaginal Thrush	24,711	24,421	24,134	23,850	23,570
Finland	**386,773**	**383,539**	**380,453**	**377,514**	**374,725**
Athlete's Foot	4,884	5,089	5,302	5,524	5,755
Dermatomycosis	33,064	34,448	35,891	37,393	38,959
Herpes Labialis	196,837	193,039	189,314	185,661	182,079
Vaginal Thrush	151,988	150,963	149,946	148,935	147,932
France	**10,587,556**	**10,563,255**	**10,544,618**	**10,531,656**	**10,524,383**
Athlete's Foot	214,455	219,473	224,609	229,865	235,244
Dermatomycosis	1,451,757	1,485,729	1,520,496	1,556,077	1,592,490
Herpes Labialis	2,646,341	2,717,060	2,789,668	2,864,217	2,940,758
Vaginal Thrush	6,275,003	6,140,993	6,009,845	5,881,497	5,755,890
Germany	**11,758,258**	**11,806,005**	**11,854,297**	**11,903,141**	**11,952,543**

Athlete's Foot	155,150	156,084	157,024	157,969	158,921
Dermatomycosis	1,050,292	1,056,615	1,062,977	1,069,377	1,075,815
Herpes Labialis	6,036,160	6,029,373	6,022,594	6,015,822	6,009,058
Vaginal Thrush	4,516,657	4,563,932	4,611,703	4,659,974	4,708,749
Greece	**590,737**	**577,031**	**563,661**	**550,620**	**537,900**
Athlete's Foot	19,385	18,999	18,622	18,251	17,889
Dermatomycosis	131,226	128,617	126,060	123,553	121,097
Herpes Labialis	422,879	412,061	401,519	391,247	381,238
Vaginal Thrush	17,247	17,353	17,461	17,568	17,677
Hungary	**1,017,199**	**987,442**	**958,563**	**930,536**	**903,335**
Athlete's Foot	25,213	24,391	23,597	22,828	22,084
Dermatomycosis	170,679	165,118	159,738	154,533	149,498
Herpes Labialis	494,091	480,996	468,248	455,838	443,757
Vaginal Thrush	327,216	316,937	306,980	297,337	287,997
Ireland	**780,449**	**816,720**	**855,107**	**895,748**	**938,792**
Athlete's Foot	12,062	12,779	13,538	14,343	15,195
Dermatomycosis	81,652	86,504	91,645	97,092	102,862
Herpes Labialis	387,251	396,225	405,407	414,802	424,414
Vaginal Thrush	299,484	321,212	344,517	369,512	396,320
Italy	**6,219,665**	**6,223,810**	**6,228,381**	**6,233,383**	**6,238,819**
Athlete's Foot	101,462	100,719	99,982	99,250	98,523
Dermatomycosis	686,848	681,820	676,829	671,874	666,956
Herpes Labialis	2,007,716	2,032,919	2,058,439	2,084,279	2,110,443
Vaginal Thrush	3,423,639	3,408,351	3,393,132	3,377,980	3,362,896
Latvia	**170,612**	**173,555**	**176,641**	**179,875**	**183,266**
Athlete's Foot	2,736	2,729	2,721	2,714	2,707
Dermatomycosis	18,520	18,471	18,422	18,373	18,324
Herpes Labialis	89,644	89,735	89,825	89,916	90,007
Vaginal Thrush	59,711	62,621	65,672	68,872	72,228
Lithuania	**302,508**	**313,417**	**324,853**	**336,867**	**349,527**

Athlete's Foot	114	152	204	273	365
Dermatomycosis	769	1,030	1,378	1,845	2,469
Herpes Labialis	192,184	197,050	202,039	207,154	212,399
Vaginal Thrush	109,441	115,186	121,232	127,596	134,294
Luxembourg	**81,949**	**82,878**	**87,279**	**91,933**	**96,890**
Athlete's Foot	1,625	1,640	1,743	1,853	1,969
Dermatomycosis	11,002	11,102	11,802	12,544	13,329
Herpes Labialis	28,967	28,912	29,365	29,798	30,234
Vaginal Thrush	40,354	41,225	44,368	47,738	51,357
Malta	**72,169**	**84,582**	**84,101**	**83,623**	**83,168**
Athlete's Foot	1,430	1,718	1,759	1,801	1,844
Dermatomycosis	9,684	11,630	11,908	12,192	12,481
Herpes Labialis	19,199	23,165	23,364	23,548	23,732
Vaginal Thrush	41,856	48,069	47,069	46,082	45,111
Netherlands	**1,076,751**	**1,102,650**	**1,133,761**	**1,170,175**	**1,212,012**
Athlete's Foot	22,268	23,169	24,106	25,082	26,096
Dermatomycosis	150,745	156,843	163,189	169,791	176,660
Herpes Labialis	310,058	286,156	264,097	243,738	224,949
Vaginal Thrush	593,680	636,481	682,368	731,564	784,306
Poland	**4,770,497**	**5,331,031**	**6,141,481**	**7,308,671**	**8,985,124**
Athlete's Foot	116,141	114,560	113,001	111,462	109,945
Dermatomycosis	786,219	775,516	764,959	754,546	744,274
Herpes Labialis	2,503,831	2,492,980	2,482,175	2,471,417	2,460,706
Vaginal Thrush	1,364,306	1,947,975	2,781,346	3,971,245	5,670,199
Portugal	**1,664,592**	**1,738,629**	**1,816,622**	**1,898,806**	**1,985,431**
Athlete's Foot	25,348	25,745	26,148	26,557	26,973
Dermatomycosis	171,596	174,281	177,009	179,779	182,593
Herpes Labialis	706,411	727,340	748,889	771,076	793,921
Vaginal Thrush	761,237	811,263	864,577	921,394	981,945
Romania	**730,807**	**736,906**	**744,334**	**753,079**	**763,131**

Athlete's Foot	25,947	25,709	25,474	25,241	25,010
Dermatomycosis	175,646	174,039	172,447	170,869	169,305
Herpes Labialis	127,440	118,607	110,386	102,735	95,614
Vaginal Thrush	401,774	418,550	436,028	454,234	473,201
Slovakia	**597,665**	**637,453**	**683,761**	**737,655**	**800,379**
Athlete's Foot	18,332	18,173	18,016	17,860	17,705
Dermatomycosis	124,100	123,025	121,960	120,903	119,856
Herpes Labialis	214,487	215,957	217,436	218,926	220,426
Vaginal Thrush	240,745	280,298	326,349	379,966	442,391
Slovenia	**255,809**	**262,336**	**267,310**	**272,453**	**277,839**
Athlete's Foot	6,391	6,308	6,227	6,146	6,066
Dermatomycosis	43,264	42,704	42,151	41,605	41,066
Herpes Labialis	89,258	91,534	92,046	92,505	92,976
Vaginal Thrush	116,897	121,789	126,887	132,198	137,731
Spain	**2,670,837**	**2,761,600**	**2,855,878**	**2,953,816**	**3,055,566**
Athlete's Foot	8,645	8,582	8,519	8,457	8,395
Dermatomycosis	58,524	58,097	57,672	57,251	56,833
Herpes Labialis	1,430,859	1,466,816	1,503,677	1,541,464	1,580,200
Vaginal Thrush	1,172,809	1,228,106	1,286,010	1,346,644	1,410,137
Sweden	**921,603**	**946,318**	**984,580**	**1,024,870**	**1,067,737**
Athlete's Foot	13,564	13,803	14,400	15,020	15,667
Dermatomycosis	91,822	93,442	97,478	101,680	106,057
Herpes Labialis	454,591	459,878	465,100	470,071	475,157
Vaginal Thrush	361,626	379,195	407,602	438,099	470,855
UK	**2,815,579**	**2,819,443**	**2,824,603**	**2,831,038**	**2,838,732**
Athlete's Foot	69,733	70,441	71,157	71,880	72,611
Dermatomycosis	472,057	476,854	481,699	486,595	491,539
Herpes Labialis	821,915	795,834	770,581	746,129	722,454
Vaginal Thrush	1,451,875	1,476,314	1,501,165	1,526,434	1,552,128

A.3. Excess appointments

The following chart and table details the number of excess appointments per indication in each country for a single year for the general population. We estimate that ~60 million additional visits to doctor's practice will occur as people seek treatment. There will be a shift of self-care patients into the healthcare system as they seek treatment from doctors, either immediately (Scenario 1) or eventually as their symptoms worsen (Scenario 2 & 3).

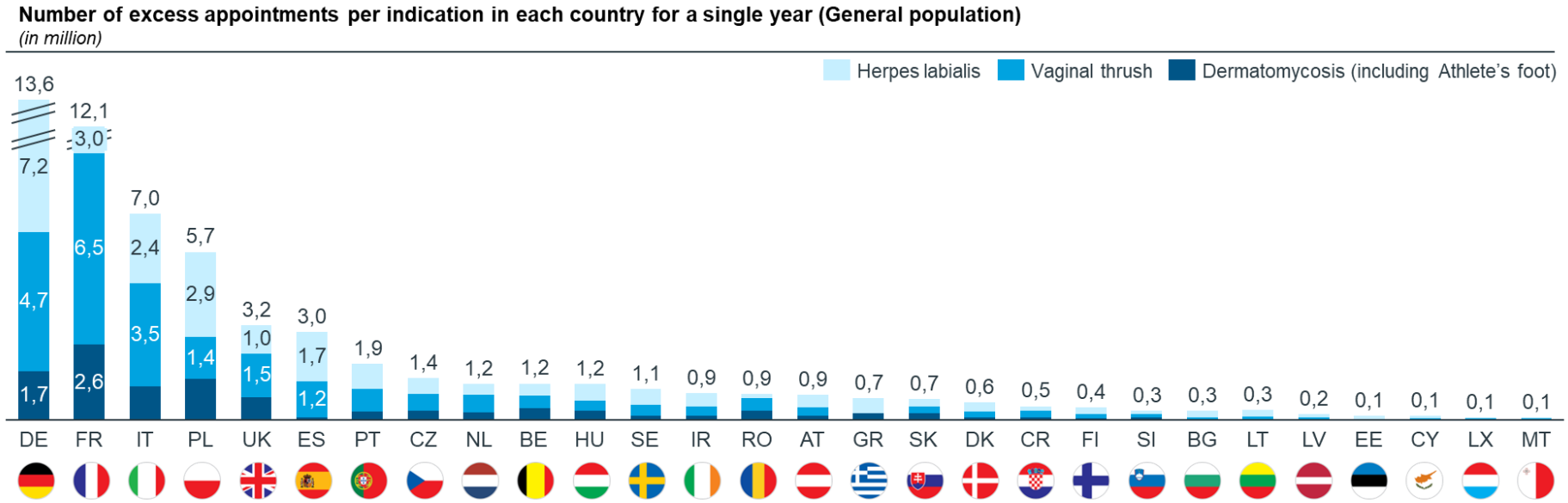


Figure 44 Excess appointments per indication in each country for a single year (General population)

Table 59 Number of excess appointments per indication in each country for a single year (General population)

Country and Indications	Excess appointments for Seeking Rx decision pathways	Excess appointments for Seeking Alternative decision pathways	Excess appointments for Do nothing decision pathways	Total excess appointments
Austria	**680,917**	**134,072**	**43,700**	**858,688**
Athlete's Foot	9,070	4,692	1,564	15,326
Dermatomycosis	76,223	31,759	10,586	118,568
Herpes Labialis	330,610	97,621	-	428,231
Vaginal Thrush	265,014	-	31,549	296,563
Belgium	**956,472**	**200,495**	**82,137**	**1,239,105**
Athlete's Foot	26,683	13,802	4,601	45,085
Dermatomycosis	224,231	93,430	31,143	348,804
Herpes Labialis	315,855	93,264	-	409,119
Vaginal Thrush	389,703	-	46,393	436,096
Bulgaria	**248,909**	**60,613**	**9,528**	**319,050**
Athlete's Foot	2,355	1,218	406	3,979
Dermatomycosis	19,787	8,245	2,748	30,780
Herpes Labialis	173,229	51,150	-	224,379
Vaginal Thrush	53,538	-	6,374	59,912
Croatia	**360,197**	**95,717**	**14,453**	**470,367**
Athlete's Foot	7,714	2,128	-	9,842
Dermatomycosis	64,825	14,406	-	79,231
Herpes Labialis	91,776	36,132	14,453	142,361
Vaginal Thrush	195,881	43,051	-	238,932
Cyprus	**93,588**	**47,508**	**-**	**141,096**
Athlete's Foot	1,767	871	-	2,638
Dermatomycosis	14,852	5,893	-	20,745
Herpes Labialis	49,248	21,543	-	70,791
Vaginal Thrush	27,721	19,201	-	46,922
Czech Republic	**1,026,506**	**407,910**	**-**	**1,434,415**

Athlete's Foot	26,676	7,359	-	34,035
Dermatomycosis	224,175	49,817	-	273,991
Herpes Labialis	334,424	210,661	-	545,085
Vaginal Thrush	441,231	140,073	-	581,304
Denmark	**397,479**	**171,483**	**20,144**	**589,106**
Athlete's Foot	5,938	2,925	585	9,449
Dermatomycosis	49,903	19,803	3,961	73,667
Herpes Labialis	194,236	101,961	-	296,197
Vaginal Thrush	147,401	46,794	15,598	209,794
Estonia	**90,336**	**31,058**	**10,108**	**131,502**
Athlete's Foot	539	149	-	688
Dermatomycosis	4,532	1,007	-	5,539
Herpes Labialis	64,184	25,269	10,108	99,560
Vaginal Thrush	21,082	4,633	-	25,715
Finland	**296,333**	**128,404**	**14,610**	**439,348**
Athlete's Foot	3,813	1,879	376	6,068
Dermatomycosis	32,046	12,717	2,543	47,306
Herpes Labialis	149,990	78,735	-	228,725
Vaginal Thrush	110,483	35,074	11,691	157,249
France	**8,897,364**	**3,220,963**	**-**	**12,118,327**
Athlete's Foot	222,114	61,273	-	283,387
Dermatomycosis	1,866,544	414,788	-	2,281,332
Herpes Labialis	1,867,141	1,176,152	-	3,043,292
Vaginal Thrush	4,941,565	1,568,751	-	6,510,316
Germany	**10,848,509**	**2,098,266**	**652,531**	**13,599,307**
Athlete's Foot	112,484	58,181	19,394	190,059
Dermatomycosis	945,263	393,859	131,286	1,470,408
Herpes Labialis	5,575,217	1,646,225	-	7,221,442
Vaginal Thrush	4,215,546	-	501,851	4,717,397
Greece	**509,919**	**221,045**	**-**	**730,963**
Athlete's Foot	16,396	8,077	-	24,473
Dermatomycosis	137,787	54,678	-	192,465

Herpes Labialis	345,251	151,028	-	496,279
Vaginal Thrush	10,484	7,262	-	17,746
Hungary	**893,829**	**262,643**	**58,128**	**1,214,600**
Athlete's Foot	26,113	7,204	-	33,317
Dermatomycosis	219,445	48,765	-	268,210
Herpes Labialis	369,115	145,321	58,128	572,564
Vaginal Thrush	279,156	61,353	-	340,509
Ireland	**626,544**	**273,758**	**-**	**900,302**
Athlete's Foot	12,492	3,446	-	15,939
Dermatomycosis	104,981	23,329	-	128,310
Herpes Labialis	273,227	172,112	-	445,339
Vaginal Thrush	235,844	74,871	-	310,715
Italy	**4,527,379**	**2,487,036**	**-**	**7,014,416**
Athlete's Foot	85,820	42,276	-	128,096
Dermatomycosis	721,191	286,187	-	1,007,377
Herpes Labialis	1,639,157	717,041	-	2,356,198
Vaginal Thrush	2,081,212	1,441,532	-	3,522,744
Latvia	**144,556**	**43,635**	**10,546**	**198,737**
Athlete's Foot	2,834	782	-	3,615
Dermatomycosis	23,812	5,292	-	29,104
Herpes Labialis	66,969	26,366	10,546	103,882
Vaginal Thrush	50,941	11,196	-	62,137
Lithuania	**238,046**	**77,297**	**22,610**	**337,953**
Athlete's Foot	118	32	-	150
Dermatomycosis	989	220	-	1,209
Herpes Labialis	143,573	56,525	22,610	222,707
Vaginal Thrush	93,367	20,520	-	113,887
Luxembourg	**68,046**	**26,571**	**-**	**94,617**
Athlete's Foot	1,683	464	-	2,148
Dermatomycosis	14,146	3,144	-	17,289
Herpes Labialis	20,438	12,874	-	33,312
Vaginal Thrush	31,779	10,089	-	41,868

Malta	**52,496**	**29,111**	**-**	**81,608**
Athlete's Foot	1,210	596	-	1,806
Dermatomycosis	10,168	4,035	-	14,202
Herpes Labialis	15,675	6,857	-	22,532
Vaginal Thrush	25,444	17,623	-	43,067
Netherlands	**831,316**	**327,570**	**58,976**	**1,217,862**
Athlete's Foot	17,386	8,565	1,713	27,664
Dermatomycosis	146,106	57,979	11,596	215,681
Herpes Labialis	236,264	124,023	-	360,287
Vaginal Thrush	431,560	137,003	45,668	614,230
Poland	**4,165,575**	**1,250,046**	**294,568**	**5,710,189**
Athlete's Foot	120,289	33,183	-	153,472
Dermatomycosis	1,010,853	224,634	-	1,235,487
Herpes Labialis	1,870,509	736,421	294,568	2,901,498
Vaginal Thrush	1,163,924	255,807	-	1,419,731
Portugal	**1,241,102**	**654,870**	**-**	**1,895,972**
Athlete's Foot	21,440	10,562	-	32,002
Dermatomycosis	180,176	71,498	-	251,674
Herpes Labialis	576,734	252,290	-	829,024
Vaginal Thrush	462,752	320,521	-	783,272
Romania	**690,673**	**170,413**	**14,993**	**876,079**
Athlete's Foot	26,873	7,413	-	34,287
Dermatomycosis	225,831	50,185	-	276,015
Herpes Labialis	95,205	37,482	14,993	147,680
Vaginal Thrush	342,763	75,333	-	418,096
Slovakia	**544,164**	**148,919**	**25,234**	**718,317**
Athlete's Foot	18,987	5,238	-	24,225
Dermatomycosis	159,557	35,457	-	195,014
Herpes Labialis	160,234	63,084	25,234	248,553
Vaginal Thrush	205,386	45,140	-	250,525
Slovenia	**217,277**	**83,081**	**-**	**300,358**
Athlete's Foot	6,619	1,826	-	8,445

Dermatomycosis	55,625	12,361	-	67,987
Herpes Labialis	62,976	39,670	-	102,646
Vaginal Thrush	92,056	29,224	-	121,280
Spain	**1,949,901**	**1,032,822**	**-**	**2,982,724**
Athlete's Foot	7,312	3,602	-	10,915
Dermatomycosis	61,450	24,385	-	85,835
Herpes Labialis	1,168,194	511,021	-	1,679,215
Vaginal Thrush	712,944	493,814	-	1,206,758
Sweden	**708,860**	**305,822**	**35,924**	**1,050,606**
Athlete's Foot	10,590	5,217	1,043	16,851
Dermatomycosis	88,997	35,316	7,063	131,377
Herpes Labialis	346,398	181,836	-	528,235
Vaginal Thrush	262,874	83,452	27,817	374,144
UK	**2,193,677**	**872,194**	**153,359**	**3,219,231**
Athlete's Foot	54,445	26,820	5,364	86,629
Dermatomycosis	457,532	181,560	36,312	675,404
Herpes Labialis	626,299	328,766	-	955,065
Vaginal Thrush	1,055,401	335,048	111,683	1,502,132
Grand Total	**43,499,973**	**14,863,323**	**1,521,549**	**59,884,845**

A.4. Emergency visits

In accordance with the approach and assumption elaborated in the methodology section, the following chart and table detail the number of emergency visits across the 28 in-scope countries for a single year. The additional healthcare visits include ~12,1 million visits to the emergency department. Overall, Germany and France having the highest estimates for the additional emergency visits across all countries. However, Spain, Portugal, and the UK are expected to receive the highest proportional increase on additional visits to the emergency department.

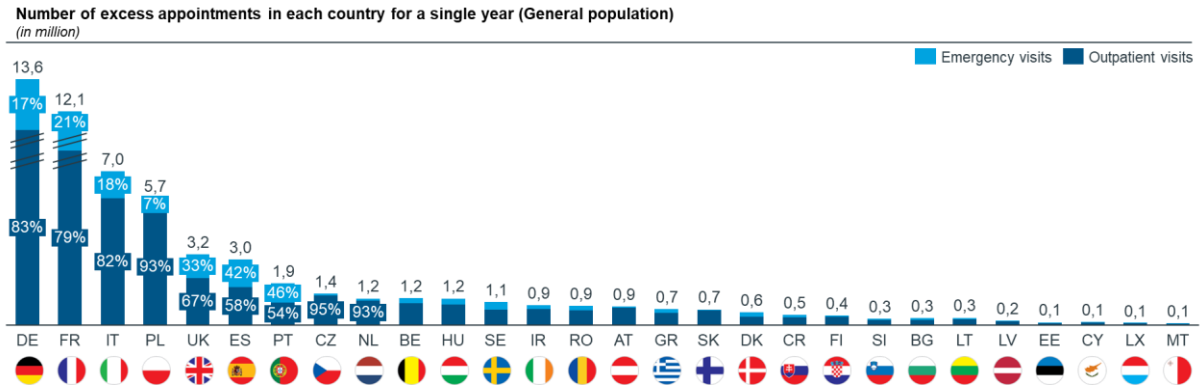


Figure 45 Number of emergency visits in each country for a single year in millions (General Population)

Table 60 Detailed number of emergency visits in each country for a single year in millions (General Population)

Country	Emergency visits	Outpatient visits	Total excess appointments
Austria	59,643	799,045	858,688
Belgium	254,416	984,689	1,239,105
Bulgaria	72,502	246,548	319,050
Croatia	103,338	367,028	470,367
Cyprus	25,840	115,256	141,096
Czech Republic	72,547	1,361,868	1,434,415
Denmark	193,398	395,708	589,106
Estonia	33,327	98,175	131,502
Finland	70,295	369,052	439,348
France	2,567,636	9,550,691	12,118,327
Germany	2,331,075	11,268,231	13,599,307
Greece	159,184	571,779	730,963
Hungary	264,426	950,174	1,214,600
Ireland	179,819	720,483	900,302
Italy	1,235,053	5,779,363	7,014,416
Latvia	31,295	167,443	198,737
Lithuania	62,290	275,663	337,953
Luxembourg	19,884	74,733	94,617
Malta	14,388	67,220	81,608
Netherlands	90,619	1,127,243	1,217,862

Poland	418,624	5,291,565	5,710,189
Portugal	873,934	1,022,038	1,895,972
Romania	200,056	676,022	876,079
Slovakia	54,089	664,228	718,317
Slovenia	63,883	236,476	300,358
Spain	1,261,015	1,721,709	2,982,724
Sweden	344,904	705,702	1,050,606
UK	1,074,725	2,144,506	3,219,231
Grand Total	**12,132,204**	**47,752,641**	**59,884,845**

A.5. Unresolved cases

Unresolved cases represent the number of cases that are expected to exacerbate due to patients delaying appropriate care as they seek an alternative treatment which is available for self-purchase (Non-prescription medicines), or they do nothing at all in the hope that their symptom will self-resolve. Overall, the total number of unresolved cases is 16,384,872. The following chart and tables detail the unresolved cases for each country across the indications.

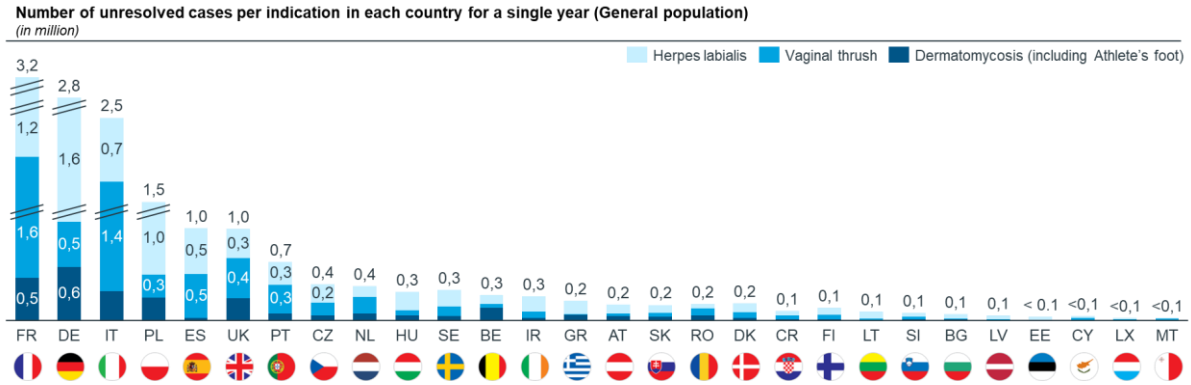


Figure 46 Number of unresolved cases per indication in each country for a single year in millions (General Population)

Table 61 Detailed number of unresolved cases per indication in each country for a single year (General Population)

Country and indications	Seek alternative treatment cases	Do nothing cases	Total unresolved cases
Austria	**134,072**	**43,700**	**177,772**
Athlete's Foot	4,692	1,564	6,255
Dermatomycosis	31,759	10,586	42,346
Herpes Labialis	97,621	-	97,621
Vaginal Thrush	-	31,549	31,549
Belgium	**200,495**	**82,137**	**282,632**
Athlete's Foot	13,802	4,601	18,402

Dermatomycosis	93,430	31,143	124,573
Herpes Labialis	93,264	-	93,264
Vaginal Thrush	-	46,393	46,393
Bulgaria	**60,613**	**9,528**	**70,141**
Athlete's Foot	1,218	406	1,624
Dermatomycosis	8,245	2,748	10,993
Herpes Labialis	51,150	-	51,150
Vaginal Thrush	-	6,374	6,374
Croatia	**95,717**	**14,453**	**110,170**
Athlete's Foot	2,128	-	2,128
Dermatomycosis	14,406	-	14,406
Herpes Labialis	36,132	14,453	50,585
Vaginal Thrush	43,051	-	43,051
Cyprus	**47,508**	**-**	**47,508**
Athlete's Foot	871	-	871
Dermatomycosis	5,893	-	5,893
Herpes Labialis	21,543	-	21,543
Vaginal Thrush	19,201	-	19,201
Czech Republic	**407,910**	**-**	**407,910**
Athlete's Foot	7,359	-	7,359
Dermatomycosis	49,817	-	49,817
Herpes Labialis	210,661	-	210,661
Vaginal Thrush	140,073	-	140,073
Denmark	**171,483**	**20,144**	**191,627**
Athlete's Foot	2,925	585	3,510
Dermatomycosis	19,803	3,961	23,763
Herpes Labialis	101,961	-	101,961
Vaginal Thrush	46,794	15,598	62,392
Estonia	**31,058**	**10,108**	**41,166**
Athlete's Foot	149	-	149
Dermatomycosis	1,007	-	1,007
Herpes Labialis	25,269	10,108	35,377
Vaginal Thrush	4,633	-	4,633
Finland	**128,404**	**14,610**	**143,015**
Athlete's Foot	1,879	376	2,254
Dermatomycosis	12,717	2,543	15,260
Herpes Labialis	78,735	-	78,735
Vaginal Thrush	35,074	11,691	46,765
France	**3,220,963**	**-**	**3,220,963**
Athlete's Foot	61,273	-	61,273
Dermatomycosis	414,788	-	414,788
Herpes Labialis	1,176,152	-	1,176,152
Vaginal Thrush	1,568,751	-	1,568,751
Germany	**2,098,266**	**652,531**	**2,750,797**
Athlete's Foot	58,181	19,394	77,575
Dermatomycosis	393,859	131,286	525,146

Herpes Labialis	1,646,225	-	1,646,225
Vaginal Thrush	-	501,851	501,851
Greece	**221,045**	**-**	**221,045**
Athlete's Foot	8,077	-	8,077
Dermatomycosis	54,678	-	54,678
Herpes Labialis	151,028	-	151,028
Vaginal Thrush	7,262	-	7,262
Hungary	**262,643**	**58,128**	**320,771**
Athlete's Foot	7,204	-	7,204
Dermatomycosis	48,765	-	48,765
Herpes Labialis	145,321	58,128	203,449
Vaginal Thrush	61,353	-	61,353
Ireland	**273,758**	**-**	**273,758**
Athlete's Foot	3,446	-	3,446
Dermatomycosis	23,329	-	23,329
Herpes Labialis	172,112	-	172,112
Vaginal Thrush	74,871	-	74,871
Italy	**2,487,036**	**-**	**2,487,036**
Athlete's Foot	42,276	-	42,276
Dermatomycosis	286,187	-	286,187
Herpes Labialis	717,041	-	717,041
Vaginal Thrush	1,441,532	-	1,441,532
Latvia	**43,635**	**10,546**	**54,181**
Athlete's Foot	782	-	782
Dermatomycosis	5,292	-	5,292
Herpes Labialis	26,366	10,546	36,912
Vaginal Thrush	11,196	-	11,196
Lithuania	**77,297**	**22,610**	**99,907**
Athlete's Foot	32	-	32
Dermatomycosis	220	-	220
Herpes Labialis	56,525	22,610	79,135
Vaginal Thrush	20,520	-	20,520
Luxembourg	**26,571**	**-**	**26,571**
Athlete's Foot	464	-	464
Dermatomycosis	3,144	-	3,144
Herpes Labialis	12,874	-	12,874
Vaginal Thrush	10,089	-	10,089
Malta	**29,111**	**-**	**29,111**
Athlete's Foot	596	-	596
Dermatomycosis	4,035	-	4,035
Herpes Labialis	6,857	-	6,857
Vaginal Thrush	17,623	-	17,623
Netherlands	**327,570**	**58,976**	**386,546**
Athlete's Foot	8,565	1,713	10,278
Dermatomycosis	57,979	11,596	69,574
Herpes Labialis	124,023	-	124,023

Vaginal Thrush	137,003	45,668	182,671
Poland	**1,250,046**	**294,568**	**1,544,614**
Athlete's Foot	33,183	-	33,183
Dermatomycosis	224,634	-	224,634
Herpes Labialis	736,421	294,568	1,030,989
Vaginal Thrush	255,807	-	255,807
Portugal	**654,870**	**-**	**654,870**
Athlete's Foot	10,562	-	10,562
Dermatomycosis	71,498	-	71,498
Herpes Labialis	252,290	-	252,290
Vaginal Thrush	320,521	-	320,521
Romania	**170,413**	**14,993**	**185,406**
Athlete's Foot	7,413	-	7,413
Dermatomycosis	50,185	-	50,185
Herpes Labialis	37,482	14,993	52,475
Vaginal Thrush	75,333	-	75,333
Slovakia	**148,919**	**25,234**	**174,153**
Athlete's Foot	5,238	-	5,238
Dermatomycosis	35,457	-	35,457
Herpes Labialis	63,084	25,234	88,318
Vaginal Thrush	45,140	-	45,140
Slovenia	**83,081**	**-**	**83,081**
Athlete's Foot	1,826	-	1,826
Dermatomycosis	12,361	-	12,361
Herpes Labialis	39,670	-	39,670
Vaginal Thrush	29,224	-	29,224
Spain	**1,032,822**	**-**	**1,032,822**
Athlete's Foot	3,602	-	3,602
Dermatomycosis	24,385	-	24,385
Herpes Labialis	511,021	-	511,021
Vaginal Thrush	493,814	-	493,814
Sweden	**305,822**	**35,924**	**341,746**
Athlete's Foot	5,217	1,043	6,260
Dermatomycosis	35,316	7,063	42,380
Herpes Labialis	181,836	-	181,836
Vaginal Thrush	83,452	27,817	111,270
UK	**872,194**	**153,359**	**1,025,553**
Athlete's Foot	26,820	5,364	32,184
Dermatomycosis	181,560	36,312	217,872
Herpes Labialis	328,766	-	328,766
Vaginal Thrush	335,048	111,683	446,731
Grand Total	**14,863,323**	**1,521,549**	**16,384,872**

A.6. Total costs

Cumulatively, the total costs of reverse-switching for five years amount to €52.6 billion, increasing by 2.06% year-on-year. Approximately 82% of these costs, equivalent to €42.9 billion, are healthcare-related expenditures. Of these healthcare costs, 81% are borne by public payers, followed by 14% by individuals, and 5% by private health insurance. The remaining 18% of the total costs, equivalent to €9.7 billion, are attributed to productivity losses due to disability and individuals seeking care at doctors' practices. The largest costs are attributed to vaginal thrush (€21.4 billion), followed by herpes labialis (€20.5 billion), and dermatomycosis (€10.7 billion).

A.6.1. Projected total costs

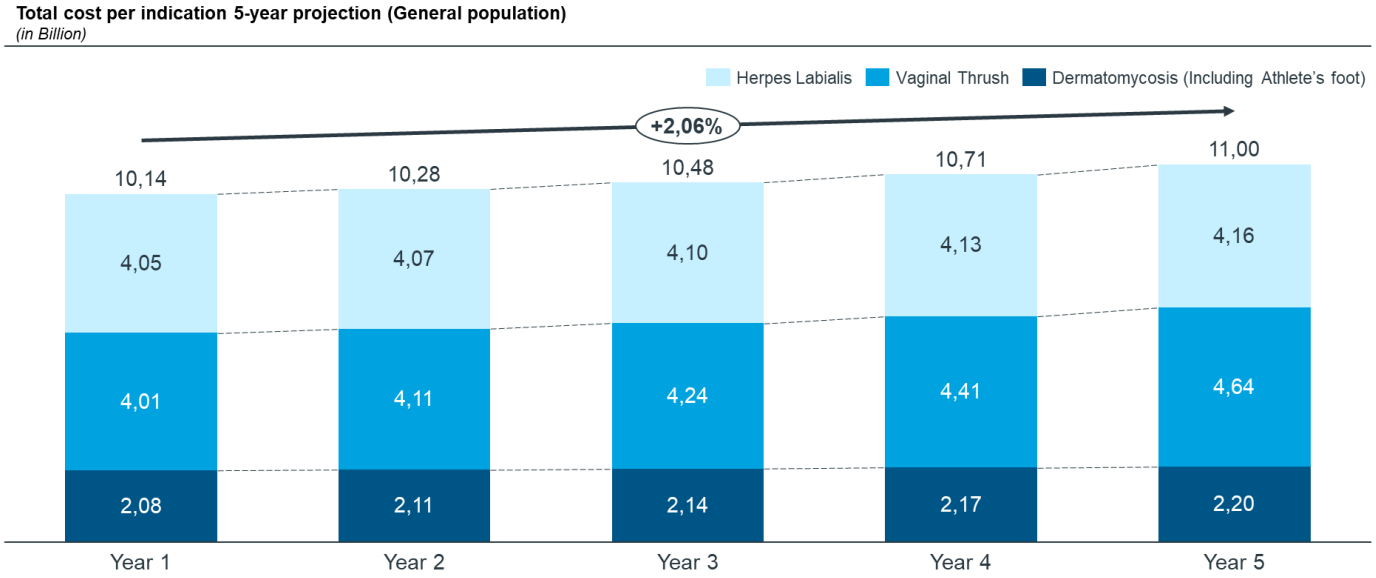


Figure 47 5-year projection of the total cost per indication (General Population)

Table 62 Total cost by indication for 5 years (General Population)

Indications	Year 1	Year 2	Year 3	Year 4	Year 5
Athlete's Foot	205,147,133	207,482,157	210,377,428	213,395,827	216,543,411
Dermatomycosis	1,878,879,560	1,900,467,270	1,927,257,634	1,955,194,357	1,984,334,908
Herpes Labialis	4,049,206,873	4,069,010,226	4,096,644,231	4,126,800,471	4,159,706,087
Vaginal Thrush	4,007,524,738	4,106,469,003	4,241,310,786	4,414,920,650	4,642,077,576

A.6.2. Total costs by country and indications for a single year

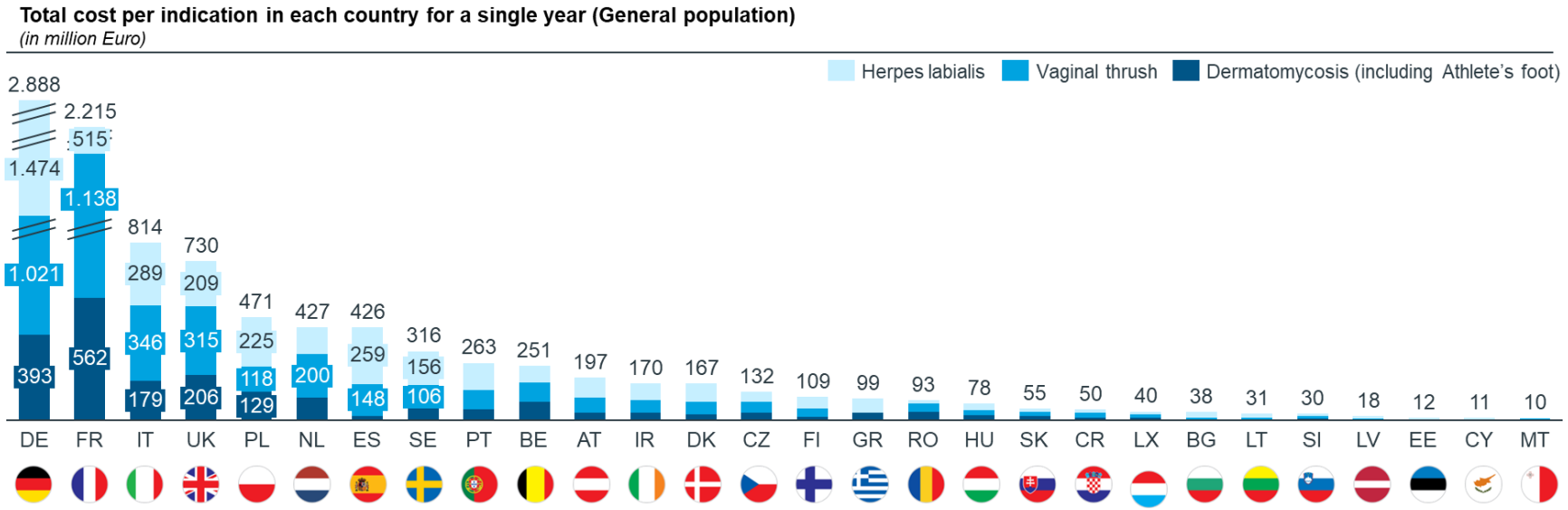


Figure 48 Total cost per indication in each country for a single year (General Population)

Table 63 5-year total costs by country and indication (General Population)

Country and indications	Total Rx cost	Total Outpatient cost	Productivity cost	Total overall cost
Austria	**6,025,116**	**153,809,483**	**37,551,309**	**197,385,907**
Athlete's Foot	122,203	2,451,980	654,329	3,228,512
Dermatomycosis	1,315,639	22,714,028	6,408,619	30,438,286
Herpes Labialis	2,750,001	73,644,298	18,235,722	94,630,021
Vaginal Thrush	1,837,272	54,999,177	12,252,639	69,089,089
Belgium	**10,682,902**	**184,789,553**	**55,036,668**	**250,509,123**
Athlete's Foot	414,895	5,917,100	1,884,481	8,216,477
Dermatomycosis	4,466,754	54,813,337	18,456,972	77,737,063
Herpes Labialis	2,901,765	57,715,214	17,056,034	77,673,013
Vaginal Thrush	2,899,488	66,343,902	17,639,180	86,882,569
Bulgaria	**1,695,651**	**26,574,959**	**9,612,798**	**37,883,408**
Athlete's Foot	24,582	300,826	117,779	443,187
Dermatomycosis	264,652	2,786,713	1,153,552	4,204,917
Herpes Labialis	1,227,864	18,236,351	6,625,158	26,089,373
Vaginal Thrush	178,552	5,251,069	1,716,310	7,145,931
Croatia	**2,191,314**	**34,307,519**	**13,583,811**	**50,082,643**
Athlete's Foot	50,236	765,796	297,193	1,113,224
Dermatomycosis	518,416	6,742,468	2,712,107	9,972,991
Herpes Labialis	466,484	9,310,895	4,097,125	13,874,504
Vaginal Thrush	1,156,178	17,488,360	6,477,387	25,121,925
Cyprus	**810,684**	**7,877,570**	**2,512,441**	**11,200,695**
Athlete's Foot	24,330	161,259	50,269	235,857
Dermatomycosis	257,566	1,461,397	478,503	2,197,466
Herpes Labialis	297,172	4,112,710	1,314,393	5,724,275
Vaginal Thrush	231,616	2,142,203	669,277	3,043,097
Czech Republic	**11,827,432**	**94,853,582**	**25,517,645**	**132,198,659**
Athlete's Foot	270,241	2,509,320	639,370	3,418,931

Dermatomycosis	2,788,788	22,093,363	5,834,736	30,716,887
Herpes Labialis	5,574,916	32,743,475	9,697,503	48,015,895
Vaginal Thrush	3,193,487	37,507,424	9,346,036	50,046,947
Denmark	**4,072,596**	**132,421,507**	**30,906,285**	**167,400,388**
Athlete's Foot	50,552	2,218,651	519,230	2,788,433
Dermatomycosis	540,009	20,337,272	5,018,103	25,895,384
Herpes Labialis	1,642,824	65,445,265	15,799,085	82,887,174
Vaginal Thrush	1,839,210	44,420,319	9,569,868	55,829,397
Estonia	**819,227**	**8,534,986**	**2,474,775**	**11,828,988**
Athlete's Foot	6,313	51,231	13,628	71,171
Dermatomycosis	65,147	451,063	124,363	640,573
Herpes Labialis	569,424	6,231,461	1,879,501	8,680,386
Vaginal Thrush	178,344	1,801,231	457,283	2,436,857
Finland	**4,180,233**	**90,590,870**	**14,096,520**	**108,867,623**
Athlete's Foot	66,889	1,312,786	204,990	1,584,665
Dermatomycosis	714,520	12,033,653	1,981,132	14,729,304
Herpes Labialis	2,076,439	46,565,891	7,500,507	56,142,837
Vaginal Thrush	1,322,385	30,678,540	4,409,892	36,410,817
France	**48,299,548**	**1,780,228,175**	**386,613,660**	**2,215,141,383**
Athlete's Foot	1,115,741	46,048,951	9,675,542	56,840,234
Dermatomycosis	11,514,055	405,439,021	88,296,628	505,249,704
Herpes Labialis	13,709,659	402,917,405	98,403,474	515,030,538
Vaginal Thrush	21,960,093	925,822,798	190,238,016	1,138,020,907
Germany	**80,366,206**	**2,220,333,718**	**586,823,739**	**2,887,523,663**
Athlete's Foot	1,751,892	27,797,331	8,070,766	37,619,989
Dermatomycosis	18,860,829	257,501,873	79,046,631	355,409,334
Herpes Labialis	32,603,073	1,135,276,908	305,856,921	1,473,736,901
Vaginal Thrush	27,150,412	799,757,606	193,849,421	1,020,757,439
Greece	**4,837,698**	**84,353,240**	**9,895,600**	**99,086,538**
Athlete's Foot	159,031	2,823,496	321,082	3,303,609

Dermatomycosis	1,683,584	25,587,692	3,056,352	30,327,628
Herpes Labialis	2,866,425	54,413,041	6,343,899	63,623,365
Vaginal Thrush	128,658	1,529,012	174,266	1,831,936
Hungary	**10,774,808**	**47,118,952**	**20,104,739**	**77,998,498**
Athlete's Foot	330,288	1,391,412	563,463	2,285,164
Dermatomycosis	3,408,457	12,250,720	5,142,029	20,801,207
Herpes Labialis	4,122,018	20,099,573	9,229,105	33,450,697
Vaginal Thrush	2,914,044	13,377,245	5,170,141	21,461,430
Ireland	**5,901,534**	**137,179,877**	**26,509,094**	**169,590,505**
Athlete's Foot	86,340	2,764,025	497,623	3,347,988
Dermatomycosis	891,002	24,335,916	4,541,183	29,768,101
Herpes Labialis	2,601,849	62,923,677	13,167,739	78,693,264
Vaginal Thrush	2,322,343	47,156,260	8,302,550	57,781,152
Italy	**64,162,350**	**589,666,196**	**160,454,792**	**814,283,337**
Athlete's Foot	1,850,298	12,263,954	3,272,921	17,387,173
Dermatomycosis	19,588,200	111,141,038	31,154,638	161,883,876
Herpes Labialis	15,490,716	214,383,816	58,657,187	288,531,719
Vaginal Thrush	27,233,136	251,877,388	67,370,046	346,480,569
Latvia	**1,365,368**	**12,259,571**	**4,287,617**	**17,912,556**
Athlete's Foot	11,766	244,576	80,985	337,327
Dermatomycosis	121,421	2,153,371	739,053	3,013,846
Herpes Labialis	667,460	5,907,274	2,217,910	8,792,644
Vaginal Thrush	564,721	3,954,350	1,249,669	5,768,740
Lithuania	**2,808,025**	**19,268,728**	**8,641,210**	**30,717,963**
Athlete's Foot	1,101	9,783	4,106	14,990
Dermatomycosis	11,359	86,131	37,474	134,963
Herpes Labialis	1,927,234	12,194,209	5,803,888	19,925,331
Vaginal Thrush	868,331	6,978,606	2,795,741	10,642,679
Luxembourg	**963,454**	**30,728,268**	**7,976,825**	**39,668,547**
Athlete's Foot	15,742	777,873	192,214	985,828

Dermatomycosis	162,448	6,848,797	1,754,099	8,765,343
Herpes Labialis	260,642	9,830,529	2,823,530	12,914,701
Vaginal Thrush	524,623	13,271,069	3,206,982	17,002,674
Malta	**826,760**	**7,250,172**	**2,305,329**	**10,382,260**
Athlete's Foot	27,533	182,491	56,887	266,911
Dermatomycosis	291,478	1,653,809	541,504	2,486,790
Herpes Labialis	156,350	2,163,801	691,535	3,011,686
Vaginal Thrush	351,400	3,250,071	1,015,403	4,616,874
Netherlands	**8,490,359**	**369,359,327**	**48,807,027**	**426,656,713**
Athlete's Foot	205,118	8,702,486	1,169,394	10,076,999
Dermatomycosis	2,191,103	79,771,364	11,301,632	93,264,099
Herpes Labialis	2,088,778	106,650,236	14,783,008	123,522,021
Vaginal Thrush	4,005,361	174,235,241	21,552,992	199,793,594
Poland	**28,663,053**	**328,607,991**	**114,110,667**	**471,381,712**
Athlete's Foot	299,734	9,553,065	3,130,618	12,983,416
Dermatomycosis	3,093,145	84,110,173	28,569,252	115,772,570
Herpes Labialis	16,832,896	151,812,808	56,410,332	225,056,036
Vaginal Thrush	8,437,279	83,131,946	26,000,465	117,569,689
Portugal	**14,117,507**	**215,016,687**	**33,572,417**	**262,706,611**
Athlete's Foot	239,231	4,059,975	620,805	4,920,011
Dermatomycosis	2,532,624	36,793,183	5,909,383	45,235,189
Herpes Labialis	7,239,581	99,952,612	15,669,310	122,861,504
Vaginal Thrush	4,106,071	74,210,916	11,372,919	89,689,906
Romania	**5,348,965**	**61,092,383**	**26,068,101**	**92,509,449**
Athlete's Foot	216,650	2,453,902	1,035,322	3,705,874
Dermatomycosis	2,235,748	21,605,439	9,448,099	33,289,285
Herpes Labialis	800,289	8,884,410	4,250,204	13,934,903
Vaginal Thrush	2,096,279	28,148,632	11,334,476	41,579,386
Slovakia	**6,358,504**	**37,091,580**	**11,423,511**	**54,873,595**
Athlete's Foot	172,763	1,317,293	391,357	1,881,412

Dermatomycosis	1,782,853	11,598,132	3,571,426	16,952,412
Herpes Labialis	2,719,113	11,360,971	3,827,093	17,907,177
Vaginal Thrush	1,683,774	12,815,184	3,633,635	18,132,594
Slovenia	**1,446,980**	**22,779,593**	**6,159,678**	**30,386,251**
Athlete's Foot	36,952	705,792	181,557	924,300
Dermatomycosis	381,333	6,214,159	1,656,840	8,252,331
Herpes Labialis	515,936	6,989,365	2,089,835	9,595,136
Vaginal Thrush	512,759	8,870,278	2,231,446	11,614,483
Spain	**19,394,288**	**339,472,547**	**66,932,529**	**425,799,365**
Athlete's Foot	138,882	1,421,313	275,243	1,835,439
Dermatomycosis	1,470,275	12,880,531	2,620,017	16,970,823
Herpes Labialis	9,926,090	207,812,494	41,259,398	258,997,982
Vaginal Thrush	7,859,042	117,358,209	22,777,871	147,995,122
Sweden	**8,069,989**	**262,397,786**	**45,922,152**	**316,389,927**
Athlete's Foot	100,171	4,396,334	771,498	5,268,003
Dermatomycosis	1,070,047	40,299,006	7,456,156	48,825,209
Herpes Labialis	3,255,312	129,682,052	23,475,095	156,412,459
Vaginal Thrush	3,644,459	88,020,395	14,219,403	105,884,257
UK	**19,645,179**	**605,365,223**	**105,381,593**	**730,391,996**
Athlete's Foot	381,282	16,733,763	2,946,964	20,062,008
Dermatomycosis	4,072,921	153,390,082	28,480,978	185,943,980
Herpes Labialis	4,357,689	173,597,537	31,536,103	209,491,330
Vaginal Thrush	10,833,287	261,643,842	42,417,548	314,894,678
Grand Total	**374,145,728**	**7,903,330,044**	**1,863,282,532**	**10,140,758,304**

A.7. Health system related costs

Healthcare system related costs are the sum of prescription (Rx) and outpatient costs. Overall, out of an estimated 10.14 billion Euros in total costs in a single year, approximately 7.87 billion Euros is attributed to healthcare-related spending. These figures are subject to the assumptions in our methodology. The table below details the healthcare system-related costs for each country, with a specific breakdown of Rx and outpatient expenses.

Table 64 Health system related costs country breakdown in a single year

Country	Total Rx cost	Total Outpatient cost	Total health system related cost
Austria	5,913,670	143,303,624	149,217,294
Belgium	10,519,932	175,378,985	185,898,917
Bulgaria	1,687,870	25,128,814	26,816,684
Croatia	2,153,598	31,834,312	33,987,910
Cyprus	806,935	6,827,194	7,634,129
Czech Republic	11,958,242	90,165,716	102,123,958
Denmark	4,059,252	136,313,983	140,373,235
Estonia	814,601	7,915,314	8,729,915
Finland	4,167,442	93,451,210	97,618,651
France	48,968,321	1,752,341,436	1,801,309,757
Germany	78,697,594	2,059,694,300	2,138,391,894
Greece	4,862,796	72,823,017	77,685,814
Hungary	10,667,777	43,726,708	54,394,485
Ireland	5,982,608	126,507,526	132,490,134
Italy	63,526,071	522,799,132	586,325,204
Latvia	1,349,031	11,374,224	12,723,255
Lithuania	2,786,351	17,868,186	20,654,537
Luxembourg	978,744	29,447,739	30,426,484
Malta	818,137	6,515,495	7,333,632
Netherlands	8,461,523	373,024,833	381,486,355
Poland	28,422,496	304,942,996	333,365,492
Portugal	14,069,641	187,559,029	201,628,670
Romania	5,269,225	56,714,232	61,983,457
Slovakia	6,299,002	34,427,585	40,726,586
Slovenia	1,464,464	21,841,690	23,306,153
Spain	19,262,676	285,365,482	304,628,158
Sweden	8,043,548	270,110,862	278,154,410
UK	19,576,318	610,800,985	630,377,303
Grand Total	**371,587,867**	**7,498,204,608**	**7,869,792,475**

A.8. Costs to payers

This section details the distribution of healthcare costs among three primary stakeholders: public payers, individuals, and private insurance providers. On average, across all countries, public payers bear the majority of healthcare costs, accounting for approximately 81% of the total expenses. Individuals cover about 14% of healthcare costs through out-of-pocket expenses, co-payments, and deductibles. Private health insurance providers contribute the remaining 5%, offering supplementary coverage to alleviate financial pressure on both public payers and individuals.

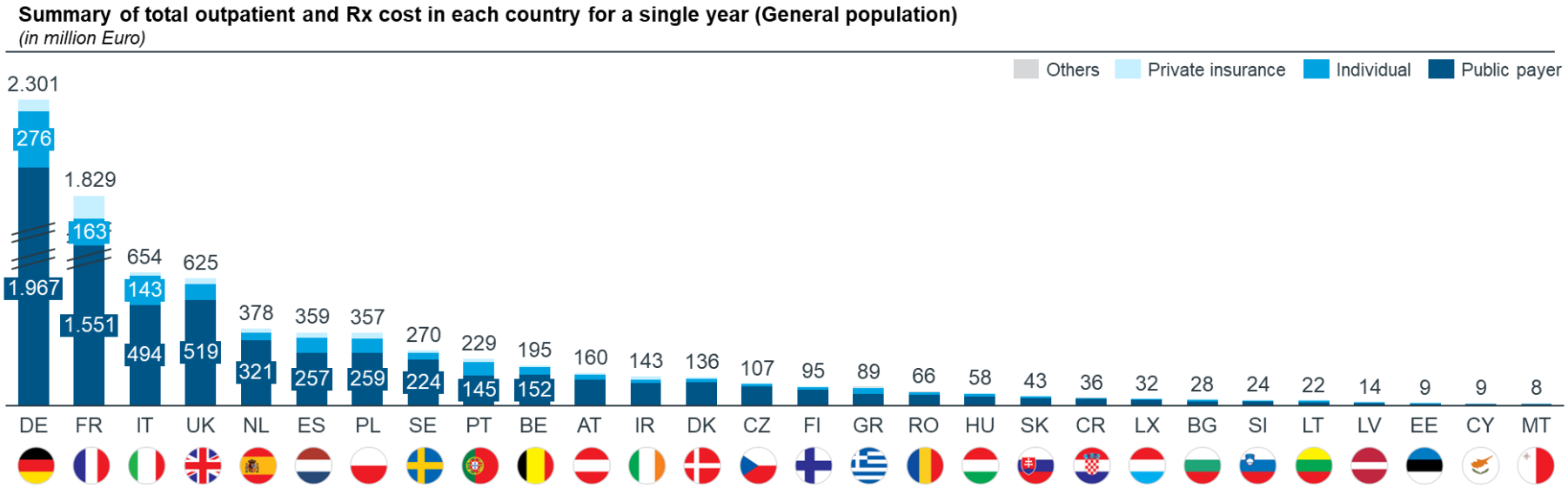


Figure 49 Total health system related cost in each country for a single year (General Population)

Table 65 Healthcare cost payers breakdown for each country for a single year (General Population)

Country	Public Payer Share	Individual share	Private Insurance share	Others	Total health system related cost
Austria	125,150,490	25,253,868	9,430,241	-	159,834,599
Belgium	151,686,627	34,989,567	8,796,261	-	195,472,455
Bulgaria	18,291,084	9,612,007	367,518	-	28,270,609
Croatia	31,024,009	3,284,895	1,861,440	328,488.51	36,498,833
Cyprus	6,559,631	1,902,727	225,895	-	8,688,254
Czech Republic	92,172,396	13,548,489	960,129	-	106,681,014
Denmark	113,290,105	17,334,752	5,869,247	-	136,494,103
Estonia	7,127,911	2,067,281	159,022	-	9,354,214
Finland	75,627,341	15,258,147	3,885,615	-	94,771,103
France	1,550,591,518	162,738,956	115,197,248	-	1,828,527,723
Germany	1,967,098,442	276,083,984	57,517,498	-	2,300,699,924
Greece	55,387,572	29,700,583	3,924,401	178,382.23	89,190,938
Hungary	41,972,975	14,241,865	1,678,919	-	57,893,760
Ireland	110,745,013	15,309,711	17,026,687	-	143,081,411
Italy	493,640,554	143,188,449	16,999,542	-	653,828,545
Latvia	9,455,708	3,678,734	490,498	-	13,624,939
Lithuania	15,122,576	6,667,180	286,998	-	22,076,753
Luxembourg	26,304,129	4,024,849	1,362,744	-	31,691,721
Malta	6,098,083	1,768,848	210,000	-	8,076,932
Netherlands	320,794,386	35,517,869	21,537,431	-	377,849,686
Poland	259,021,508	70,739,666	27,509,870	-	357,271,045
Portugal	144,812,812	66,448,914	17,872,468	-	229,134,194
Romania	51,824,249	13,952,683	465,089	199,326.44	66,441,348
Slovakia	34,629,717	8,429,316	391,051	-	43,450,084
Slovenia	17,854,985	3,125,228	3,246,361	-	24,226,573
Spain	256,948,657	75,362,033	26,556,146	-	358,866,836
Sweden	224,488,252	34,349,409	11,630,115	-	270,467,775
UK	518,758,631	79,376,324	26,875,448	-	625,010,402

Grand Total	**6,726,479,358**	**1,167,956,335**	**382,333,881**	**706,197.18**	**8,277,475,772**

A.9. Productivity costs

The Productivity cost highlights the economic impact of wage losses due to time missed from work, whether from physician consultations or the severity of the disease. Based on our methodology and assumptions made, the total productivity cost is estimated at 1.8 billion Euros. The following figure and table highlight the detailed breakdown per country and indications.

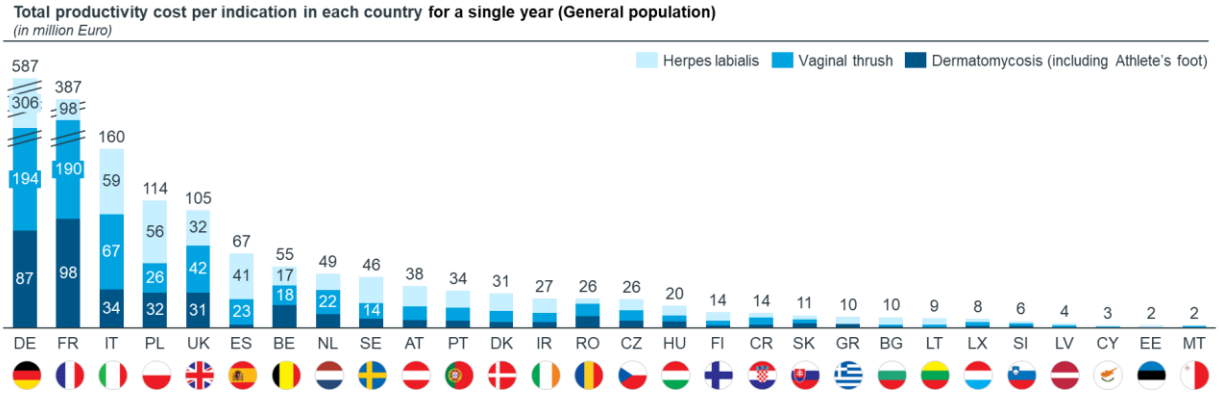


Figure 50 Total cost per indication in each country for a single year (General Population)

Table 66 Productivity cost breakdown per country and indications in a single year (General Population)

Country and indications	Total Productivity cost
Austria	**37,551,309**
Athlete's Foot	654,329
Dermatomycosis	6,408,619
Herpes Labialis	18,235,722
Vaginal Thrush	12,252,639
Belgium	**55,036,668**
Athlete's Foot	1,884,481
Dermatomycosis	18,456,972
Herpes Labialis	17,056,034
Vaginal Thrush	17,639,180
Bulgaria	**9,612,798**
Athlete's Foot	117,779
Dermatomycosis	1,153,552
Herpes Labialis	6,625,158
Vaginal Thrush	1,716,310
Croatia	**13,583,811**
Athlete's Foot	297,193
Dermatomycosis	2,712,107
Herpes Labialis	4,097,125
Vaginal Thrush	6,477,387
Cyprus	**2,512,441**
Athlete's Foot	50,269

Dermatomycosis	478,503
Herpes Labialis	1,314,393
Vaginal Thrush	669,277
Czech Republic	**25,517,645**
Athlete's Foot	639,370
Dermatomycosis	5,834,736
Herpes Labialis	9,697,503
Vaginal Thrush	9,346,036
Denmark	**30,906,285**
Athlete's Foot	519,230
Dermatomycosis	5,018,103
Herpes Labialis	15,799,085
Vaginal Thrush	9,569,868
Estonia	**2,474,775**
Athlete's Foot	13,628
Dermatomycosis	124,363
Herpes Labialis	1,879,501
Vaginal Thrush	457,283
Finland	**14,096,520**
Athlete's Foot	204,990
Dermatomycosis	1,981,132
Herpes Labialis	7,500,507
Vaginal Thrush	4,409,892
France	**386,613,660**
Athlete's Foot	9,675,542
Dermatomycosis	88,296,628
Herpes Labialis	98,403,474
Vaginal Thrush	190,238,016
Germany	**586,823,739**
Athlete's Foot	8,070,766
Dermatomycosis	79,046,631
Herpes Labialis	305,856,921
Vaginal Thrush	193,849,421
Greece	**9,895,600**
Athlete's Foot	321,082
Dermatomycosis	3,056,352
Herpes Labialis	6,343,899
Vaginal Thrush	174,266
Hungary	**20,104,739**
Athlete's Foot	563,463
Dermatomycosis	5,142,029
Herpes Labialis	9,229,105
Vaginal Thrush	5,170,141
Ireland	**26,509,094**
Athlete's Foot	497,623
Dermatomycosis	4,541,183

Herpes Labialis	13,167,739
Vaginal Thrush	8,302,550
Italy	**160,454,792**
Athlete's Foot	3,272,921
Dermatomycosis	31,154,638
Herpes Labialis	58,657,187
Vaginal Thrush	67,370,046
Latvia	**4,287,617**
Athlete's Foot	80,985
Dermatomycosis	739,053
Herpes Labialis	2,217,910
Vaginal Thrush	1,249,669
Lithuania	**8,641,210**
Athlete's Foot	4,106
Dermatomycosis	37,474
Herpes Labialis	5,803,888
Vaginal Thrush	2,795,741
Luxembourg	**7,976,825**
Athlete's Foot	192,214
Dermatomycosis	1,754,099
Herpes Labialis	2,823,530
Vaginal Thrush	3,206,982
Malta	**2,305,329**
Athlete's Foot	56,887
Dermatomycosis	541,504
Herpes Labialis	691,535
Vaginal Thrush	1,015,403
Netherlands	**48,807,027**
Athlete's Foot	1,169,394
Dermatomycosis	11,301,632
Herpes Labialis	14,783,008
Vaginal Thrush	21,552,992
Poland	**114,110,667**
Athlete's Foot	3,130,618
Dermatomycosis	28,569,252
Herpes Labialis	56,410,332
Vaginal Thrush	26,000,465
Portugal	**33,572,417**
Athlete's Foot	620,805
Dermatomycosis	5,909,383
Herpes Labialis	15,669,310
Vaginal Thrush	11,372,919
Romania	**26,068,101**
Athlete's Foot	1,035,322
Dermatomycosis	9,448,099
Herpes Labialis	4,250,204

Vaginal Thrush	11,334,476
Slovakia	**11,423,511**
Athlete's Foot	391,357
Dermatomycosis	3,571,426
Herpes Labialis	3,827,093
Vaginal Thrush	3,633,635
Slovenia	**6,159,678**
Athlete's Foot	181,557
Dermatomycosis	1,656,840
Herpes Labialis	2,089,835
Vaginal Thrush	2,231,446
Spain	**66,932,529**
Athlete's Foot	275,243
Dermatomycosis	2,620,017
Herpes Labialis	41,259,398
Vaginal Thrush	22,777,871
Sweden	**45,922,152**
Athlete's Foot	771,498
Dermatomycosis	7,456,156
Herpes Labialis	23,475,095
Vaginal Thrush	14,219,403
UK	**105,381,593**
Athlete's Foot	2,946,964
Dermatomycosis	28,480,978
Herpes Labialis	31,536,103
Vaginal Thrush	42,417,548
Grand Total	**1,863,282,532**

A.10. Volume impact

The volume impact results reveal that reverse-switching may not reduce the use of antifungal and antiviral medicines. The volume is estimated based on IQVIA NPM sales data and the following factors:

- Share of patient population who seek Rx, seek alternative treatment or do nothing
    - Share of patient population who develop recurrences
    - Severity and chronicity of conditions
    - Number of doctor's visits and refills
- We assumed that the delay in appropriate treatment for patients who seek alternative treatment or do nothing, causes worsening and chronification of conditions, which increases the use of antiviral and antifungal medicines.
- We did not account for potential changes in treatment regime, for example from topical to oral formulation, in the event of worsening or chronification of conditions.

Based on these assumptions and factors, the volume impact of herpes labialis shows a potential 67% increase, with consumption rising from 28.5 million units to 44.7 million units. Dermatomycosis, including

Athlete's foot, potentially experiences the most significant increase of 177%, with consumption jumping from 13.1 million units to 36.3 million units. These potential increases are attributed to those who seek alternative treatment or do nothing as they will delay appropriate treatment, resulting in worsening of symptoms and eventual need for a doctor's appointment as well as prescription for a more severe condition. Reverse-switch could also lead to a shift in prescribing practices, for instance, from prescribing topical/external treatment to oral/systemic treatment.

Conversely, the volume impact for Vaginal Thrush shows a potential of 13% decrease, with consumption dropping from 44.7 million units to 39.1 million units. This decline is attributed to several factors. First, most patients with vaginal thrush are women, and a majority of them seek prescription treatments rather than alternative treatments or doing nothing. Second, those who seek prescriptions tend to do so immediately, leading to better-managed conditions and fewer recurrences. Consequently, the lower recurrence rate results in a negative volume impact for vaginal thrush.

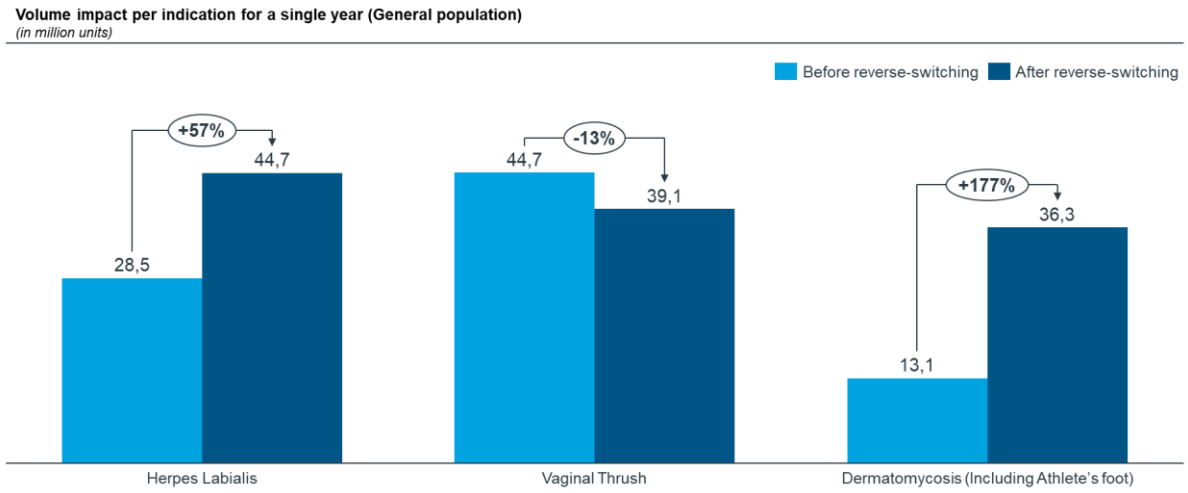


Figure 51 Volume impact per indication for a single year in million units (General Population)

These numbers show that, contrary to expectations, reverse-switching may not reduce the volume of antiviral and antifungal medicines use.

Table 67 Volume impact of reverse switch in a single year details (General Population)

	Herpes Labialis	Vaginal Thrush	Dermatomycosis (Including Athlete's foot)
Before reverse-switching	28,463,923	44,715,672	13,087,369
After reverse-switching	44,670,850	39,115,326	36,270,532

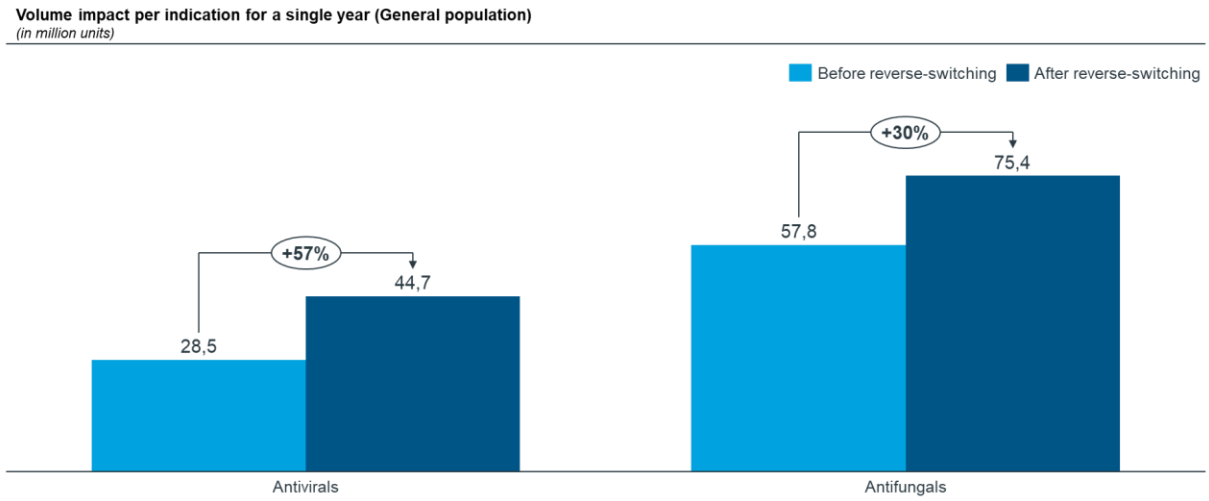


Figure 52 Volume impact for a single year for Antivirals and Antifungals (General Population)

	Antivirals	Antifungals
Before reverse-switching	21,065,559	35,450,349
After reverse-switching	33,198,414	46,761,198

Annex II: Vulnerable population summary results

A.1. Survey results

Population type distribution

This section elaborates on the distribution of the general and vulnerable populations surveyed within each country. Vulnerable population is defined as individuals who meet any of the following criteria:

5. Age 60 years and above
6. Household income below the defined threshold
7. Unemployed working status
8. Education level of no formal education or primary education

The survey results indicate the percentage of the total surveyed population that falls under each category:

Table 68 Population type parameters

Country	General population	Vulnerable Population
France	60%	40%
Germany	53%	47%
Italy	77%	23%
Poland	80%	20%
UK	59%	41%

Population parameters

The survey results provide insights on individuals' characteristics, barriers, choices and decision pathways in the event of a reverse switch. The main choices leading to decision pathways reflect the choices made by affected persons, which include:

1. Choosing to obtain Rx for the reverse-switched NPMs
2. Choosing an alternate treatment other than antifungals and antivirals
3. Doing nothing

Vulnerable Population: The distribution of decision pathways within this group is as follows:

Table 69 Vulnerable population parameters

Country	Indication	Seek Prescription	Seek Alternative treatment	Do nothing
France	Herpes Labialis	57%	14%	29%
France	Vaginal Thrush	14%	86%	0%
France	Athlete's Foot	0%	75%	25%
France	Dermatomycosis	0%	75%	25%

Germany	Herpes Labialis	25%	63%	13%
Germany	Vaginal Thrush	40%	60%	0%
Germany	Athlete's Foot	36%	64%	0%
Germany	Dermatomycosis	36%	64%	0%
Italy	Herpes Labialis	100%	0%	0%
Italy	Vaginal Thrush	100%	0%	0%
Italy	Athlete's Foot	40%	60%	0%
Italy	Dermatomycosis	40%	60%	0%
Poland	Herpes Labialis	100%	0%	0%
Poland	Vaginal Thrush	25%	50%	25%
Poland	Athlete's Foot	75%	25%	0%
Poland	Dermatomycosis	75%	25%	0%
UK	Herpes Labialis	13%	75%	13%
UK	Vaginal Thrush	17%	67%	17%
UK	Athlete's Foot	57%	43%	0%
UK	Dermatomycosis	57%	43%	0%

A.2. Total burden

Based on the approach and assumption elaborated in the methodology section, the following table details the estimated burden for the four indications across 27 European countries and the United Kingdom across the current and 5 years projection.

Table 70 Estimated burden

Country and indications	Year 1	Year 2	Year 3	Year 4	Year 5
Austria	**739,090**	**790,873**	**847,228**	**908,597**	**975,468**
Athlete's Foot	12,511	12,566	12,622	12,678	12,735
Dermatomycosis	84,692	85,068	85,447	85,826	86,208
Herpes Labialis	357,944	378,028	399,238	421,639	445,296
Vaginal Thrush	283,943	315,211	349,921	388,453	431,229
Belgium	**1,045,458**	**1,040,653**	**1,035,892**	**1,031,176**	**1,026,504**
Athlete's Foot	36,804	36,368	35,938	35,512	35,092
Dermatomycosis	249,146	246,196	243,282	240,402	237,556
Herpes Labialis	341,969	340,740	339,515	338,294	337,078
Vaginal Thrush	417,539	417,349	417,158	416,968	416,778
Bulgaria	**270,147**	**270,444**	**270,794**	**271,197**	**271,651**
Athlete's Foot	3,248	3,278	3,308	3,339	3,370
Dermatomycosis	21,986	22,190	22,397	22,605	22,815
Herpes Labialis	187,551	189,101	190,664	192,239	193,828
Vaginal Thrush	57,363	55,875	54,425	53,013	51,638
Croatia	**410,322**	**411,289**	**412,335**	**413,461**	**414,666**
Athlete's Foot	7,448	7,414	7,380	7,345	7,312
Dermatomycosis	50,420	50,187	49,956	49,725	49,496
Herpes Labialis	122,850	120,848	118,879	116,942	115,037
Vaginal Thrush	229,604	232,840	236,121	239,448	242,822
Cyprus	**122,157**	**112,856**	**116,634**	**120,538**	**124,614**

Athlete's Foot	2,089	1,882	1,909	1,935	1,961
Dermatomycosis	14,144	12,743	12,925	13,101	13,273
Herpes Labialis	60,321	55,029	55,725	56,390	57,063
Vaginal Thrush	45,602	43,202	46,075	49,111	52,318
Czech Republic	**1,234,394**	**1,232,129**	**1,229,966**	**1,227,904**	**1,225,942**
Athlete's Foot	25,756	25,234	24,722	24,221	23,729
Dermatomycosis	174,358	170,821	167,356	163,961	160,635
Herpes Labialis	473,987	472,690	471,396	470,105	468,818
Vaginal Thrush	560,293	563,384	566,492	569,617	572,759
Denmark	**516,771**	**531,480**	**552,464**	**574,636**	**598,261**
Athlete's Foot	7,606	7,752	8,080	8,422	8,778
Dermatomycosis	51,488	52,480	54,697	57,011	59,425
Herpes Labialis	254,903	258,281	260,975	263,565	266,234
Vaginal Thrush	202,774	212,967	228,712	245,638	263,824
Estonia	**114,672**	**110,719**	**106,920**	**103,269**	**99,758**
Athlete's Foot	521	492	464	438	414
Dermatomycosis	3,525	3,328	3,142	2,966	2,801
Herpes Labialis	85,915	82,479	79,181	76,014	72,974
Vaginal Thrush	24,711	24,421	24,134	23,850	23,570
Finland	**386,773**	**383,539**	**380,453**	**377,514**	**374,725**
Athlete's Foot	4,884	5,089	5,302	5,524	5,755
Dermatomycosis	33,064	34,448	35,891	37,393	38,959
Herpes Labialis	196,837	193,039	189,314	185,661	182,079
Vaginal Thrush	151,988	150,963	149,946	148,935	147,932
France	**10,587,556**	**10,563,255**	**10,544,618**	**10,531,656**	**10,524,383**
Athlete's Foot	214,455	219,473	224,609	229,865	235,244
Dermatomycosis	1,451,757	1,485,729	1,520,496	1,556,077	1,592,490
Herpes Labialis	2,646,341	2,717,060	2,789,668	2,864,217	2,940,758
Vaginal Thrush	6,275,003	6,140,993	6,009,845	5,881,497	5,755,890
Germany	**11,758,258**	**11,806,005**	**11,854,297**	**11,903,141**	**11,952,543**

Athlete's Foot	155,150	156,084	157,024	157,969	158,921
Dermatomycosis	1,050,292	1,056,615	1,062,977	1,069,377	1,075,815
Herpes Labialis	6,036,160	6,029,373	6,022,594	6,015,822	6,009,058
Vaginal Thrush	4,516,657	4,563,932	4,611,703	4,659,974	4,708,749
Greece	**590,737**	**577,031**	**563,661**	**550,620**	**537,900**
Athlete's Foot	19,385	18,999	18,622	18,251	17,889
Dermatomycosis	131,226	128,617	126,060	123,553	121,097
Herpes Labialis	422,879	412,061	401,519	391,247	381,238
Vaginal Thrush	17,247	17,353	17,461	17,568	17,677
Hungary	**1,017,199**	**987,442**	**958,563**	**930,536**	**903,335**
Athlete's Foot	25,213	24,391	23,597	22,828	22,084
Dermatomycosis	170,679	165,118	159,738	154,533	149,498
Herpes Labialis	494,091	480,996	468,248	455,838	443,757
Vaginal Thrush	327,216	316,937	306,980	297,337	287,997
Ireland	**780,449**	**816,720**	**855,107**	**895,748**	**938,792**
Athlete's Foot	12,062	12,779	13,538	14,343	15,195
Dermatomycosis	81,652	86,504	91,645	97,092	102,862
Herpes Labialis	387,251	396,225	405,407	414,802	424,414
Vaginal Thrush	299,484	321,212	344,517	369,512	396,320
Italy	**6,219,665**	**6,223,810**	**6,228,381**	**6,233,383**	**6,238,819**
Athlete's Foot	101,462	100,719	99,982	99,250	98,523
Dermatomycosis	686,848	681,820	676,829	671,874	666,956
Herpes Labialis	2,007,716	2,032,919	2,058,439	2,084,279	2,110,443
Vaginal Thrush	3,423,639	3,408,351	3,393,132	3,377,980	3,362,896
Latvia	**170,612**	**173,555**	**176,641**	**179,875**	**183,266**
Athlete's Foot	2,736	2,729	2,721	2,714	2,707
Dermatomycosis	18,520	18,471	18,422	18,373	18,324
Herpes Labialis	89,644	89,735	89,825	89,916	90,007
Vaginal Thrush	59,711	62,621	65,672	68,872	72,228
Lithuania	**302,508**	**313,417**	**324,853**	**336,867**	**349,527**

Athlete's Foot	114	152	204	273	365
Dermatomycosis	769	1,030	1,378	1,845	2,469
Herpes Labialis	192,184	197,050	202,039	207,154	212,399
Vaginal Thrush	109,441	115,186	121,232	127,596	134,294
Luxembourg	**81,949**	**82,878**	**87,279**	**91,933**	**96,890**
Athlete's Foot	1,625	1,640	1,743	1,853	1,969
Dermatomycosis	11,002	11,102	11,802	12,544	13,329
Herpes Labialis	28,967	28,912	29,365	29,798	30,234
Vaginal Thrush	40,354	41,225	44,368	47,738	51,357
Malta	**72,169**	**84,582**	**84,101**	**83,623**	**83,168**
Athlete's Foot	1,430	1,718	1,759	1,801	1,844
Dermatomycosis	9,684	11,630	11,908	12,192	12,481
Herpes Labialis	19,199	23,165	23,364	23,548	23,732
Vaginal Thrush	41,856	48,069	47,069	46,082	45,111
Netherlands	**1,076,751**	**1,102,650**	**1,133,761**	**1,170,175**	**1,212,012**
Athlete's Foot	22,268	23,169	24,106	25,082	26,096
Dermatomycosis	150,745	156,843	163,189	169,791	176,660
Herpes Labialis	310,058	286,156	264,097	243,738	224,949
Vaginal Thrush	593,680	636,481	682,368	731,564	784,306
Poland	**4,770,497**	**5,331,031**	**6,141,481**	**7,308,671**	**8,985,124**
Athlete's Foot	116,141	114,560	113,001	111,462	109,945
Dermatomycosis	786,219	775,516	764,959	754,546	744,274
Herpes Labialis	2,503,831	2,492,980	2,482,175	2,471,417	2,460,706
Vaginal Thrush	1,364,306	1,947,975	2,781,346	3,971,245	5,670,199
Portugal	**1,664,592**	**1,738,629**	**1,816,622**	**1,898,806**	**1,985,431**
Athlete's Foot	25,348	25,745	26,148	26,557	26,973
Dermatomycosis	171,596	174,281	177,009	179,779	182,593
Herpes Labialis	706,411	727,340	748,889	771,076	793,921
Vaginal Thrush	761,237	811,263	864,577	921,394	981,945
Romania	**730,807**	**736,906**	**744,334**	**753,079**	**763,131**

Athlete's Foot	25,947	25,709	25,474	25,241	25,010
Dermatomycosis	175,646	174,039	172,447	170,869	169,305
Herpes Labialis	127,440	118,607	110,386	102,735	95,614
Vaginal Thrush	401,774	418,550	436,028	454,234	473,201
Slovakia	**597,665**	**637,453**	**683,761**	**737,655**	**800,379**
Athlete's Foot	18,332	18,173	18,016	17,860	17,705
Dermatomycosis	124,100	123,025	121,960	120,903	119,856
Herpes Labialis	214,487	215,957	217,436	218,926	220,426
Vaginal Thrush	240,745	280,298	326,349	379,966	442,391
Slovenia	**255,809**	**262,336**	**267,310**	**272,453**	**277,839**
Athlete's Foot	6,391	6,308	6,227	6,146	6,066
Dermatomycosis	43,264	42,704	42,151	41,605	41,066
Herpes Labialis	89,258	91,534	92,046	92,505	92,976
Vaginal Thrush	116,897	121,789	126,887	132,198	137,731
Spain	**2,670,837**	**2,761,600**	**2,855,878**	**2,953,816**	**3,055,566**
Athlete's Foot	8,645	8,582	8,519	8,457	8,395
Dermatomycosis	58,524	58,097	57,672	57,251	56,833
Herpes Labialis	1,430,859	1,466,816	1,503,677	1,541,464	1,580,200
Vaginal Thrush	1,172,809	1,228,106	1,286,010	1,346,644	1,410,137
Sweden	**921,603**	**946,318**	**984,580**	**1,024,870**	**1,067,737**
Athlete's Foot	13,564	13,803	14,400	15,020	15,667
Dermatomycosis	91,822	93,442	97,478	101,680	106,057
Herpes Labialis	454,591	459,878	465,100	470,071	475,157
Vaginal Thrush	361,626	379,195	407,602	438,099	470,855
UK	**2,815,579**	**2,819,443**	**2,824,603**	**2,831,038**	**2,838,732**
Athlete's Foot	69,733	70,441	71,157	71,880	72,611
Dermatomycosis	472,057	476,854	481,699	486,595	491,539
Herpes Labialis	821,915	795,834	770,581	746,129	722,454
Vaginal Thrush	1,451,875	1,476,314	1,501,165	1,526,434	1,552,128

A.3. Excess appointments

The following chart and table detail the number of excess appointments per indication in each country for a single year for the vulnerable population. We estimate that ~57,3 million additional visits to doctor's practice will occur as people seek treatment. There will be a shift of self-care patients into the healthcare system as they seek treatment from doctors, either immediately (Scenario 1) or eventually as their symptoms worsen (Scenario 2 & 3).

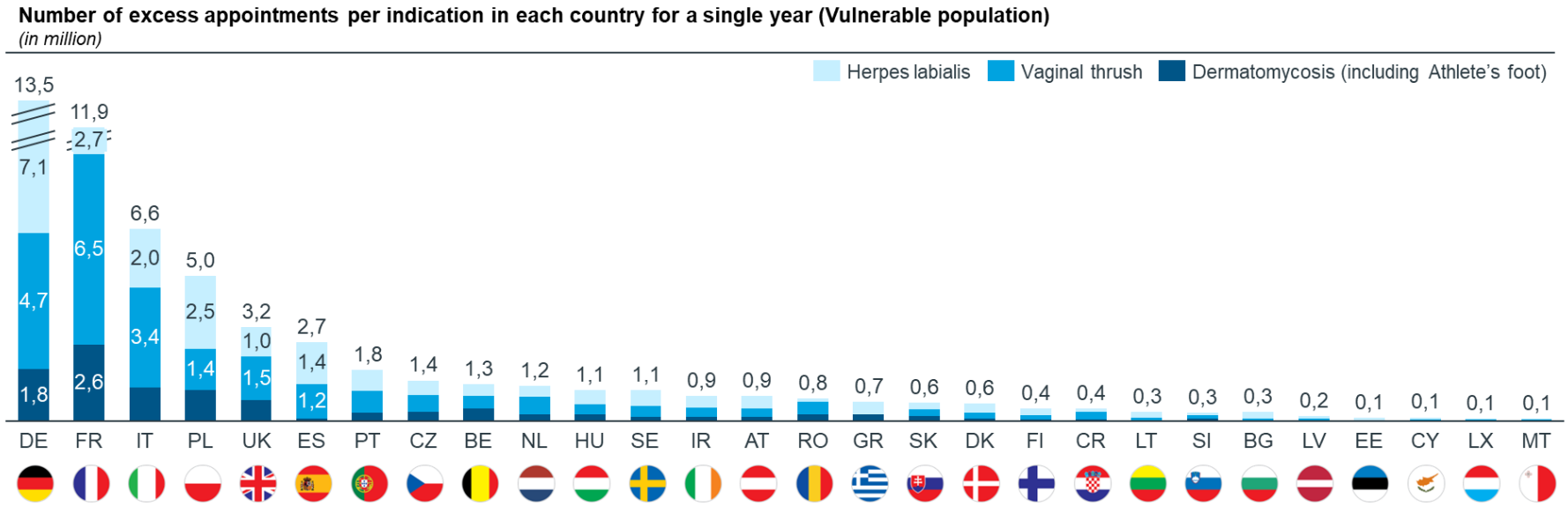


Figure 53 Excess appointments per indication in each country for a single year (Vulnerable Population)

Table 71 Number of excess appointments per indication in each country for a single year (Vulnerable Population)

Country and Indications	Excess appointments for Seeking Rx decision pathways	Excess appointments for Seeking Alternative decision pathways	Excess appointments for Do nothing decision pathways	Total excess appointments
Austria	**571,557**	**238,410**	**44,743**	**854,710**
Athlete's Foot	11,544	4,549	-	16,093
Dermatomycosis	97,010	30,797	-	127,807
Herpes Labialis	284,118	89,486	44,743	418,347
Vaginal Thrush	178,884	113,577	-	292,462
Belgium	**853,833**	**356,490**	**42,746**	**1,253,068**
Athlete's Foot	33,960	13,383	-	47,343
Dermatomycosis	285,385	90,598	-	375,983
Herpes Labialis	271,438	85,492	42,746	399,676
Vaginal Thrush	263,050	167,016	-	430,065
Bulgaria	**213,188**	**79,009**	**23,444**	**315,640**
Athlete's Foot	2,997	1,181	-	4,178
Dermatomycosis	25,184	7,995	-	33,179
Herpes Labialis	148,869	46,888	23,444	219,200
Vaginal Thrush	36,138	22,945	-	59,083
Croatia	**145,931**	**223,652**	**57,401**	**426,984**
Athlete's Foot	2,700	5,586	-	8,286
Dermatomycosis	22,689	37,815	-	60,504
Herpes Labialis	-	122,850	-	122,850
Vaginal Thrush	120,542	57,401	57,401	235,344
Cyprus	**17,094**	**112,417**	**-**	**129,510**
Athlete's Foot	1,818	836	-	2,654
Dermatomycosis	15,276	5,658	-	20,934
Herpes Labialis	-	60,321	-	60,321
Vaginal Thrush	-	45,602	-	45,602
Czech Republic	**853,652**	**350,892**	**185,453**	**1,389,997**

Athlete's Foot	28,010	-	6,439	34,449
Dermatomycosis	235,383	-	43,590	278,973
Herpes Labialis	85,995	270,850	135,425	492,269
Vaginal Thrush	504,264	80,042	-	584,306
Denmark	**429,182**	**99,426**	**65,659**	**594,267**
Athlete's Foot	4,726	4,346	-	9,073
Dermatomycosis	39,719	29,421	-	69,140
Herpes Labialis	242,795	31,863	31,863	306,521
Vaginal Thrush	141,942	33,796	33,796	209,534
Estonia	**14,748**	**95,127**	**6,178**	**116,053**
Athlete's Foot	189	390	-	579
Dermatomycosis	1,586	2,643	-	4,230
Herpes Labialis	-	85,915	-	85,915
Vaginal Thrush	12,973	6,178	6,178	25,329
Finland	**322,420**	**71,620**	**49,936**	**443,976**
Athlete's Foot	3,035	2,791	-	5,826
Dermatomycosis	25,506	18,893	-	44,400
Herpes Labialis	187,487	24,605	24,605	236,696
Vaginal Thrush	106,391	25,331	25,331	157,054
France	**8,320,716**	**2,408,624**	**1,172,650**	**11,901,991**
Athlete's Foot	233,220	-	53,614	286,834
Dermatomycosis	1,959,871	-	362,939	2,322,811
Herpes Labialis	480,122	1,512,195	756,097	2,748,414
Vaginal Thrush	5,647,503	896,429	-	6,543,932
Germany	**8,982,918**	**3,754,045**	**754,520**	**13,491,483**
Athlete's Foot	143,161	56,418	-	199,580
Dermatomycosis	1,203,061	381,924	-	1,584,986
Herpes Labialis	4,791,202	1,509,040	754,520	7,054,762
Vaginal Thrush	2,845,494	1,806,663	-	4,652,156
Greece	**158,589**	**500,370**	**-**	**658,959**
Athlete's Foot	16,865	7,754	-	24,619
Dermatomycosis	141,724	52,490	-	194,215

Herpes Labialis	-	422,879	-	422,879
Vaginal Thrush	-	17,247	-	17,247
Hungary	**257,733**	**722,814**	**81,804**	**1,062,351**
Athlete's Foot	9,140	18,910	-	28,049
Dermatomycosis	76,806	128,009	-	204,815
Herpes Labialis	-	494,091	-	494,091
Vaginal Thrush	171,788	81,804	81,804	335,396
Ireland	**463,141**	**264,070**	**134,071**	**861,282**
Athlete's Foot	13,117	-	3,015	16,132
Dermatomycosis	110,230	-	20,413	130,643
Herpes Labialis	70,258	221,286	110,643	402,188
Vaginal Thrush	269,536	42,783	-	312,319
Italy	**830,068**	**5,746,679**	**-**	**6,576,747**
Athlete's Foot	88,272	40,585	-	128,857
Dermatomycosis	741,796	274,739	-	1,016,535
Herpes Labialis	-	2,007,716	-	2,007,716
Vaginal Thrush	-	3,423,639	-	3,423,639
Latvia	**40,674**	**120,514**	**14,928**	**176,116**
Athlete's Foot	992	2,052	-	3,044
Dermatomycosis	8,334	13,890	-	22,225
Herpes Labialis	-	89,644	-	89,644
Vaginal Thrush	31,348	14,928	14,928	61,204
Lithuania	**57,844**	**220,206**	**27,360**	**305,411**
Athlete's Foot	41	85	-	126
Dermatomycosis	346	577	-	923
Herpes Labialis	-	192,184	-	192,184
Vaginal Thrush	57,456	27,360	27,360	112,177
Luxembourg	**58,195**	**22,318**	**11,433**	**91,946**
Athlete's Foot	1,767	-	406	2,174
Dermatomycosis	14,853	-	2,751	17,604
Herpes Labialis	5,255	16,553	8,276	30,084
Vaginal Thrush	36,319	5,765	-	42,084

Malta	**11,703**	**65,501**	**-**	**77,203**
Athlete's Foot	1,244	572	-	1,817
Dermatomycosis	10,458	3,873	-	14,332
Herpes Labialis	-	19,199	-	19,199
Vaginal Thrush	-	41,856	-	41,856
Netherlands	**841,033**	**236,568**	**137,704**	**1,215,305**
Athlete's Foot	13,838	12,725	-	26,563
Dermatomycosis	116,289	86,140	-	202,428
Herpes Labialis	295,330	38,757	38,757	372,845
Vaginal Thrush	415,576	98,947	98,947	613,469
Poland	**1,112,161**	**3,521,678**	**341,077**	**4,974,915**
Athlete's Foot	42,101	87,106	-	129,207
Dermatomycosis	353,799	589,664	-	943,463
Herpes Labialis	-	2,503,831	-	2,503,831
Vaginal Thrush	716,261	341,077	341,077	1,398,414
Portugal	**207,376**	**1,546,425**	**-**	**1,753,802**
Athlete's Foot	22,053	10,139	-	32,192
Dermatomycosis	185,323	68,638	-	253,962
Herpes Labialis	-	706,411	-	706,411
Vaginal Thrush	-	761,237	-	761,237
Romania	**299,378**	**379,078**	**100,443**	**778,899**
Athlete's Foot	9,406	19,460	-	28,866
Dermatomycosis	79,041	131,735	-	210,775
Herpes Labialis	-	127,440	-	127,440
Vaginal Thrush	210,931	100,443	100,443	411,818
Slovakia	**188,882**	**381,498**	**60,186**	**630,566**
Athlete's Foot	6,645	13,749	-	20,395
Dermatomycosis	55,845	93,075	-	148,920
Herpes Labialis	-	214,487	-	214,487
Vaginal Thrush	126,391	60,186	60,186	246,764
Slovenia	**186,758**	**67,704**	**37,916**	**292,378**
Athlete's Foot	6,950	-	1,598	8,548

Dermatomycosis	58,407	-	10,816	69,223
Herpes Labialis	16,194	51,004	25,502	92,701
Vaginal Thrush	105,207	16,700	-	121,906
Spain	**70,727**	**2,630,535**	**-**	**2,701,263**
Athlete's Foot	7,521	3,458	-	10,979
Dermatomycosis	63,206	23,410	-	86,616
Herpes Labialis	-	1,430,859	-	1,430,859
Vaginal Thrush	-	1,172,809	-	1,172,809
Sweden	**765,400**	**177,316**	**117,095**	**1,059,810**
Athlete's Foot	8,429	7,751	-	16,180
Dermatomycosis	70,834	52,470	-	123,304
Herpes Labialis	432,998	56,824	56,824	546,646
Vaginal Thrush	253,138	60,271	60,271	373,680
UK	**2,206,678**	**654,312**	**344,719**	**3,205,709**
Athlete's Foot	43,334	39,847	-	83,181
Dermatomycosis	364,158	269,747	-	633,904
Herpes Labialis	782,874	102,739	102,739	988,353
Vaginal Thrush	1,016,312	241,979	241,979	1,500,271
Grand Total	**28,481,579**	**25,047,297**	**3,811,466**	**57,340,342**

A.4. Emergency visits

In accordance with the approach and assumption elaborated in the methodology section, the following chart and table detail the number of emergency visits across the 28 in-scope countries for a single year. The additional healthcare visits include ~8,7 million visits to the emergency department. Overall, Germany and France having the highest estimates for the additional emergency visits across all countries. However, only UK and Sweden are expected to receive the highest proportional increase on additional visits to the emergency department.

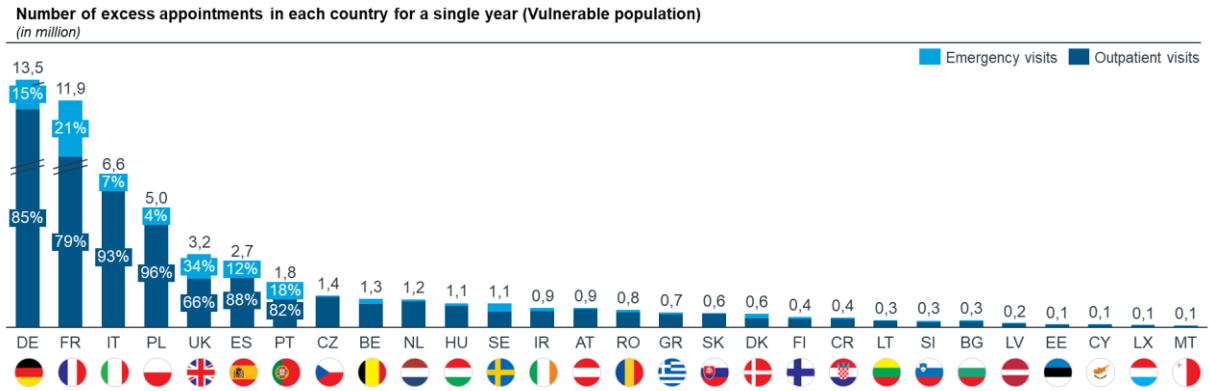


Figure 54 Number of emergency visits in each country for a single year in millions (Vulnerable Population)

Table 72 Detailed number of emergency visits in each country for a single year in millions (General Population)

Country	Emergency visits	Outpatient visits	Total excess appointments
Austria	51,213	803,497	854,710
Belgium	227,247	1,025,821	1,253,068
Bulgaria	63,907	251,733	315,640
Croatia	57,883	369,101	426,984
Cyprus	9,938	119,572	129,510
Czech Republic	64,328	1,325,669	1,389,997
Denmark	204,837	389,430	594,267
Estonia	13,482	102,571	116,053
Finland	74,823	369,154	443,976
France	2,471,793	9,430,198	11,901,991
Germany	1,983,037	11,508,446	13,491,483
Greece	84,883	574,076	658,959
Hungary	135,723	926,629	1,062,351
Ireland	147,728	713,554	861,282
Italy	436,440	6,140,307	6,576,747
Latvia	15,368	160,749	176,116
Lithuania	27,000	278,411	305,411
Luxembourg	17,974	73,972	91,946

Malta	5,472	71,731	77,203
Netherlands	91,810	1,123,495	1,215,305
Poland	209,991	4,764,924	4,974,915
Portugal	312,255	1,441,547	1,753,802
Romania	121,822	657,078	778,899
Slovakia	30,011	600,554	630,566
Slovenia	57,887	234,490	292,378
Spain	316,766	2,384,497	2,701,263
Sweden	365,305	694,505	1,059,810
UK	1,086,156	2,119,553	3,205,709
Grand Total	**8,685,078**	**48,655,264**	**57,340,342**

A.5. Unresolved cases

Unresolved cases represent the number of cases that are expected to exacerbate due to patients delaying appropriate care as they seek an alternative treatment which is available for self-purchase (Non-prescription medicines), or they do nothing at all in the hope that their symptom will self-resolve. Overall, the total number of unresolved cases is 28,858,763. The following chart and tables detail the unresolved cases for each country across the indications.

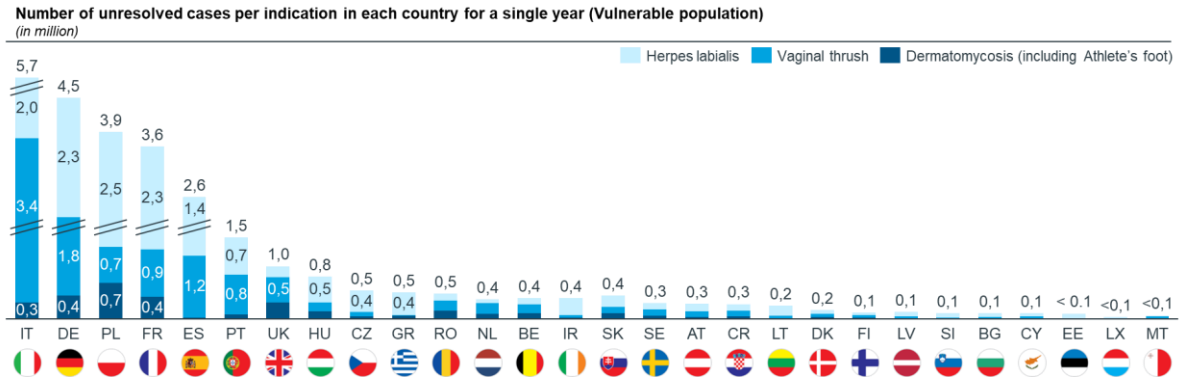


Figure 55 Number of unresolved cases per indication in each country for a single year in millions (Vulnerable Population)

Table 73 Detailed number of unresolved cases per indication in each country for a single year (Vulnerable Population)

Country and indications	Seek alternative treatment cases	Do nothing cases	Total unresolved cases
Austria	**238,410**	**44,743**	**283,153**
Athlete's Foot	4,549	-	4,549
Dermatomycosis	30,797	-	30,797
Herpes Labialis	89,486	44,743	134,229
Vaginal Thrush	113,577	-	113,577

Belgium	**356,490**	**42,746**	**399,236**
Athlete's Foot	13,383	-	13,383
Dermatomycosis	90,598	-	90,598
Herpes Labialis	85,492	42,746	128,238
Vaginal Thrush	167,016	-	167,016
Bulgaria	**79,009**	**23,444**	**102,453**
Athlete's Foot	1,181	-	1,181
Dermatomycosis	7,995	-	7,995
Herpes Labialis	46,888	23,444	70,332
Vaginal Thrush	22,945	-	22,945
Croatia	**223,652**	**57,401**	**281,053**
Athlete's Foot	5,586	-	5,586
Dermatomycosis	37,815	-	37,815
Herpes Labialis	122,850	-	122,850
Vaginal Thrush	57,401	57,401	114,802
Cyprus	**112,417**	**-**	**112,417**
Athlete's Foot	836	-	836
Dermatomycosis	5,658	-	5,658
Herpes Labialis	60,321	-	60,321
Vaginal Thrush	45,602	-	45,602
Czech Republic	**350,892**	**185,453**	**536,345**
Athlete's Foot	-	6,439	6,439
Dermatomycosis	-	43,590	43,590
Herpes Labialis	270,850	135,425	406,275
Vaginal Thrush	80,042	-	80,042
Denmark	**99,426**	**65,659**	**165,085**
Athlete's Foot	4,346	-	4,346
Dermatomycosis	29,421	-	29,421
Herpes Labialis	31,863	31,863	63,726
Vaginal Thrush	33,796	33,796	67,591
Estonia	**95,127**	**6,178**	**101,305**
Athlete's Foot	390	-	390
Dermatomycosis	2,643	-	2,643
Herpes Labialis	85,915	-	85,915
Vaginal Thrush	6,178	6,178	12,356
Finland	**71,620**	**49,936**	**121,556**
Athlete's Foot	2,791	-	2,791
Dermatomycosis	18,893	-	18,893
Herpes Labialis	24,605	24,605	49,209
Vaginal Thrush	25,331	25,331	50,663
France	**2,408,624**	**1,172,650**	**3,581,274**
Athlete's Foot	-	53,614	53,614
Dermatomycosis	-	362,939	362,939
Herpes Labialis	1,512,195	756,097	2,268,292
Vaginal Thrush	896,429	-	896,429
Germany	**3,754,045**	**754,520**	**4,508,565**

Athlete's Foot	56,418	-	56,418
Dermatomycosis	381,924	-	381,924
Herpes Labialis	1,509,040	754,520	2,263,560
Vaginal Thrush	1,806,663	-	1,806,663
Greece	**500,370**	**-**	**500,370**
Athlete's Foot	7,754	-	7,754
Dermatomycosis	52,490	-	52,490
Herpes Labialis	422,879	-	422,879
Vaginal Thrush	17,247	-	17,247
Hungary	**722,814**	**81,804**	**804,618**
Athlete's Foot	18,910	-	18,910
Dermatomycosis	128,009	-	128,009
Herpes Labialis	494,091	-	494,091
Vaginal Thrush	81,804	81,804	163,608
Ireland	**264,070**	**134,071**	**398,141**
Athlete's Foot	-	3,015	3,015
Dermatomycosis	-	20,413	20,413
Herpes Labialis	221,286	110,643	331,929
Vaginal Thrush	42,783	-	42,783
Italy	**5,746,679**	**-**	**5,746,679**
Athlete's Foot	40,585	-	40,585
Dermatomycosis	274,739	-	274,739
Herpes Labialis	2,007,716	-	2,007,716
Vaginal Thrush	3,423,639	-	3,423,639
Latvia	**120,514**	**14,928**	**135,442**
Athlete's Foot	2,052	-	2,052
Dermatomycosis	13,890	-	13,890
Herpes Labialis	89,644	-	89,644
Vaginal Thrush	14,928	14,928	29,856
Lithuania	**220,206**	**27,360**	**247,567**
Athlete's Foot	85	-	85
Dermatomycosis	577	-	577
Herpes Labialis	192,184	-	192,184
Vaginal Thrush	27,360	27,360	54,720
Luxembourg	**22,318**	**11,433**	**33,751**
Athlete's Foot	-	406	406
Dermatomycosis	-	2,751	2,751
Herpes Labialis	16,553	8,276	24,829
Vaginal Thrush	5,765	-	5,765
Malta	**65,501**	**-**	**65,501**
Athlete's Foot	572	-	572
Dermatomycosis	3,873	-	3,873
Herpes Labialis	19,199	-	19,199
Vaginal Thrush	41,856	-	41,856
Netherlands	**236,568**	**137,704**	**374,272**
Athlete's Foot	12,725	-	12,725

Dermatomycosis	86,140	-	86,140
Herpes Labialis	38,757	38,757	77,515
Vaginal Thrush	98,947	98,947	197,893
Poland	**3,521,678**	**341,077**	**3,862,754**
Athlete's Foot	87,106	-	87,106
Dermatomycosis	589,664	-	589,664
Herpes Labialis	2,503,831	-	2,503,831
Vaginal Thrush	341,077	341,077	682,153
Portugal	**1,546,425**	**-**	**1,546,425**
Athlete's Foot	10,139	-	10,139
Dermatomycosis	68,638	-	68,638
Herpes Labialis	706,411	-	706,411
Vaginal Thrush	761,237	-	761,237
Romania	**379,078**	**100,443**	**479,522**
Athlete's Foot	19,460	-	19,460
Dermatomycosis	131,735	-	131,735
Herpes Labialis	127,440	-	127,440
Vaginal Thrush	100,443	100,443	200,887
Slovakia	**381,498**	**60,186**	**441,684**
Athlete's Foot	13,749	-	13,749
Dermatomycosis	93,075	-	93,075
Herpes Labialis	214,487	-	214,487
Vaginal Thrush	60,186	60,186	120,373
Slovenia	**67,704**	**37,916**	**105,620**
Athlete's Foot	-	1,598	1,598
Dermatomycosis	-	10,816	10,816
Herpes Labialis	51,004	25,502	76,507
Vaginal Thrush	16,700	-	16,700
Spain	**2,630,535**	**-**	**2,630,535**
Athlete's Foot	3,458	-	3,458
Dermatomycosis	23,410	-	23,410
Herpes Labialis	1,430,859	-	1,430,859
Vaginal Thrush	1,172,809	-	1,172,809
Sweden	**177,316**	**117,095**	**294,411**
Athlete's Foot	7,751	-	7,751
Dermatomycosis	52,470	-	52,470
Herpes Labialis	56,824	56,824	113,648
Vaginal Thrush	60,271	60,271	120,542
UK	**654,312**	**344,719**	**999,031**
Athlete's Foot	39,847	-	39,847
Dermatomycosis	269,747	-	269,747
Herpes Labialis	102,739	102,739	205,479
Vaginal Thrush	241,979	241,979	483,958
Grand Total	**25,047,297**	**3,811,466**	**28,858,763**

A.6. Total costs

Cumulatively, the total costs of reverse-switching for five years amount to €43.3 billion, increasing by 1.7% year-on-year. Approximately 80% of these costs, equivalent to €34.6 billion, are healthcare-related expenditures. Of these healthcare costs, 82% are borne by public payers, followed by 13% by individuals, and 5% by private health insurance. The remaining 20% of the total costs, equivalent to €8.7 billion, are attributed to productivity losses due to disability and individuals seeking care at doctors' practices. The largest costs are attributed to vaginal thrush (€17.1 billion), followed by herpes labialis (€15.6 billion), and dermatomycosis (€10.7 billion).

A.6.1. Projected total costs

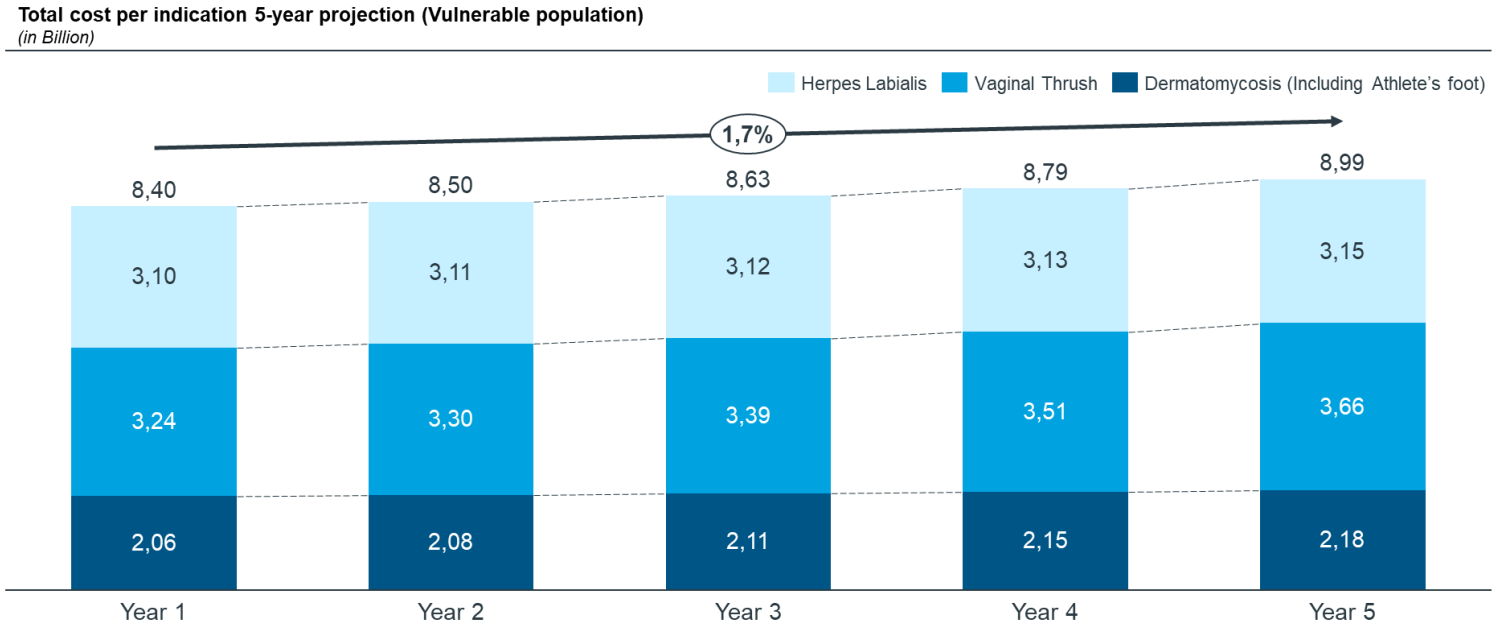


Figure 56 5-year projection of the total cost per indication (Vulnerable Population)

Table 74 Total cost by indication for 5 years (Vulnerable Population)

Indications	Year 1	Year 2	Year 3	Year 4	Year 5
Athlete's Foot	201,808,013	204,207,880	207,125,749	210,161,467	213,320,647
Dermatomycosis	1,858,541,875	1,880,541,812	1,907,553,482	1,935,681,472	1,964,980,993
Herpes Labialis	3,101,191,505	3,106,058,318	3,117,637,614	3,131,370,505	3,147,484,064
Vaginal Thrush	3,242,682,104	3,304,583,688	3,393,711,914	3,510,097,761	3,663,930,086

A.6.2. Total costs by country and indications for a single year

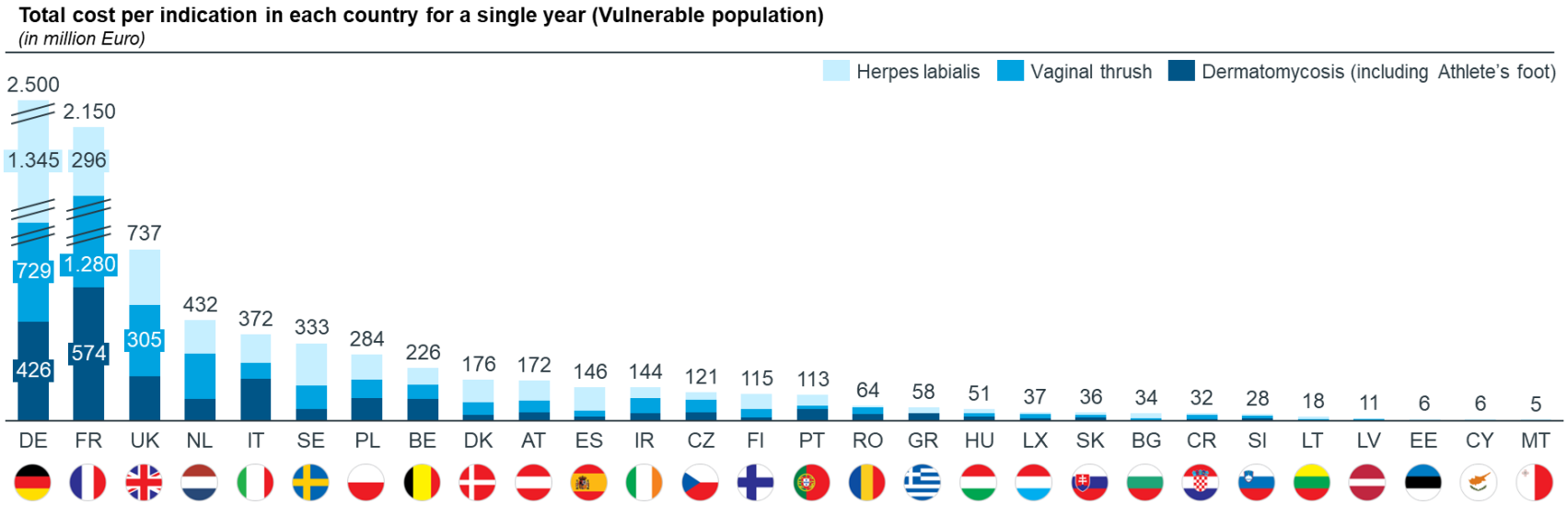


Figure 57 Total cost per indication in each country for a single year (Vulnerable Population)

Table 75 5-year total costs by country and indication (Vulnerable Population)

Country and indications	Total Rx cost	Total Outpatient cost	Productivity cost	Total overall cost
Austria	**5,812,329**	**132,068,808**	**34,299,193**	**172,180,330**
Athlete's Foot	126,620	2,803,938	696,094	3,626,653
Dermatomycosis	1,326,512	25,096,618	6,511,431	32,934,561
Herpes Labialis	2,764,408	66,091,898	17,486,160	86,342,465
Vaginal Thrush	1,594,790	38,076,353	9,605,507	49,276,651
Belgium	**10,367,341**	**165,056,205**	**50,941,111**	**226,364,658**
Athlete's Foot	429,892	6,766,445	2,004,767	9,201,104
Dermatomycosis	4,503,669	60,562,987	18,753,073	83,819,730
Herpes Labialis	2,916,966	51,796,380	16,354,962	71,068,308
Vaginal Thrush	2,516,814	45,930,393	13,828,308	62,275,516
Bulgaria	**1,681,593**	**23,424,557**	**8,995,700**	**34,101,850**
Athlete's Foot	25,471	344,006	125,297	494,774
Dermatomycosis	266,839	3,079,026	1,172,058	4,517,923
Herpes Labialis	1,234,296	16,366,169	6,352,837	23,953,303
Vaginal Thrush	154,987	3,635,355	1,345,508	5,135,851
Croatia	**2,013,987**	**19,216,816**	**10,749,154**	**31,979,956**
Athlete's Foot	44,386	460,417	238,493	743,296
Dermatomycosis	504,016	4,675,202	2,567,609	7,746,827
Herpes Labialis	480,440	2,929,199	3,071,171	6,480,810
Vaginal Thrush	985,146	11,151,998	4,871,880	17,009,024
Cyprus	**749,425**	**3,029,601**	**1,785,017**	**5,564,042**
Athlete's Foot	24,435	163,860	50,646	238,941
Dermatomycosis	257,825	1,479,004	479,432	2,216,261
Herpes Labialis	306,915	1,216,435	962,869	2,486,220
Vaginal Thrush	160,250	170,301	292,070	622,620
Czech Republic	**12,119,541**	**84,106,351**	**24,659,216**	**120,885,109**
Athlete's Foot	272,661	2,586,293	649,084	3,508,038

Dermatomycosis	2,794,747	22,614,433	5,858,648	31,267,828
Herpes Labialis	5,691,739	16,374,885	7,969,779	30,036,404
Vaginal Thrush	3,360,394	42,530,740	10,181,704	56,072,838
Denmark	**4,031,339**	**140,254,412**	**31,604,139**	**175,889,890**
Athlete's Foot	49,095	1,971,997	492,994	2,514,086
Dermatomycosis	536,421	18,667,545	4,953,520	24,157,486
Herpes Labialis	1,630,283	76,728,932	16,802,894	95,162,109
Vaginal Thrush	1,815,540	42,885,938	9,354,732	54,056,209
Estonia	**807,336**	**3,452,590**	**1,881,471**	**6,141,397**
Athlete's Foot	5,578	30,801	10,936	47,315
Dermatomycosis	63,338	312,766	117,737	493,840
Herpes Labialis	586,459	1,960,412	1,408,859	3,955,730
Vaginal Thrush	151,961	1,148,611	343,939	1,644,512
Finland	**4,140,687**	**96,425,834**	**14,438,080**	**115,004,600**
Athlete's Foot	64,960	1,166,839	194,632	1,426,432
Dermatomycosis	709,772	11,045,669	1,955,634	13,711,075
Herpes Labialis	2,060,589	54,594,493	7,977,058	64,632,140
Vaginal Thrush	1,305,366	29,618,832	4,310,755	35,234,953
France	**49,769,172**	**1,713,777,120**	**386,600,775**	**2,150,147,067**
Athlete's Foot	1,125,735	47,461,495	9,822,546	58,409,777
Dermatomycosis	11,538,657	415,001,262	88,658,499	515,198,419
Herpes Labialis	13,996,946	201,497,440	80,871,737	296,366,123
Vaginal Thrush	23,107,833	1,049,816,923	207,247,993	1,280,172,748
Germany	**77,172,896**	**1,888,829,800**	**534,154,703**	**2,500,157,398**
Athlete's Foot	1,815,214	31,787,378	8,585,921	42,188,513
Dermatomycosis	19,016,704	284,512,559	80,314,759	383,844,022
Herpes Labialis	32,773,869	1,018,851,520	293,284,963	1,344,910,352
Vaginal Thrush	23,567,109	553,678,342	151,969,060	729,214,511
Greece	**4,894,416**	**44,980,565**	**8,109,104**	**57,984,085**
Athlete's Foot	159,718	2,869,036	323,493	3,352,248

Dermatomycosis	1,685,276	25,895,977	3,062,287	30,643,540
Herpes Labialis	2,960,406	16,093,998	4,647,275	23,701,680
Vaginal Thrush	89,016	121,553	76,049	286,618
Hungary	**10,333,917**	**24,184,882**	**16,126,954**	**50,645,753**
Athlete's Foot	291,826	836,555	452,172	1,580,552
Dermatomycosis	3,313,778	8,494,603	4,868,068	16,676,450
Herpes Labialis	4,245,340	6,323,307	6,918,061	17,486,708
Vaginal Thrush	2,482,972	8,530,417	3,888,653	14,902,043
Ireland	**6,080,110**	**112,698,405**	**24,931,644**	**143,710,159**
Athlete's Foot	87,114	2,848,811	505,183	3,441,108
Dermatomycosis	892,906	24,909,877	4,559,794	30,362,577
Herpes Labialis	2,656,371	31,467,888	10,821,751	44,946,010
Vaginal Thrush	2,443,719	53,471,830	9,044,916	64,960,465
Italy	**56,306,764**	**208,374,871**	**106,882,432**	**371,564,067**
Athlete's Foot	1,858,295	12,461,759	3,297,496	17,617,551
Dermatomycosis	19,607,887	112,480,087	31,215,132	163,303,106
Herpes Labialis	15,998,609	63,409,300	42,969,800	122,377,709
Vaginal Thrush	18,841,974	20,023,726	29,400,003	68,265,702
Latvia	**1,297,056**	**6,020,222**	**3,367,116**	**10,684,394**
Athlete's Foot	10,396	147,045	64,990	222,431
Dermatomycosis	118,048	1,493,139	699,678	2,310,865
Herpes Labialis	687,429	1,858,423	1,662,527	4,208,379
Vaginal Thrush	481,182	2,521,615	939,922	3,942,719
Lithuania	**2,736,788**	**8,352,016**	**6,492,099**	**17,580,904**
Athlete's Foot	973	5,882	3,295	10,149
Dermatomycosis	11,043	59,723	35,477	106,243
Herpes Labialis	1,984,892	3,836,287	4,350,547	10,171,726
Vaginal Thrush	739,880	4,450,125	2,102,780	7,292,785
Luxembourg	**996,823**	**27,776,713**	**7,770,639**	**36,544,175**
Athlete's Foot	15,883	801,734	195,134	1,012,751

Dermatomycosis	162,795	7,010,325	1,761,288	8,934,407
Herpes Labialis	266,103	4,916,210	2,320,485	7,502,798
Vaginal Thrush	552,042	15,048,445	3,493,732	19,094,218
Malta	**724,024**	**2,757,540**	**1,549,577**	**5,031,140**
Athlete's Foot	27,652	185,434	57,314	270,401
Dermatomycosis	291,771	1,673,734	542,555	2,508,060
Herpes Labialis	161,476	639,998	506,590	1,308,063
Vaginal Thrush	243,125	258,374	443,117	944,617
Netherlands	**8,402,392**	**374,211,956**	**49,057,214**	**431,671,563**
Athlete's Foot	199,204	7,735,006	1,110,307	9,044,516
Dermatomycosis	2,176,544	73,221,991	11,156,180	86,554,715
Herpes Labialis	2,072,833	125,038,207	15,722,260	142,833,300
Vaginal Thrush	3,953,812	168,216,752	21,068,468	193,239,032
Poland	**27,797,713**	**164,837,078**	**91,400,022**	**284,034,812**
Athlete's Foot	264,830	5,743,560	2,512,278	8,520,668
Dermatomycosis	3,007,225	58,321,677	27,047,120	88,376,021
Herpes Labialis	17,336,498	47,760,165	42,284,719	107,381,382
Vaginal Thrush	7,189,161	53,011,676	19,555,905	79,756,741
Portugal	**13,093,274**	**76,824,996**	**22,988,098**	**112,906,367**
Athlete's Foot	240,265	4,125,459	625,466	4,991,190
Dermatomycosis	2,535,169	37,236,474	5,920,857	45,692,501
Herpes Labialis	7,476,945	29,563,450	11,478,681	48,519,075
Vaginal Thrush	2,840,895	5,899,613	4,963,094	13,703,601
Romania	**4,975,474**	**37,201,361**	**21,486,542**	**63,663,378**
Athlete's Foot	191,421	1,475,352	830,832	2,497,605
Dermatomycosis	2,173,644	14,981,130	8,944,716	26,099,490
Herpes Labialis	824,232	2,795,027	3,185,918	6,805,177
Vaginal Thrush	1,786,178	17,949,852	8,525,076	28,261,106
Slovakia	**6,121,133**	**20,580,245**	**9,296,951**	**35,998,329**
Athlete's Foot	152,645	791,992	314,058	1,258,695

Dermatomycosis	1,733,329	8,042,101	3,381,145	13,156,576
Herpes Labialis	2,800,463	3,574,151	2,868,757	9,243,371
Vaginal Thrush	1,434,695	8,172,002	2,732,991	12,339,688
Slovenia	**1,485,736**	**20,641,777**	**5,996,421**	**28,123,934**
Athlete's Foot	37,283	727,442	184,315	949,040
Dermatomycosis	382,147	6,360,719	1,663,631	8,406,497
Herpes Labialis	526,748	3,495,355	1,717,506	5,739,608
Vaginal Thrush	539,558	10,058,261	2,430,969	13,028,789
Spain	**17,300,259**	**85,275,357**	**43,067,489**	**145,643,105**
Athlete's Foot	139,482	1,444,238	277,310	1,861,030
Dermatomycosis	1,471,752	13,035,719	2,625,104	17,132,575
Herpes Labialis	10,251,536	61,465,669	30,224,909	101,942,113
Vaginal Thrush	5,437,488	9,329,732	9,940,167	24,707,387
Sweden	**7,988,237**	**277,918,958**	**46,959,059**	**332,866,254**
Athlete's Foot	97,283	3,907,581	732,516	4,737,379
Dermatomycosis	1,062,937	36,990,385	7,360,195	45,413,517
Herpes Labialis	3,230,462	152,041,026	24,966,607	180,238,094
Vaginal Thrush	3,597,554	84,979,967	13,899,742	102,477,263
UK	**19,434,433**	**611,804,106**	**105,916,240**	**737,154,779**
Athlete's Foot	370,288	14,873,422	2,798,059	18,041,769
Dermatomycosis	4,045,858	140,796,479	28,114,428	172,956,764
Herpes Labialis	4,324,425	203,528,146	33,539,778	241,392,349
Vaginal Thrush	10,693,862	252,606,058	41,463,976	304,763,896
Grand Total	**358,634,194**	**6,374,083,142**	**1,671,506,161**	**8,404,223,497**

A.7. Health system related costs

Healthcare system related costs are the sum of prescription (Rx) and outpatient costs. Overall, out of an estimated 8.4 billion Euros in total costs in a single year, approximately 6.7 billion Euros is attributed to healthcare-related spending. These figures are subject to the assumptions in our methodology. The table below details the healthcare system-related costs for each country, with a specific breakdown of Rx and outpatient expenses.

Table 76 Health system related costs country breakdown in a single year

Country	Total Rx cost	Total Outpatient cost	Total health system related cost
Austria	5,812,329	132,068,808	137,881,137
Belgium	10,367,341	165,056,205	175,423,547
Bulgaria	1,681,593	23,424,557	25,106,150
Croatia	2,013,987	19,216,816	21,230,803
Cyprus	749,425	3,029,601	3,779,025
Czech Republic	12,119,541	84,106,351	96,225,893
Denmark	4,031,339	140,254,412	144,285,751
Estonia	807,336	3,452,590	4,259,926
Finland	4,140,687	96,425,834	100,566,520
France	49,769,172	1,713,777,120	1,763,546,292
Germany	77,172,896	1,888,829,800	1,966,002,695
Greece	4,894,416	44,980,565	49,874,981
Hungary	10,333,917	24,184,882	34,518,799
Ireland	6,080,110	112,698,405	118,778,515
Italy	56,306,764	208,374,871	264,681,636
Latvia	1,297,056	6,020,222	7,317,278
Lithuania	2,736,788	8,352,016	11,088,805
Luxembourg	996,823	27,776,713	28,773,536
Malta	724,024	2,757,540	3,481,563
Netherlands	8,402,392	374,211,956	382,614,349
Poland	27,797,713	164,837,078	192,634,790
Portugal	13,093,274	76,824,996	89,918,269
Romania	4,975,474	37,201,361	42,176,836
Slovakia	6,121,133	20,580,245	26,701,378
Slovenia	1,485,736	20,641,777	22,127,513
Spain	17,300,259	85,275,357	102,575,616
Sweden	7,988,237	277,918,958	285,907,195
UK	19,434,433	611,804,106	631,238,539
Grand Total	**358,634,194**	**6,374,083,142**	**6,732,717,336**

A.8. Costs to payers

This section details the distribution of healthcare costs among three primary stakeholders: public payers, individuals, and private insurance providers. On average, across all countries, public payers bear the majority of healthcare costs, accounting for approximately 82% of the total expenses. Individuals cover about 13% of healthcare costs through out-of-pocket expenses, co-payments, and deductibles. Private health insurance providers contribute the remaining 5%, offering supplementary coverage to alleviate financial pressure on both public payers and individuals.

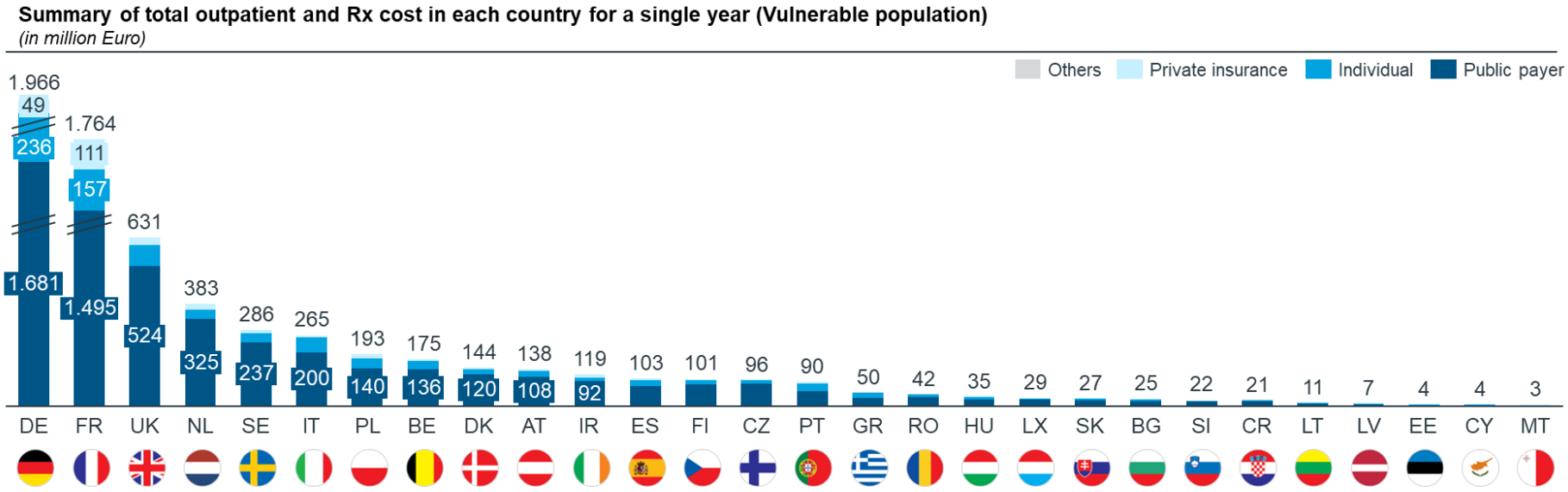


Figure 58 Total health system related cost in each country for a single year (Vulnerable Population)

Table 77 Healthcare cost payers breakdown for each country for a single year (Vulnerable Population)

Country	Public Payer Share	Individual share	Private Insurance share	Others	Total health system related cost
Austria	107,960,929	21,785,221	8,134,987	-	137,881,137
Belgium	136,128,674	31,400,813	7,894,060	-	175,423,547
Bulgaria	16,243,679	8,536,091	326,380	-	25,106,150
Croatia	18,046,183	1,910,772	1,082,771	191,077	21,230,803
Cyprus	2,853,164	827,607	98,255	-	3,779,025
Czech Republic	83,139,171	12,220,689	866,033	-	96,225,893
Denmark	119,757,172	18,324,291	6,204,287	-	144,285,751
Estonia	3,246,064	941,444	72,419	-	4,259,926
Finland	80,252,084	16,191,210	4,123,227	-	100,566,520
France	1,495,487,264	156,955,609	111,103,418	-	1,763,546,292
Germany	1,680,932,310	235,920,318	49,150,067	-	1,966,002,695
Greece	30,972,363	16,608,369	2,194,499	99,750	49,874,981
Hungary	25,026,129	8,491,625	1,001,045	-	34,518,799
Ireland	91,934,571	12,709,301	14,134,643	-	118,778,515
Italy	199,834,636	57,965,277	6,881,722	-	264,681,636
Latvia	5,078,191	1,975,665	263,422	-	7,317,278
Lithuania	7,595,831	3,348,819	144,154	-	11,088,805
Luxembourg	23,882,035	3,654,239	1,237,262	-	28,773,536
Malta	2,628,580	762,462	90,521	-	3,481,563
Netherlands	324,839,585	35,965,748	21,809,016	-	382,614,349
Poland	139,660,223	38,141,688	14,832,879	-	192,634,790
Portugal	56,828,347	26,076,297	7,013,625	-	89,918,269
Romania	32,897,931	8,857,135	295,238	126,532	42,176,836
Slovakia	21,280,998	5,180,067	240,312	-	26,701,378
Slovenia	16,307,977	2,854,449	2,965,087	-	22,127,513
Spain	73,444,142	21,540,879	7,590,596	-	102,575,616
Sweden	237,302,970	36,310,215	12,294,010	-	285,907,195
UK	523,927,984	80,167,297	27,143,258	-	631,238,539

Grand Total	5,557,489,187	865,623,597	309,187,193	417,359	6,732,717,336

A.9. Productivity costs

The productivity cost represents hypothetical wage losses through lost time incurred due to physician consultations or due to the severity of the disease. Although a significant portion of the vulnerable population may be unemployed, and therefore, do not cause any direct impact in terms of workforce absenteeism, we considered this cost to be relevant from other aspects such as indirect costs to caregivers, future employment opportunities and social welfare. Even if unemployed individuals do not contribute to the formal economy, their well-being and quality of life matter. Health conditions can reduce their overall welfare, affecting their ability to engage in non-work activities or participate in social life.

Based on our methodology and assumptions made, the total productivity cost is estimated at 1.67 billion Euros. The following figure and table highlight the detailed breakdown per country and indications.

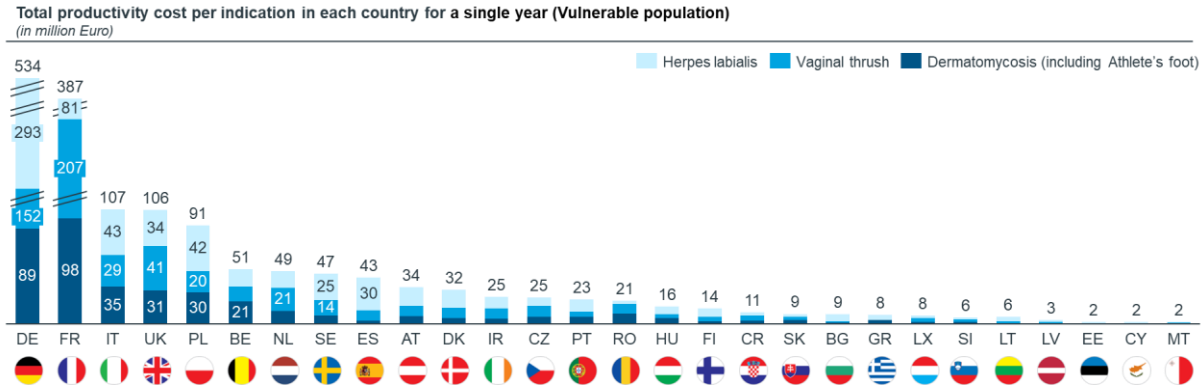


Figure 59 Total cost per indication in each country for a single year (Vulnerable Population)

Table 78 Productivity cost breakdown per country and indications in a single year (Vulnerable Population)

Country and indications	Total Productivity cost
Austria	**34,299,193**
Athlete's Foot	696,094
Dermatomycosis	6,511,431
Herpes Labialis	17,486,160
Vaginal Thrush	9,605,507
Belgium	**50,941,111**
Athlete's Foot	2,004,767
Dermatomycosis	18,753,073
Herpes Labialis	16,354,962
Vaginal Thrush	13,828,308
Bulgaria	**8,995,700**
Athlete's Foot	125,297
Dermatomycosis	1,172,058
Herpes Labialis	6,352,837
Vaginal Thrush	1,345,508
Croatia	**10,749,154**
Athlete's Foot	238,493
Dermatomycosis	2,567,609

Herpes Labialis	3,071,171
Vaginal Thrush	4,871,880
Cyprus	**1,785,017**
Athlete's Foot	50,646
Dermatomycosis	479,432
Herpes Labialis	962,869
Vaginal Thrush	292,070
Czech Republic	**24,659,216**
Athlete's Foot	649,084
Dermatomycosis	5,858,648
Herpes Labialis	7,969,779
Vaginal Thrush	10,181,704
Denmark	**31,604,139**
Athlete's Foot	492,994
Dermatomycosis	4,953,520
Herpes Labialis	16,802,894
Vaginal Thrush	9,354,732
Estonia	**1,881,471**
Athlete's Foot	10,936
Dermatomycosis	117,737
Herpes Labialis	1,408,859
Vaginal Thrush	343,939
Finland	**14,438,080**
Athlete's Foot	194,632
Dermatomycosis	1,955,634
Herpes Labialis	7,977,058
Vaginal Thrush	4,310,755
France	**386,600,775**
Athlete's Foot	9,822,546
Dermatomycosis	88,658,499
Herpes Labialis	80,871,737
Vaginal Thrush	207,247,993
Germany	**534,154,703**
Athlete's Foot	8,585,921
Dermatomycosis	80,314,759
Herpes Labialis	293,284,963
Vaginal Thrush	151,969,060
Greece	**8,109,104**
Athlete's Foot	323,493
Dermatomycosis	3,062,287
Herpes Labialis	4,647,275
Vaginal Thrush	76,049
Hungary	**16,126,954**
Athlete's Foot	452,172
Dermatomycosis	4,868,068
Herpes Labialis	6,918,061
Vaginal Thrush	3,888,653
Ireland	**24,931,644**

Athlete's Foot	505,183
Dermatomycosis	4,559,794
Herpes Labialis	10,821,751
Vaginal Thrush	9,044,916
Italy	**106,882,432**
Athlete's Foot	3,297,496
Dermatomycosis	31,215,132
Herpes Labialis	42,969,800
Vaginal Thrush	29,400,003
Latvia	**3,367,116**
Athlete's Foot	64,990
Dermatomycosis	699,678
Herpes Labialis	1,662,527
Vaginal Thrush	939,922
Lithuania	**6,492,099**
Athlete's Foot	3,295
Dermatomycosis	35,477
Herpes Labialis	4,350,547
Vaginal Thrush	2,102,780
Luxembourg	**7,770,639**
Athlete's Foot	195,134
Dermatomycosis	1,761,288
Herpes Labialis	2,320,485
Vaginal Thrush	3,493,732
Malta	**1,549,577**
Athlete's Foot	57,314
Dermatomycosis	542,555
Herpes Labialis	506,590
Vaginal Thrush	443,117
Netherlands	**49,057,214**
Athlete's Foot	1,110,307
Dermatomycosis	11,156,180
Herpes Labialis	15,722,260
Vaginal Thrush	21,068,468
Poland	**91,400,022**
Athlete's Foot	2,512,278
Dermatomycosis	27,047,120
Herpes Labialis	42,284,719
Vaginal Thrush	19,555,905
Portugal	**22,988,098**
Athlete's Foot	625,466
Dermatomycosis	5,920,857
Herpes Labialis	11,478,681
Vaginal Thrush	4,963,094
Romania	**21,486,542**
Athlete's Foot	830,832
Dermatomycosis	8,944,716
Herpes Labialis	3,185,918

Vaginal Thrush	8,525,076
Slovakia	**9,296,951**
Athlete's Foot	314,058
Dermatomycosis	3,381,145
Herpes Labialis	2,868,757
Vaginal Thrush	2,732,991
Slovenia	**5,996,421**
Athlete's Foot	184,315
Dermatomycosis	1,663,631
Herpes Labialis	1,717,506
Vaginal Thrush	2,430,969
Spain	**43,067,489**
Athlete's Foot	277,310
Dermatomycosis	2,625,104
Herpes Labialis	30,224,909
Vaginal Thrush	9,940,167
Sweden	**46,959,059**
Athlete's Foot	732,516
Dermatomycosis	7,360,195
Herpes Labialis	24,966,607
Vaginal Thrush	13,899,742
UK	**105,916,240**
Athlete's Foot	2,798,059
Dermatomycosis	28,114,428
Herpes Labialis	33,539,778
Vaginal Thrush	41,463,976
Grand Total	**1,671,506,161**

A.10. Volume impact

The volume impact results reveal that reverse-switching may not reduce the use of antifungal and antiviral medicines. The volume is estimated based on IQVIA NPM sales data and the following factors:

- Share of patient population who seek Rx, seek alternative treatment or do nothing
    - Share of patient population who develop recurrences
    - Severity and chronicity of conditions
    - Number of doctor's visits and refills
- We assumed that the delay in appropriate treatment for patients who seek alternative treatment or do nothing, causes worsening and chronification of conditions, which increases the use of antiviral and antifungal medicines.
- We did not account for potential changes in treatment regime, for example from topical to oral formulation, in the event of worsening or chronification of conditions.

Based on these assumptions and factors, the volume impact of herpes labialis shows a potential 60% increase, with consumption rising from 28.5 million units to 45.5 million units. Dermatomycosis, including Athlete's foot, potentially experiences the most significant increase of 176%, with consumption jumping from 13.1 million units to 36.1 million units. These potential increases are attributed to those who seek

alternative treatment or do nothing as they will delay appropriate treatment, resulting in worsening of symptoms and eventual need for a doctor's appointment as well as prescription for a more severe condition. Reverse-switch could also lead to a shift in prescribing practices, for instance, from prescribing topical/external treatment to oral/systemic treatment.

Conversely, the volume impact for Vaginal Thrush shows a potential of 22% decrease, with consumption dropping from 44.7 million units to 35 million units. This decline is attributed to several factors. First, most patients with vaginal thrush are women, and a majority of them seek prescription treatments rather than alternative treatments or doing nothing. Second, those who seek prescriptions tend to do so immediately, leading to better-managed conditions and fewer recurrences. Consequently, the lower recurrence rate results in a negative volume impact for vaginal thrush.

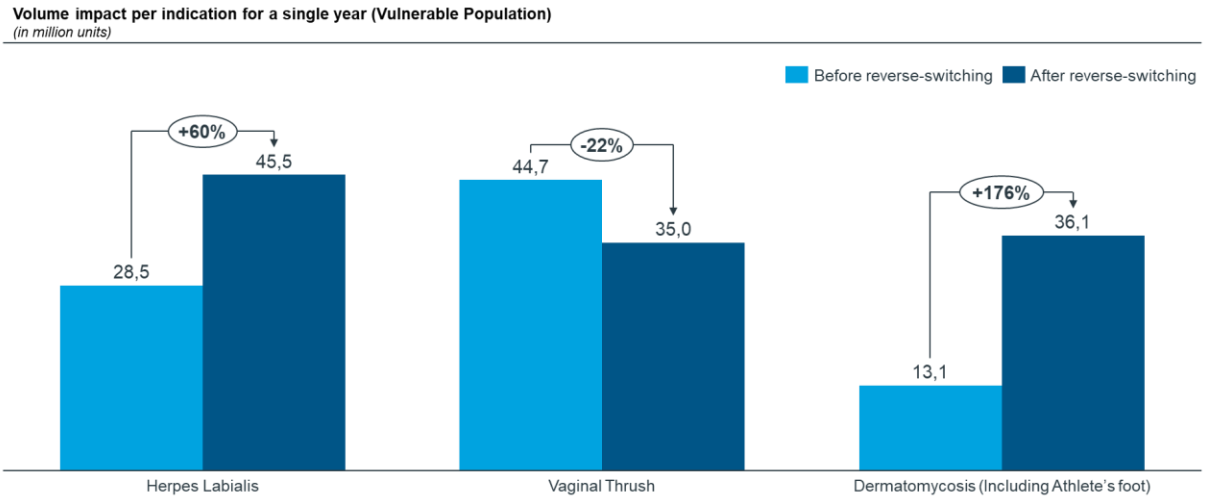


Figure 60 Volume impact per indication for a single year in million units (Vulnerable Population)

Table 79 Volume impact per indication for a single year details (Vulnerable Population)

	Herpes Labialis	Vaginal Thrush	Dermatomycosis (Including Athlete's foot)
Before reverse-switching	28,463,923	44,715,672	13,087,369
After reverse-switching	45,516,687	35,043,683	36,144,879

These numbers show that, contrary to expectations, reverse-switching may not reduce the volume of antivirals and antifungals use.

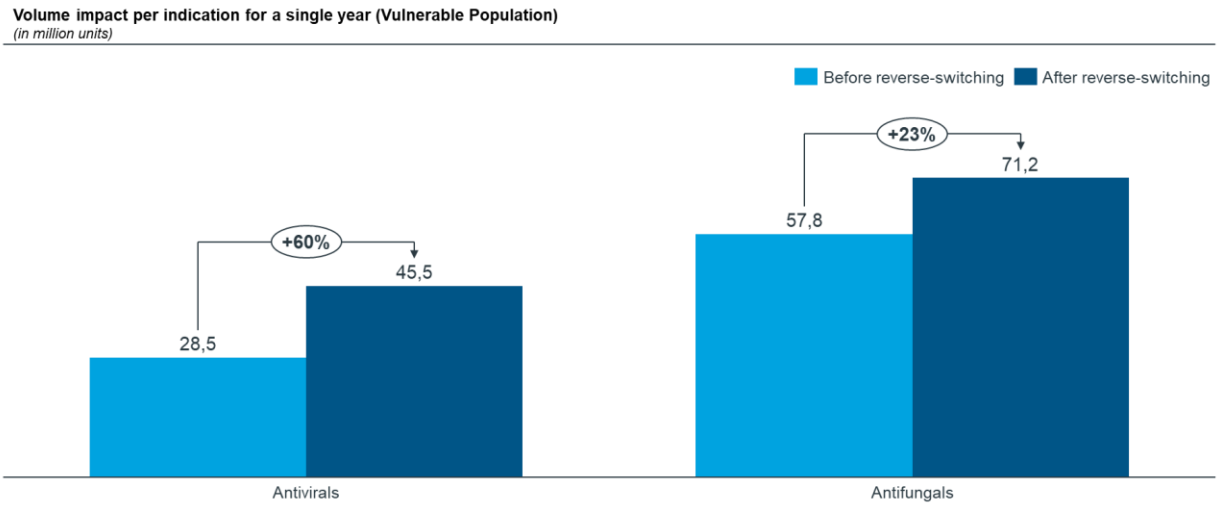


Figure 61 Volume impact in a single year for Antivirals and Antifungals (Vulnerable Population)

Table 80 Volume impact in a single year for Antivirals and Antifungals details (Vulnerable Population)

	Antivirals	Antifungals
Before reverse-switching	28,463,923	57,803,041
After reverse-switching	45,516,687	71,188,562

Annex III: Survey discussion guide

Health economic study on impact of reverse-switching antifungal, antiviral and antiseptics

Note:
SA: Single Answer
MA: Multiple Answers

DEMOGRAPHIC PROFILE AND SCREENER

[ALL] We would like to invite you to participate in our survey to improve our understanding on the potential impact of reclassifying antifungal, antiviral and antiseptic non-prescription medicines to prescription status.

Should you agree to participate, we will proceed to the screener and main survey which would take about ~**30 minutes** to complete**.** Would you be interested in participating?

Interest to Participate	CODE [SA]	Remark
Yes	1	**CONTINUE**
No	2	**THANKS & TERMINATE**

IF CONTINUE, SHOW [Thank you for agreeing to participate in this study. Please be assured that all your responses will be kept in strict confidence. We will ensure that the strictest standards of privacy are maintained with the content of your responses during the discussion. Rest assured that no identifying information will be collected, and all responses will remain anonymous.**]**

IF TERMINATE, SHOW [Thank you for your time. We hope to have the opportunity to include you in future research studies.]

S1. **[ASK Germany/ Italy/ Poland/ France]** What is your preferred language for the study? **[SA]**
This question (S1) will be asked in both **English and **local language**.*
For UK, only **English will be used. Hence S1 will be skipped.*

Language	CODE [SA]	Remark
[SHOW ALL] English	1	**CONTINUE**
[SHOW Germany only] German	2	
[SHOW Italy only] Italian	3	
[SHOW Poland only] Polish	4	
[SHOW France only] French	5	
Others	99	**THANKS & TERMINATE**

S2. **[ASK ALL]** Have you experienced any of the following conditions in the past 12 months? You may choose more than one **[MA]**

Conditions	CODE [MA]	Remark
Vaginal thrush	1	**CHECK QUOTA, CONTINUE TO Q2a**
Dermatomycosis (fungal infection of the skin, including athlete's foot)	2	
Herpes labialis	3	
Wound	4	
Pharyngitis	5	
No; I never had any of the conditions you mentioned above.	6	**THANKS & TERMINATE**

S2a. **[ASK ALL]** Have you used products without prescription to **treat any of the selected** indication(s) in the past 12 months? **[SA]**[76]

	Please select	Remark
Yes	1	**CONTINUE**
No	2	**THANKS & TERMINATE**

S2b. **If 1-5 selected** How many times had you had **[insert indication selected in S2]** in the past 12 months? **[SA]**

Status of condition	CODE [SA]	Remark
One-time episode	1	**CONTINUE**
Recurrent (More than once/ongoing)	2	

S3. **[ASK ALL]** What sex was attributed at birth? **[SA]**

Gender	CODE [SA]	Remark
Male	1	**CONTINUE**
Female	2	
Others	3	

S4. **[ASK ALL]** Can you please tell me your age? **[SA]**

Age Group	CODE [SA]	Remark

[76] S2a to be repeated for each indication selected in S2

Below 18 years	1	**THANKS & TERMINATE**
18-24 years	2	**CHECK QUOTA, CONTINUE**
25-29 years	3	
30-34 years	4	**CHECK QUOTA, CONTINUE**
34-39 years	5	
40-44 years	6	
45-49 years	7	**CHECK QUOTA, CONTINUE**
50-54 years	8	
55-59 years	9	
60 years and above	10	**CHECK QUOTA, CONTINUE**

S5. **[ASK ALL]** Monthly household income **[SA]**

S5a. Including yourself, how many people are in your household?

	Write in	**Remark**
Household size	**RANGE 1-10** #	**CONTINUE**

S5b. What is your **[weekly (UK ONLY)/ monthly]** household income after deductions and taxes? **[SA]**

	Write in	**Remark**
Household income	**RANGE 1-20000** #	**CONTINUE**
Prefer not to answer	99	**THANKS & TERMINATE**

[UK ONLY]

Weekly Net Household Income	**CODE [SA]**	**Remark**
Less than £373 per week	1	**CHECK QUOTA, CONTINUE**
£373 per week and more	2	**CHECK QUOTA, CONTINUE**
Prefer not to answer	99	**THANKS & TERMINATE**

[GERMANY ONLY]

Monthly Household Income	**CODE [SA]**	**Remark**

Less than €1,250 pm	1	**CHECK QUOTA, CONTINUE**
€1,250 pm and more	2	**CHECK QUOTA, CONTINUE**
Prefer not to answer	99	**THANKS & TERMINATE**

[ITALY ONLY]

Monthly Household Income	CODE [SA]	Remark
Less than €1,150 pm	1	**CHECK QUOTA, CONTINUE**
€1,150 pm and more	2	**CHECK QUOTA, CONTINUE**
Prefer not to answer	99	**THANKS & TERMINATE**

[POLAND ONLY]

Monthly Household Income	CODE [SA]	Remark
Less than XX	1	**CHECK QUOTA, CONTINUE**
XX and more	2	**CHECK QUOTA, CONTINUE**
Prefer not to answer	99	**THANKS & TERMINATE**

[FRANCE ONLY]

Monthly Household Income	CODE [SA]	Remark
Less than €1,150 pm	1	**CHECK QUOTA, CONTINUE**
€1,150 pm and more	2	**CHECK QUOTA, CONTINUE**
Prefer not to answer	99	**THANKS & TERMINATE**

S6. **[ASK ALL]** Please select your working status. **[SA]**

Employment	CODE [SA]	Remark
Self-employed	1	**CONTINUE**
Full-time employee	2	
Part-time employee	3	

Unemployed	4	
Retired	5	
Student	6	

S7. **[ASK ALL]** Please select your highest education level. **[SA]**

Education	CODE [SA]	Remark
No formal education	1	**CONTINUE**
Primary education	2	
Lower secondary education	3	
Upper secondary education	5	
Post-secondary non-tertiary education	6	
Short-cycle tertiary education	7	
Tertiary education – Bachelors	8	
Tertiary education - Masters	9	
Tertiary education – PhD	10	
None of the above	11	

S8. **[ASK ALL]** Do you have any of these conditions? You may choose more than one **[MA]**

Medical Condition	CODE [MA]	Remark
Cardiovascular Disease	1	**CONTINUE**
Cancer	2	
Chronic Respiratory Disease	4	
Chronic Kidney Disease	5	**CONTINUE**
Communication disabilities	6	**THANKS & TERMINATE**
Terminal Illness/ End Stage disease	7	**THANKS & TERMINATE**
Psychiatric Illness	8	**THANKS & TERMINATE**
No; I do not have any of the conditions you mentioned above.	9	**CONTINUE**

[RESPONDENT HAS BEEN TERMINATED] Thank you for your willingness to participate in our study. Unfortunately, based on the specific criteria we have set for this research, we are unable to

include you in the study at this time. We genuinely appreciate your interest and value your opinion. We hope to have the opportunity to include you in future research studies.

Section A: Background Information

We would like to ask you some background questions on your access to healthcare.

1. **[ASK ALL]** How far are you from the nearest retail pharmacy? [SA]

Distance	Please select	Remark
Less than 3 km	1	**CONTINUE**
3 – 5 km	2	
5 – 10 km	3	
More than 10 km	4	

2. **[ASK for UK and Italy only]** How far are you from the nearest retail outlet selling over-the-counter medicines? [SA]

Distance	Please select	Remark
Less than 3 km	1	**CONTINUE**
3 – 5 km	2	
5 – 10 km	3	
More than 10 km	4	
Not applicable	5	

3. **[ASK ALL]** How far are you from the nearest health clinic/GP? [SA]

Distance	Please select	Remark
Less than 3 km	1	**CONTINUE**
3 – 5 km	2	
5 – 10 km	3	
More than 10 km	4	

4. **[ASK ALL]** How far are you from the nearest emergency care unit? [SA]

Distance	Please select	Remark
Less than 3 km	1	**CONTINUE**
3 – 5 km	2	
5 – 10 km	3	
More than 10 km	4	

5. **[ASK ALL]** In the past 12 months, did you have problem accessing healthcare due to any of these reasons? You may choose more than one [MA except 5 and 6]

Reason	Please select [MA]	Remark
Long distance or lack of transportation	1	**CONTINUE**
Long waiting list	2	
Could not afford to pay for medical examination	3	
Could not afford to pay for treatment including medicines	4	
Could not take time off	5	
None of the above, I have other reason(s). Please state	FREE TEXT	
No, did not have any problem accessing healthcare	6	
No, did not need care	7	

6. **[ASK ALL]** Have you used products without prescription to treat **[insert in-scope indication(s)]** in the past 12 months? [SA][77]

	Please select	Remark
Yes	1	**CONTINUE TO Q7**
No	2	**SKIP TO Q9, THEN TERMINATE BEFORE SECTION B, MARK AS COMPLETED**

7. **If respondent selects yes to Q6** What products without prescription have you used for **[insert in-scope indication]** in the past 12 months? [SA]

	Please select [MA]	Remark
Please specify	FREE TEXT	**CONTINUE to Q8**
Do not remember	99	

8. **If respondent selects yes to Q6** Where did you purchase the products without prescription from? [MA]

[77] Question 6-10 to be repeated for each indication selected

	Please select	Remark
Retail chain	1	**CONTINUE TO Q9**
Pharmacy	2	
Clinics	3	
Online	4	
Others	FREE TEXT	

9. **[ASK ALL]** Have you used prescription medicines for **[insert in-scope indication(s)]** in the past 12 months? [SA]

	Please select	Remark
Yes	1	**CONTINUE TO Q10**
No	2	**SKIP TO Q11**

10. **If respondent selects yes to Q9** What medicines were you prescribed for **[insert in-scope indication(s)]** in the past 12 months? [SA]

Prescription Medicine	Please select [MA]	Remark
Please specify	FREE TEXT	**CONTINUE**
Do not remember	99	

11. **If respondent selects no to Q9** Were products available without prescription your only treatment choice for **insert in-scope indication(s)]** in the past 12 months? [SA]

	Please select	Remark
Yes	1	**CONTINUE TO SECTION B INTRO**
No, I also use _____	2 FREE TEXT	

IF CONTINUE, SHOW [INTRO TO SECTION B]

IF TERMINATE, SHOW [Thank you for joining the survey]

Section B: Scenario[78]

In this next section, imagine that the products that you have been using for **[insert in-scope indications selected]**, along with the entire class of medicines, are no longer available over the counter and they must be prescribed by a doctor for you to obtain them. Please consider this scenario as if you are making real-world decisions on your condition and indicate your most preferred option.

12. Considering this change in policy, what would you do to get treated for **[insert in-scope indications selected]**? [SA]

Option	Please select	Remark
Switch to an alternate treatment	1	**CONTINUE TO Q13**
Get a prescription	2	**SKIP Q13, CONTINUE TO Q14**
Do nothing	3	**SKIP Q13 & Q14, CONTINUE TO Q15**

13. **If respondent selects 1 in Q12** If you opt to use an alternative, what would it be? [SA]

Alternative	Please select	Remark
Product from another class available as OTC (OTCs are products available without prescription e.g. painkillers, anti-itch products etc.)	1	**CONTINUE TO Q13(a)**
Home remedies	2	**THANKS & TERMINATE, OR LOOP BACK TO Q12 TO REPEAT FOR ANOTHER INDICATION SELECTED**
Get the same product online or from other market	3	
Other	4 FREE TEXT	

a. **If respondent selects 1 in Q13** If you opt for product from another class of OTC, what would it be? [SA]

Prescription Medicine	Please select [MA]	Remark
Please specify	FREE TEXT	**CONTINUE**
Do not remember	99	

14. **If respondent selects 2 in Q12** What would you do to get a prescription? [SA]

[78] Questions for Section B will be repeated for each indication if more than one were selected

Option	Please select	Remark
Visit a general practitioner or specialist doctor	1	**THANKS & TERMINATE, OR LOOP BACK TO Q12 TO REPEAT FOR ANOTHER INDICATION SELECTED**
Go to emergency care unit	2	
Visit a specialist clinic	3	
Others	4 FREE TEXT	

15. **If respondent selects 3 in Q12** If the condition does not resolve, what would you do? [SA]

Option	Please select	Remark
Switch to an alternate treatment	1	**LOOP BACK TO Q13**
Get a prescription	2	**LOOP BACK TO Q14**
Other	3 FREE TEXT	**THANKS & TERMINATE, OR LOOP BACK TO Q12 TO REPEAT FOR ANOTHER INDICATION SELECTED**
Do nothing	4	

THANK YOU FOR JOINING THIS SURVEY!

Annex IV: Survey results

Section A: Background information

Question 1

[ASK ALL] ***"How far are you from the nearest retail pharmacy?"*** [Single answer]

Table 81 Survey results: Retail pharmacy distance

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	378	90	83	79	66	60
	100%	100%	100%	100%	100%	100%
Less than 3 km	75%	66%	73%	73%	94%	70%
3 - 5 km	18%	27%	22%	22%	2%	15%
5 - 10 km	6%	8%	5%	4%	3%	12%
More than 10 km	1%	-	-	1%	2%	3%

Question 2

[ASK for UK and Italy only] ***"How far are you from the nearest retail outlet selling over-the-counter medicines?"*** [Single answer]

Table 82 Survey results: OTC retail distance

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	145	-	-	79	66	-
	100%			100%	100%	
Less than 3 km	79%	-	-	68%	92%	-
3 - 5 km	12%	-	-	20%	3%	-
5 - 10 km	6%	-	-	9%	3%	-
More than 10 km	2%	-	-	3%	2%	-
Not applicable	-	-	-	-	-	-

Question 3

[ASK ALL] ***"How far are you from the nearest health clinic/GP?"*** [Single answer]

Table 83 Survey results: Health clinic/GP distance

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	378	90	83	79	66	60

	100%	100%	100%	100%	100%	100%
Less than 3 km	54%	47%	47%	63%	58%	58%
3 - 5 km	25%	24%	28%	22%	33%	17%
5 - 10 km	17%	22%	19%	14%	8%	23%
More than 10 km	4%	7%	6%	1%	2%	2%

Question 4

[ASK ALL] ***"How far are you from the nearest emergency care unit?"*** [Single answer]

Table 84 Survey results: Emergency care distance

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	378	90	83	79	66	60
	100%	100%	100%	100%	100%	100%
Less than 3 km	25%	27%	19%	19%	27%	33%
3 - 5 km	28%	32%	19%	32%	33%	23%
5 - 10 km	26%	24%	33%	23%	23%	27%
More than 10 km	21%	17%	29%	27%	17%	17%

Question 5

[ASK ALL] ***"In the past 12 months, did you have problem accessing healthcare due to any of these reasons? You may choose more than one"*** [Multiple answer except 5 and 6]

Table 85 Survey results: Problem accessing healthcare

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	378	90	83	79	66	60
	100%	100%	100%	100%	100%	100%
Long distance or lack of transportation	11%	14%	17%	9%	8%	5%
Long waiting list	47%	33%	51%	46%	56%	55%
Could not afford to pay for medical examination	10%	7%	6%	11%	11%	17%
Could not afford to pay for treatment including medicines	7%	6%	10%	8%	6%	8%
Could not take time off	11%	13%	7%	13%	11%	12%
None of the above, I have other reason(s). Please state	1%	-	1%	1%	-	-
No, did not have any problem accessing healthcare	34%	43%	29%	34%	29%	30%
No, did not need care	7%	10%	6%	10%	3%	5%

Question 6

[ASK ALL] ***"Have you used products without prescription to treat [insert in-scope indication(s)] in the past 12 months?"*** [Single answer]

Table 86 Survey results: OTC use - vaginal thrush

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	102	21	20	20	21	20
	100%	100%	100%	100%	100%	100%
Yes	92%	90%	75%	95%	100%	100%
No	8%	10%	25%	5%	-	-

Table 87 Survey results: OTC use - Dermatomycosis (including athlete's foot)

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	101	20	21	20	20	20
	100%	100%	100%	100%	100%	100%
Yes	91%	95%	86%	100%	85%	90%
No	9%	5%	14%	-	15%	10%

Table 88 Survey results: OTC use - Herpes labialis

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	100	20	20	20	20	20
	100%	100%	100%	100%	100%	100%
Yes	92%	95%	80%	90%	100%	95%
No	8%	5%	20%	10%	-	5%

Table 89 Survey results: OTC use - Wound

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	101	21	20	20	20	20
	100%	100%	100%	100%	100%	100%
Yes	84%	81%	80%	80%	90%	90%
No	16%	19%	20%	20%	10%	10%

Table 90 Survey results: OTC use - Pharyngitis

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	103	22	21	20	20	20

	100%	100%	100%	100%	100%	100%
Yes	88%	100%	76%	90%	75%	100%
No	12%	-	24%	10%	25%	-

Question 8

[If respondent selects yes to question 6] **Where did you purchase the products without prescription from?** [Multiple answer]

Table 91 Survey results: OTC channel - Vaginal thrush

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	94	19	15	19	21	20
	100%	100%	100%	100%	100%	100%
Retail chain	13%	5%	13%	26%	5%	15%
Pharmacy	82%	68%	67%	89%	90%	90%
Clinics	5%	11%	7%	-	-	10%
Online	19%	32%	40%	-	19%	10%
Others	1%	-	-	-	-	5%

Table 92 Survey results: OTC channel - Dermatomycosis (including athlete's foot)

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	92	19	18	20	17	18
	100%	100%	100%	100%	100%	100%
Retail chain	25%	5%	17%	65%	12%	22%
Pharmacy	73%	68%	83%	50%	88%	78%
Clinics	5%	-	-	-	-	28%
Online	16%	37%	17%	5%	12%	11%
Others	-	-	-	-	-	-

Table 93 Survey results: OTC channel - Herpes labialis

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	92	19	16	18	20	19
	100%	100%	100%	100%	100%	100%
Retail chain	11%	5%	6%	28%	5%	11%
Pharmacy	86%	95%	94%	61%	85%	95%
Clinics	1%	-	-	-	-	5%
Online	14%	16%	6%	39%	10%	-
Others	1%	-	-	-	5%	-

Table 94 Survey results: OTC channel - Wound

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	85	17	16	16	18	18
	100%	100%	100%	100%	100%	100%
Retail chain	29%	41%	6%	81%	11%	11%
Pharmacy	76%	76%	100%	25%	78%	100%
Clinics	4%	-	6%	-	6%	6%
Online	11%	29%	6%	-	11%	6%
Others	-	-	-	-	-	-

Table 95 Survey results: OTC channel - Pharyngitis

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	91	22	16	18	15	20
	100%	100%	100%	100%	100%	100%
Retail chain	11%	18%	-	22%	-	10%
Pharmacy	85%	82%	100%	61%	93%	90%
Clinics	3%	5%	-	-	7%	5%
Online	21%	45%	-	33%	13%	5%
Others	1%	-	-	-	7%	-

Question 9

[ASK ALL] ***"Have you used prescription medicines for [insert in-scope indication(s)] in the past 12 months?"*** [Single answer]

Table 96 Survey results: Rx use - Vaginal thrush

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	102	21	20	20	21	20
	100%	100%	100%	100%	100%	100%
Yes	61%	43%	75%	60%	48%	80%
No	39%	57%	25%	40%	52%	20%

Table 97 Survey results: Rx use - Dermatomycosis (including athlete's foot)

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	101	20	21	20	20	20
	100%	100%	100%	100%	100%	100%
Yes	52%	40%	62%	50%	40%	70%
No	48%	60%	38%	50%	60%	30%

Table 98 Survey results: Rx use - Herpes labialis

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	100	20	20	20	20	20
	100%	100%	100%	100%	100%	100%
Yes	44%	50%	55%	45%	40%	30%
No	56%	50%	45%	55%	60%	70%

Table 99 Survey results: Rx use - Wound

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	101	21	20	20	20	20
	100%	100%	100%	100%	100%	100%
Yes	41%	33%	65%	35%	35%	35%
No	59%	67%	35%	65%	65%	65%

Table 100 Survey results: Rx use - Pharyngitis

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	103	22	21	20	20	20
	100%	100%	100%	100%	100%	100%
Yes	43%	32%	48%	20%	60%	55%
No	57%	68%	52%	80%	40%	45%

Question 11

[If respondent selects no to question 9] ***"Were products available without prescription your only treatment choice for insert in-scope indication(s)] in the past 12 months?"*** [Single answer]

Table 101 Survey results: OTC sole option - Vaginal thrush

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	40	12	5	8	11	4
	100%	100%	100%	100%	100%	100%
Yes	98%	100%	80%	100%	100%	100%
No, I also use	3%	-	20%	-	-	-

Table 102 Survey results: OTC sole option - Dermatomycosis (including athlete's foot)

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	48	12	8	10	12	6
	100%	100%	100%	100%	100%	100%
Yes	98%	100%	88%	100%	100%	100%
No, I also use	2%	-	13%	-	-	-

Table 103 Survey results: OTC sole option - Herpes labialis

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	56	10	9	11	12	14
	100%	100%	100%	100%	100%	100%
Yes	93%	100%	100%	82%	92%	93%
No, I also use	7%	-	-	18%	8%	7%

Table 104 Survey results: OTC sole option - Wound

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	60	14	7	13	13	13
	100%	100%	100%	100%	100%	100%
Yes	87%	93%	57%	92%	85%	92%
No, I also use	13%	7%	43%	8%	15%	8%

Table 105 Survey results: OTC sole option - Pharyngitis

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	59	15	11	16	8	9
	100%	100%	100%	100%	100%	100%
Yes	86%	93%	82%	88%	75%	89%
No, I also use	14%	7%	18%	13%	25%	11%

Section B: Scenario[79]

From question 12 until the end, respondents are given the following introduction:

> *"In this next section, imagine that the products that you have been using for **[insert in-scope indications selected],** along with the entire class of medicines, are no longer available over the counter and they must be prescribed by a doctor for you to obtain them. Please consider this scenario as if you are making real-world decisions on your condition and indicate your most preferred option."*

Question 12

"Considering this change in policy, what would you do to get treated for [insert in-scope indications selected]?" [Single answer]

Table 106 Survey results: Reverse switch treatment options - Vaginal thrush

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	94	19	15	19	21	20
	100%	100%	100%	100%	100%	100%
Switch to an alternate treatment	27%	21%	20%	21%	48%	20%
Get a prescription	69%	74%	80%	68%	52%	75%
Do nothing	4%	5%	-	11%	-	5%

Table 107 Survey results: Reverse switch treatment options - Dermatomycosis (including athlete's foot)

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	92	19	18	20	17	18
	100%	100%	100%	100%	100%	100%
Switch to an alternate treatment	37%	37%	22%	45%	41%	39%
Get a prescription	60%	58%	72%	50%	59%	61%
Do nothing	3%	5%	6%	5%	-	-

Table 108 Survey results: Reverse switch treatment options - Herpes labialis

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	92	19	16	18	20	19
	100%	100%	100%	100%	100%	100%
Switch to an alternate treatment	39%	26%	50%	28%	55%	37%
Get a prescription	54%	68%	38%	67%	45%	53%

[79] Note: Questions for Section B will be repeated for each indication if more than one were selected

Do nothing	7%	5%	13%	6%	-	11%

Table 109 Survey results: Reverse switch treatment options - Wound

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	85	17	16	16	18	18
	100%	100%	100%	100%	100%	100%
Switch to an alternate treatment	48%	41%	38%	50%	61%	50%
Get a prescription	48%	59%	63%	38%	39%	44%
Do nothing	4%	-	-	13%	-	6%

Table 110 Survey results: Reverse switch treatment options - Pharyngitis

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	91	22	16	18	15	20
	100%	100%	100%	100%	100%	100%
Switch to an alternate treatment	35%	32%	31%	44%	27%	40%
Get a prescription	56%	59%	50%	50%	73%	50%
Do nothing	9%	9%	19%	6%	-	10%

Question 13

[If respondent selects "Switch to alternate treatments" in question 12] ***"If you opt to use an alternative, what would it be?"*** [Single answer]

Table 111 Survey results: Choice of alternative treatment - Vaginal thrush

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	26	5	3	4	10	4
	100%	100%	100%	100%	100%	100%
Product from another class available as OTC (OTCs are products available without prescription e.g. painkillers, anti-itc	73%	100%	100%	50%	60%	75%
Home remedies	27%	-	-	50%	40%	25%
Get the same product online or from other market	-	-	-	-	-	-

Other	-	-	-	-	-	-

Table 112 Survey results: Choice of alternative treatment – Dermatomycosis (including athlete's foot)

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	34	7	4	9	7	7
	100%	100%	100%	100%	100%	100%
Product from another class available as OTC (OTCs are products available without prescription e.g. painkillers, anti-itc	71%	100%	75%	44%	71%	71%
Home remedies	12%	-	25%	22%	14%	-
Get the same product online or from other market	18%	-	-	33%	14%	29%
Other	-	-	-	-	-	-

Table 113 Survey results: Choice of alternative treatment - Herpes labialis

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	39	5	9	5	11	9
	100%	100%	100%	100%	100%	100%
Product from another class available as OTC (OTCs are products available without prescription e.g. painkillers, anti-itc	67%	60%	78%	80%	64%	56%
Home remedies	26%	20%	11%	20%	36%	33%
Get the same product online or from other market	8%	20%	11%	-	-	11%
Other	-	-	-	-	-	-

Table 114 Survey results: Choice of alternative treatment - Wound

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND

Total	41	7	6	8	11	9
	100%	100%	100%	100%	100%	100%
Product from another class available as OTC (OTCs are products available without prescription e.g. painkillers, anti-itc	61%	100%	67%	38%	55%	56%
Home remedies	32%	-	17%	38%	45%	44%
Get the same product online or from other market	7%	-	17%	25%	-	-
Other	-	-	-	-	-	-

Table 115 Survey results: Choice of alternative treatment - Pharyngitis

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	34	7	7	8	4	8
	100%	100%	100%	100%	100%	100%
Product from another class available as OTC (OTCs are products available without prescription e.g. painkillers, anti-itc	65%	86%	86%	63%	50%	38%
Home remedies	26%	14%	-	25%	50%	50%
Get the same product online or from other market	9%	-	14%	13%	-	13%
Other	-	-	-	-	-	-

Question 14

[If respondent selects “Get a prescription” in question 12] ***“What would you do to get a prescription?”*** [Single answer]

Table 116 Survey results: Choice of Rx - Vaginal thrush

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	68	14	12	15	11	16

	100%	100%	100%	100%	100%	100%
Visit a general practitioner or specialist doctor	85%	86%	92%	100%	91%	63%
Go to emergency care unit	3%	-	-	-	9%	6%
Visit a specialist clinic	12%	14%	8%	-	-	31%
Others	-	-	-	-	-	-

Table 117 Survey results: Choice of Rx – Dermatomycosis (including athelete's foot)

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	57	11	14	11	10	11
	100%	100%	100%	100%	100%	100%
Visit a general practitioner or specialist doctor	91%	100%	79%	100%	100%	82%
Go to emergency care unit	5%	-	21%	-	-	-
Visit a specialist clinic	4%	-	-	-	-	18%
Others	-	-	-	-	-	-

Table 118 Survey results: Choice of Rx - Herpes labialis

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	52	14	7	12	9	10
	100%	100%	100%	100%	100%	100%
Visit a general practitioner or specialist doctor	96%	100%	100%	92%	89%	100%
Go to emergency care unit	-	-	-	-	-	-
Visit a specialist clinic	4%	-	-	8%	11%	-
Others	-	-	-	-	-	-

Table 119 Survey results: Choice of Rx - Wound

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	43	10	10	8	7	8
	100%	100%	100%	100%	100%	100%
Visit a general practitioner or specialist doctor	91%	100%	90%	100%	86%	75%
Go to emergency care unit	2%	-	-	-	-	13%

Visit a specialist clinic	7%	-	10%	-	14%	13%
Others	-	-	-	-	-	-

Table 120 Survey results: Choice of Rx - Pharyngitis

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	54	14	9	10	11	10
	100%	100%	100%	100%	100%	100%
Visit a general practitioner or specialist doctor	94%	93%	89%	100%	100%	90%
Go to emergency care unit	4%	-	11%	-	-	10%
Visit a specialist clinic	2%	7%	-	-	-	-
Others	-	-	-	-	-	-

Question 15

[If respondent selects "Do nothing" in question 12] **If the condition does not resolve, what would you do?** [Single answer]

Table 121 Survey results: Choice of do nothing - Vaginal thrush

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	4	1	-	2	-	1
	100%	100%		100%		100%
Switch to an alternate treatment	25%	100%	-	-	-	-
Get a prescription	75%	-	-	100%	-	100%
Other	-	-	-	-	-	-
Do nothing	-	-	-	-	-	-

Table 122 Survey results: Choice of do nothing - Dermatomycosis (including athlete's foot)

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	3	1	1	1	-	-
	100%	100%	100%	100%		
Switch to an alternate treatment	-	-	-	-	-	-
Get a prescription	67%	-	100%	100%	-	-
Other	33%	100%	-	-	-	-
Do nothing	-	-	-	-	-	-

Table 123 Survey results: Choice of do nothing - Herpes labialis

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	6	1	2	1	-	2
	100%	100%	100%	100%		100%
Switch to an alternate treatment	50%	-	50%	-	-	100%
Get a prescription	33%	100%	50%	-	-	-
Other	-	-	-	-	-	-
Do nothing	17%	-	-	100%	-	-

Table 124 Survey results: Choice of do nothing - Wound

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	3	-	-	2	-	1
	100%			100%		100%
Switch to an alternate treatment	-	-	-	-	-	-
Get a prescription	67%	-	-	100%	-	-
Other	-	-	-	-	-	-
Do nothing	33%	-	-	-	-	100%

Table 125 Survey results: Choice of do nothing - Pharyngitis

	TOTAL	GERMANY	FRANCE	UK	ITALY	POLAND
Total	8	2	3	1	-	2
	100%	100%	100%	100%		100%
Switch to an alternate treatment	25%	-	67%	-	-	-
Get a prescription	38%	50%	33%	100%	-	-
Other	-	-	-	-	-	-
Do nothing	38%	50%	-	-	-	100%

Annex V: Disability weight

In this section, we provide additional insights on how reverse-switching impacts disability weights, which are defined as the number of days lost due to ill-health, disability, or early death. We calculated the disability weight for each of the three decision pathways: Seek Rx, Seek alternative treatment, and Do nothing. The formulas used for these calculations are detailed below.

Methodology of calculating Disability weight

1. **Disability weight for Seeking Rx decision pathway**

$$Disability\ weight_{Seek\ Rx} = \left(Burden\ \times a\%\ \times \left(\frac{DALY}{365\ days}\right) \times Length\ of\ First\ episode_{\ Lower\ bound}\right) + \left(Burden\ \times recurrence\ rate\ \times a\%\ \times \left(\frac{DALY}{365\ days}\right) \times\ Length\ of\ recurrent\ episode_{\ Lower\ bound}\ \times\ Length\ of\ Episode_{Lower\ bound}\right)$$

Where:

- Burden: The number of individuals infected with any of the specified indications who exhibit symptoms and receive Non-prescription medicine (NPM)treatment.
- a%: the % of total burden who chose to seek Rx as their decision pathways in case of reverse-switch.
- Recurrence rate: The estimated % share of total burden who experience recurrences based on the natural history.
- $Number\ of\ episodes_{lower\ bound}$: The least number of bound episode range based on the natural history[80].
- DALY = Disability-adjusted life year, defined as a measure of overall disease burden, expressed as the number of years lost due to ill-health, disability, or early death. Data obtained from IHME[81].

2. **Disability weight for Seeking alternative treatment decision pathway**

$$Disability\ weight_{Seek\ alternative\ product} = \left(Burden\ \times b\%\ \times \left(\frac{DALY}{365\ days}\right) \times Length\ of\ First\ episode_{\ Upper\ bound}\right) + \left(Burden\ \times recurrence\ rate\ \times b\%\ \times \left(\frac{DALY}{365\ days}\right) \times\ Length\ of\ recurrent\ episode_{\ Upper\ bound}\ \times\ Length\ of\ Episode_{Upper\ bound}\right)$$

Where:

- Burden: The number of individuals infected with any of the specified indications who exhibit symptoms and receive Non-prescription medicine (NPM)treatment.

[80] It is assumed that individuals who seek prescription medication immediately, resulting in better-controlled conditions and fewer number of episodes.

[81] GBD Results. (n.d.-b). Institute for Health Metrics and Evaluation. https://vizhub.healthdata.org/gbd-results/

- b%: The % of total burden who chose to Seek alternative treatment as their decision pathways in case of reverse-switch.
- Recurrence rate: The estimated % share of total burden who experience recurrences based on the natural history.
- Upper bound episode: The greatest number of bound episode range based on the natural history[82].
- DALY = Disability-adjusted life year, defined as a measure of overall disease burden, expressed as the number of years lost due to ill-health, disability, or early death. Data obtained from IHME[83].

3. Disability weight for seeking alternative treatment decision pathway

$$Disability\ weight_{Do\ nothing} = \left(Burden\ \times c\%\ \times \left(\frac{DALY}{365\ days}\right) \times Length\ of\ First\ episode_{\ Upper\ bound}\right) + \left(Burden\ \times recurrence\ rate\ \times c\%\ \times \left(\frac{DALY}{365\ days}\right) \times\ Length\ of\ recurrent\ episode_{Upper\ bound}\ \times\ Length\ of\ Episode_{Upper\ bound}\right)$$

Where:

- Burden: The number of individuals infected with any of the specified indications who exhibit symptoms and receive Non-prescription medicine (NPM)treatment.
- c%: The % of total burden who chose to Seek alternative treatment as their decision pathways in case of reverse-switch.
- Recurrence rate: The estimated % share of total burden who experience recurrences based on the natural history.
- Upper bound episode: The greatest number of bound episode range based on the natural history[84].
- DALY = Disability-adjusted life year, defined as a measure of overall disease burden, expressed as the number of years lost due to ill-health, disability, or early death. Data obtained from IHME[85].

4. Total disability weight

$$Disability\ weight_{Total} = Disability\ weight_{Seek\ Rx} + Disability\ weight_{Seek\ alternative\ product} + Disability\ weight_{Do\ nothing}$$

These formulas account for the initial and recurrent episodes of the conditions under each decision pathway, using the lower bound estimates for episode duration. By applying these formulas, we can quantify the impact of delayed treatment and alternative care-seeking behaviors on disability weights.

[82] It is assumed that individuals who seek alternative and do nothing are more likely to experience higher episodes due to delayed or alternative treatments.

[83] GBD Results. (n.d.-b). Institute for Health Metrics and Evaluation. https://vizhub.healthdata.org/gbd-results/

[84] It is assumed that individuals who seek alternative and do nothing are more likely to experience higher episodes due to delayed or alternative treatments.

[85] GBD Results. (n.d.-b). Institute for Health Metrics and Evaluation. https://vizhub.healthdata.org/gbd-results/

Disability weight result

The following table presents the calculated disability weights based on these formulas, offering an additional insight of how reverse-switching influences the number of days lost due to ill-health, disability, or early death for each decision pathway.

Table 126 Disability weight impact in each country for a single year

Country	Total Disability Weight
Austria	311
Belgium	773
Bulgaria	99
Croatia	162
Cyprus	53
Czech Republic	490
Denmark	216
Estonia	28
Finland	145
France	3,766
Germany	4,166
Greece	464
Hungary	566
Ireland	270
Italy	2,382
Latvia	69
Lithuania	44
Luxembourg	31
Malta	31
Netherlands	546
Poland	2,659
Portugal	642
Romania	499
Slovakia	380
Slovenia	115
Spain	494
Sweden	386
UK	1,680
Grand Total	**21,469**

Annex VI: Basic reproduction number (R0)

The Basic Reproduction Number (R0) is a crucial parameter in understanding the transmission dynamics of infectious diseases. This section explains the methodologies used to determine the R0 values for Herpes Labialis, Vaginal Thrush, and Dermatomycosis. The R0 values are calculated on a scenario analysis basis, with detailed impact detailed in the "Scenario analysis" under result section.

Herpes Labialis R0

The R0 value for Herpes Labialis was calculated using a three-step approach, as illustrated in the attached methodology:

1. Literature Review:
    a. Insights from Lipstich et al. (2000) indicate that the formula used to calculate R0 is:

$$R0 = \frac{1}{(1 - equilibrium\ seroprevalence)}$$

2. Collect data
    a. Equilibrium seroprevalence is calculated as:

$$\text{Equilibrium seroprevalence} = \frac{Total\ herpes\ labialis\ prevalence}{Total\ Population\ within\ in{-}scope\ European\ countries} = \sim 4{,}1\%$$

Where:

- Total herpes labialis prevalence: The total burden of herpes labialis within inscope countries calculated in our estimates.
- Total population: Population data from the Institute for Health Metrics and Evaluation (IHME).

3. Calculate R0:
    a. Applying the formula:

$$R0 = \frac{1}{(1 - \sim 0.041)} = \sim 1{,}05$$

Vaginal Thrush R0

For Vaginal Thrush, we use an R0 value of 0. This assumption is based on the following rationale:

1. Vaginal Thrush is primarily caused by the overgrowth of Candida species, which are part of the normal vaginal flora in many women. The condition is generally not transmitted from person to person.
2. Candida infections are usually opportunistic and do not spread between individuals under normal circumstances, with some medical literatures saying it is not a sexually transmitted infection[86].

[86] Yeast infection (vaginal) - Symptoms and causes - Mayo Clinic. (2023, January 11). Mayo Clinic. https://www.mayoclinic.org/diseases-conditions/yeast-infection/symptoms-causes/syc-20378999

3. No medical literature has quantified the R0 value for Vaginal Thrush, supporting the assumption that transmission is very low and thus not significant.

Dermatomycosis R0

For Dermatomycosis, including Athlete's foot, we also use an R0 value of 0. This assumption is based on the following rationale:

1. Dermatomycosis is caused by dermatophytes, which are fungi that infect keratinized tissues such as skin, hair, and nails. While these infections can be spread through direct contact with infected individuals or contaminated surfaces, the transmission rate is relatively low.
2. According to a review by Havlickova et al. (2008)[87], dermatophyte infections are typically spread in environments conducive to fungal growth, such as communal showers and locker rooms, rather than through casual contact.

The absence of quantified R0 values in medical literature supports the assumption that the transmission rate is not significant enough to warrant an R0 calculation.

R0 application

This section elaborates on how the Basic Reproduction Number (R0) is calculated and applied through a scenario analysis for Herpes Labialis, Vaginal Thrush, and Dermatomycosis. As elaborated earlier, the R0 values are as follows:

- Herpes Labialis: ~1.05
- Vaginal Thrush: 0
- Dermatomycosis: 0

Application of R0 in Scenario Analysis

The R0 values are used to analyze potential changes in disease burden and their subsequent impact on health outcomes and costs.

1. Herpes Labialis: The R0 value of ~1.05 indicates a ~5% increase in the disease burden. This increase affects all related health outcomes and costs, which are dependent on the burden in their calculations. This adjustment reflects a higher transmission rate, leading to more cases and greater demands on healthcare resources and associated costs.
2. Vaginal Thrush and Dermatomycosis: With R0 values of 0, there is no anticipated change in the burden for these conditions. This means we assume their transmission rates do not contribute to an increase in cases, and the burden remains constant.

It is important to note that the calculated health outcomes and costs presented in this report do not incorporate the R0 values. This section specifically addresses the potential variations introduced by R0, offering an understanding of how transmission dynamics could influence the burden, health outcomes, and economic implications of the three indications.

[87] Havlickova, B., Czaika, V. A., & Friedrich, M. (2008). Epidemiological trends in skin mycoses worldwide. Mycoses, 51(S4), 2-15 (https://onlinelibrary.wiley.com/doi/full/10.1111/j.1439-0507.2008.01606.x)

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