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Observational study on the therapeutic management and economic burden of adult patients with moderate to severe plaque psoriasis in France – the POP study

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ABSTRACT

Background: Data on the therapeutic management and healthcare cost of moderate to severe psoriasis in France are scarce.

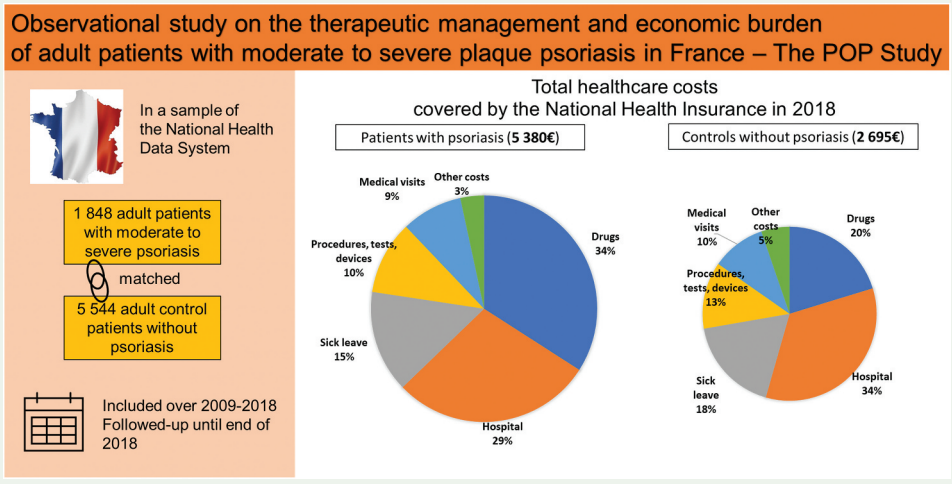
Objective: To assess the therapeutic management and economic burden of patients with moderate to severe psoriasis.

Setting: This is a retrospective observational study on the Generalist Beneficiaries Sample of the National Health Data System.

Patients and outcome measures: Adults with moderate to severe psoriasis (with a topical vitamin D derivative followed by systemic treatment or hospitalization for psoriasis) were included and followed-up from 1 January 2009 to 31 December 2018. Patients were matched to controls without psoriasis. Patients' characteristics and healthcare cost from the National Health Insurance's (NHI) perspective were described.

Results: Overall, 1,848 and 5,544 adults were included in the psoriatic and control cohorts, respectively. The most frequent treatments were methotrexate (18.5% to 21.4% of patients by year), phototherapy (29.9% in 2010 down to 6.2% in 2018), and acitretin (25.9% in 2010 down to 8.6% in 2018). Overall, 19% of patients used biotherapies. The mean healthcare costs reimbursed by NHI was €5,365/psoriatic patient (including €2,685 potentially attributable to psoriasis), which was twice as high as in controls. In both cohorts, healthcare costs increased over time.

Conclusion: Moderate to severe psoriasis healthcare costs are high.



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Introduction

Based on studies mostly conducted in high-income countries, the estimates of the prevalence of psoriasis in adults range from 0.5% to 11.4% [1]. In France, psoriasis affects between 1.3% (based on claims database) [2] and 4% (based on self-questionnaire) [3] of the population. Eighty to ninety percent of people with psoriasis experience plaque psoriasis [4]. The disease course is unpredictable, progressing in flare-ups of varying intensity, interspersed with remissions of varying duration. Beyond the high medical impact of the disease, psoriasis also has a considerable emotional and psychosocial effect on patients [5]. The odds of suicidal behaviors of patients with psoriasis compared with individuals without psoriasis are 1.3 [6] and suicide prevalence in adults with psoriasis is 0.8% [7]. Psychiatric disorders can both result from and contribute to progression of psoriasis, suggesting that psoriasis and psychiatric conditions, may have overlapping biological mechanisms [8,9].

For mild-to-moderate cases, first-line therapy involves topical drugs, including corticosteroids, vitamin D3 analogues and combination treatment. For more severe cases, systemic therapies may be administered, including phototherapy, conventional systemic treatments and immunosuppressive biotherapies. New treatments have recently been developed for moderate to severe psoriasis and, in France, biotherapies are now offered to patients as a third-line option [10]. It is important to monitor the integration of these new treatments into the wide psoriasis therapeutic arsenal and their effect on healthcare costs.

Data on the cost of psoriasis in France are scarce. Two studies examined patients' out-of-pocket costs [11,12]. One regional study examined, from the French National Health Insurance's (NHI) perspective, in 2009–2011, the healthcare costs among patients with moderate to severe psoriasis [13]. Over a six-month period, the total cost per patient was €1,678 for patients without biotherapy and €8,107 for those with biotherapy.

The POP study aimed to assess the therapeutic management and the economic burden, including the cost potentially attributable to psoriasis, of adult patients living with moderate to severe psoriasis in France from the NHI's perspective over 2009–2018. For the therapeutic management, besides the description of treatments, a machine learning approach was used to visualize treatment sequences. As an exploratory objective, the study examined the psychological impact of psoriasis through the number of hospitalized suicide attempts. Data were obtained from the National Health Data System (SNDS) of the NHI, specifically from the Generalist Beneficiaries Sample (EGB, Echantillon Généraliste des Bénéficiaires) – a sample of the SNDS.

Materials and methods

Study design

This is a retrospective observational study carried out on the EGB database on adult patients with a moderate to severe plaque psoriasis.

Data sources

The EGB is a random sample of about 660,000 NHI beneficiaries (1/97th of beneficiaries) that is periodically renewed (Supplement Methods 1). The SNDS, from which the EGB dataset is derived, is a claims database containing anonymous sociodemographic and medical characteristics, as well as reimbursed healthcare information [14].

Study population

The study population is composed of two cohorts: the psoriasis cohort and the control cohort. The algorithm used to identify the study population was adapted from a previously published algorithm developed for the SNDS [15].

The psoriasis cohort encompassed adults (≥18 years old) with ≥ 1 reimbursement of a topical vitamin D derivative, followed within a two-year period with ≥ 1 reimbursement of a systemic treatment: phototherapy, immunosuppressant or immunomodulating drug (acitretin, cyclosporin, methotrexate, apremilast), biotherapy originator and biosimilar (etanercept, infliximab, adalimumab, certolizumab pegol, ustekinumab, secukinumab, brodalumab, ixekizumab, guzelkumab, risankizumab) (timeframes of treatments in Supplement Table 1). As the selected systemic treatments have multiple indications other than psoriasis treatment (psoriatic arthritis, Crohn disease, etc.), association of a topical drug delivery with systemic treatments was used to ascertain inclusion of patients treated for a psoriasis. The ATC codes for drugs and the CCAM codes for medical procedures are in Supplement Table 2-4. Patients were also included if they had ≥ 1 hospitalization with a primary diagnosis of psoriasis (ICD-10 code L40).

The control cohort was established for the analysis of the cost potentially attributable to psoriasis. Adults failing the treatment and diagnosis inclusion criteria of the psoriasis cohort were pre-selected for the control cohort.

Individuals (with or without psoriasis) with <2 years of continuous presence in the EGB prior to the index date were excluded. Only patients with a unique, permanent social security number were included.

Table 1. Participant's characteristics at index date×.

Variable	Patients with moderate to severe plaque psoriasis (*n* = 1,848)	Matched cohort (*n* = 5,544)
Inclusion year		
2009	197 (10.66%)	581 (10.48%)
2010	174 (9.42%)	522 (9.42%)
2011	160 (8.66%)	482 (8.69%)
2012	153 (8.28%)	458 (8.26%)
2013	213 (11.53%)	651 (11.74%)
2014	159 (8.60%)	489 (8.82%)
2015	143 (7.74%)	416 (7.50%)
2016	149 (8.06%)	430 (7.76%)
2017	220 (11.90%)	678 (12.23%)
2018	280 (15.15%)	837 (15.10%)
Age (years), mean (±SD)	51.4 (±15.8)	51.51 (±16.15)
Median [Q1; Q3]	52.0 [39.0; 63.0]	51.0 [39.0; 63.0]
Sex, N men (%)	1,012 (54.8%)	3,022 (54.5%)
State-funded free complementary healthcare benefit, N yes (%)	165 (8.9%)	478 (8.6%)
Charlson Comorbity Index, mean (±SD)	1.0 (±1.2)	0.2 (±0.5)
Median [Q1; Q3]	2.0 [1.0; 3.0]	0.0 [0.0; 0.0]
Diabetes, N (%)	203 (11.0%)	600 (10.8%)
Inflammatory diseases: Psoriatic Arthritis, Inflammatory Bowel Disease, Ankylosing Spondylitis, N (%)	203 (11.0%)	603 (10.9%)
Psoriatic Arthritis	116 (6.3%)	27 (0.5%)
Inflammatory Bowel Disease	67 (3.6%)	486 (8.8%)
Ankylosing Spondylitis	44 (2.4%)	106 (1.9%)
Infections, N (%)	131 (7.1%)	392 (7.1%)
Infections including Opportunistic Infections	121 (6.6%)	363 (6.6%)
Cytopenia	19 (1.0%)	70 (1.3%)
Cerebrovascular disease, N (%)	114 (6.17%)	324 (5.8%)
Chronic Coronary Disease	77 (4.2%)	197 (3.6%)
Heart Failure	41 (2.2%)	158 (2.9%)
Cerebrovascular Accident	20 (1.1%)	82 (1.5%)
Acute coronary syndrome, N (%)	2 (0.1%)	9 (0.2%)
Acute pulmonary embolism, N (%)	2 (0.1%)	5 (0.1%)
Morbid obesity, N (%)	88 (4.8%)	274 (4.9%)
Mental health, N (%)	50 (2.7%)	150 (2.7%)
Mood Disorders	36 (2.0%)	121 (2.2%)
Addiction	15 (0.8%)	32 (0.6%)
Cancer, N (%)	43 (2.3%)	129 (2.3%)
Cancer excluding Cutaneous Cancer	35 (1.9%)	119 (2.2%)
Cutaneous cancer excluding melanoma	7 (0.4%)	9 (0.2%)
Melanoma	2 (0.1%)	4 (0.1%)

*Index date: the date of the first reimbursement of the systemic treatment of interest or phototherapy, or the first day of hospitalization for psoriasis, during the inclusion period, whichever occurred first.

For the psoriasis cohort, the index date was defined as the date of the first reimbursement of the systemic treatment of interest or phototherapy, or the first day of hospitalization for psoriasis, whichever occurred first. For the control cohort, the index date was defined as December 31st of the individual's first year of presence in the EGB during the inclusion period.

Study period

The inclusion period lasted from 1 January 2009 until 31 December 2018 (Supplement Fig. S1). Patients were followed-up from inclusion (index date) until 31 December 2018 (the end of the study period), death, or the last healthcare claim preceding two consecutive years without any healthcare claim, whichever occurred first.

To capture comorbidities and medical history, a look-back period started two years prior to the index date (i.e., as early as 1 January 2007 for the first enrolled patients).

Outcomes

Patient demographic and medical characteristics at index date were described including comorbidities, medical history and long-term disease status (LTD) (details in Supplement Methods 2).

Healthcare consumption (hospital stays, hospital outpatient or doctor office visits, visits to other healthcare professionals, sick leaves, drugs, medical devices, biological tests, imaging procedures, transportation to a healthcare facility, and other consumptions) were collected to compute their cost, by year. Year 2009 was excluded from the healthcare

consumption and cost analysis as no patient was fully present throughout the year. The treatment sequences were explored with a machine learning approach (more to be found below). Treatments administered in 2009 contributed to the treatment sequences' analysis.

The number of patients hospitalized for a suicide attempt was reported (codes in Supplement Methods 2).

Healthcare cost calculation

Costs were determined from the perspective of the NHI based on reimbursements available in the database and updated to EUR2021 using the Consumer Price Index [16]. Sick leaves are financially compensated by the NHI allowing an analysis of the loss of productivity cost. Given that all healthcare consumptions are reported in the database, no replacement of missing values was performed.

Statistical methods

Continuous data were summarized by their mean, standard deviation (±SD) and/or median, first (Q1), and third (Q3) quartiles. Categorical data were summarized by percentages. Statistical analyses were performed using SAS version 9.4 and Python 3.7.

Cohort matching

The psoriasis and the control cohorts were matched 1:3 using a propensity score (Supplement Method 3) encompassing gender, age group, state-funded free complementary healthcare benefit, inclusion year, comorbidities, and density of dermatologists in the area.

Visualization of treatment sequences

The visualization of psoriasis treatment switch and sequences was made possible using the TAK® method (Time-sequence Analysis through K-clustering, by HEVA) [17]. In brief, an unsupervised hierarchical clustering method is applied to identify clusters of patients with similar treatment sequences, followed by a time sequence analysis. If two treatments were delivered on the same day (<1% of administrations), only one was displayed on the TAK, with the following priority order: biotherapy > systemic treatment > phototherapy.

A treatment switch is a change of treatment among the list of treatments of interest.

Psoriasis potentially attributable healthcare cost

The healthcare cost potentially attributable to psoriasis was computed in two steps. First, a negative binomial Generalized Estimating Equations (GEE) model was built, including patients' covariates, to estimate the relative increase in the average cost among patients with psoriasis compared to control patients. The obtained relative risk associated with the cost was tested for statistical significance (Wald X^2). Second, the theoretical healthcare cost of patients with psoriasis was calculated as the difference between the average observed cost in patients with psoriasis and this same average cost divided by the obtained relative risk.

$$\text{Psoriasis potentially attributable healthcare cost} = C - C/RR$$

C: Average observed healthcare cost in patients with moderate to severe psoriasis

RR: relative risk of additional cost

The computations were performed for the overall healthcare costs and by item. The 95% confidence intervals of the estimated costs were computed using the bootstrap method.

Compliance with ethical standards

In accordance with the regulations in force, patient consent was not necessary because this study uses secondary data and the protection of patients' rights and freedom were guaranteed. Access to the data was granted by the Health Data Hub (File No. 3358814) on 20 January 2021.

Results

Study population

Out of the 827,755 individuals with valid data in the EGB over 2009–2018, 1,848 patients suffered from moderate to severe plaque psoriasis (psoriasis cohort) (Figure 1); 351 patients (19%) were treated with biotherapies.

Patients in the psoriasis cohort were followed for 4.5 years (±3.1), on average, (median 4.4), and up to 10 years.

Patients with psoriasis were more likely to be men (54.8%) and were, on average, 51.4 years old (±15.8) at index date (Table 1). Their main comorbidities were diabetes (11.0%) and inflammatory diseases (11.0%).

Forty-two percent of patients (768 patients) benefitted from LTD status. The main reasons for obtaining

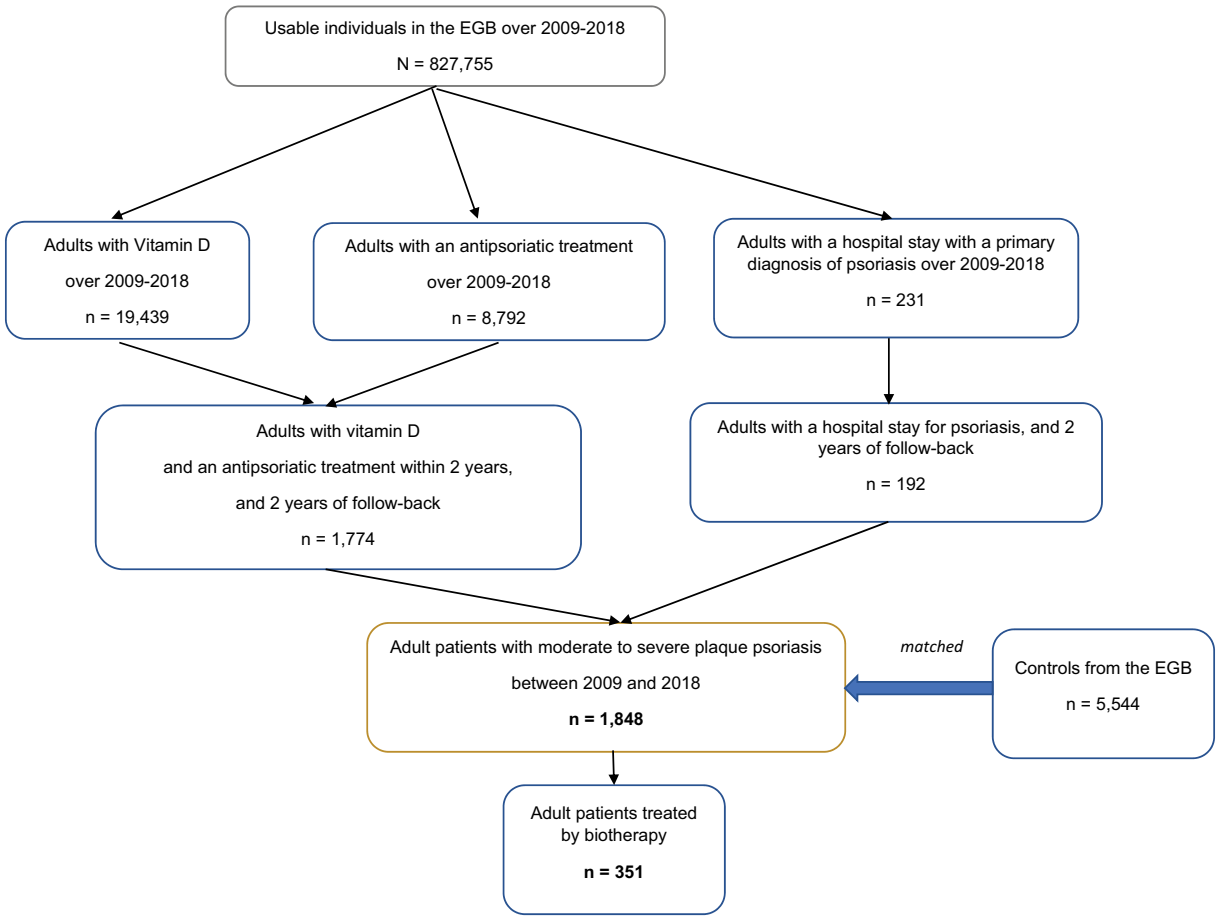

Figure 1. Study population selection process.

EGB: The Echantillon Généraliste des Bénéficiaires is a sample (1/97th of the beneficiaries) of the National Health Data System (SNDS, Système National des Données de Santé) of the National Health Insurance.

the LTD status were diabetes (13.7%), psoriatic arthritis (13.4%), ankylosing spondylitis (6.0%) and chronic ischemic heart disease (4.5%). Besides, 3.3% of patients had an LTD for psoriasis.

The 1,848 patients with moderate to severe psoriasis were matched to 5,544 control patients.

Systemic treatments and phototherapy

The number of patients treated with either conventional systemic treatment, phototherapy or biotherapy increased steadily from 342 in 2010 to 1,301 in 2018. The most frequent treatment was methotrexate (dispensed to 18.5% to 21.4% of patients over time), followed by phototherapy (which decreased from 29.9% in 2010 to 6.2% in 2018) and acitretin (from 25.9% in 2010 to 8.6% in 2018). Meanwhile, the proportion of patients using vitamin D analogues and topical corticosteroids decreased from 54.7% to 36.9% and from 50.4% to 38.5%, respectively (Table 2).

Figure 2 shows the treatment sequences in patients identified with moderate to severe psoriasis starting from their index date. For more than 75% of patients, the first-line treatment was one of the following: phototherapy (31%), acitretin (26%), and methotrexate (22%). Patients hardly switched treatment during the study: 7% of patients started with phototherapy before switching to acitretin or methotrexate and 5% started with acitretin before switching to phototherapy or methotrexate. Around a quarter of patients were only treated with phototherapy, for 3–4 months.

Among the 351 patients treated with biotherapies (Figure 3), 40% were not previously treated by a conventional systemic treatment or phototherapy. Most of them also suffered from other inflammatory diseases (e.g., 35% had inflammatory bowel disease, 21% had ankylosing spondylitis, and 21% had psoriatic arthritis). When excluding patients with a reimbursement of a biotherapy prior to the index date,

Table 2. Proportion of patients with moderate to severe psoriasis who used at least once systemic treatments or phototherapy, by study year ($n = 1,848$ patients).

Treatment	2010	2011	2012	2013	2014	2015	2016	2017	2018
Any antipsoriatic drug below	342 (92.18%)	437 (84.36%)	545 (81.83%)	699 (80.16%)	814 (79.88%)	845 (73.80%)	957 (74.59%)	1,113 (75.00%)	1,301 (74.64%)
Phototherapy	111 (29.92%)	100 (19.31%)	102 (15.32%)	119 (13.65%)	117 (11.48%)	115 (10.04%)	112 (8.73%)	96 (6.47%)	108 (6.20%)
acitretin	96 (25.88%)	93 (17.95%)	109 (16.37%)	135 (15.48%)	125 (12.27%)	124 (10.83%)	115 (8.96%)	139 (9.37%)	149 (8.55%)
methotrexate	76 (20.49%)	99 (19.11%)	123 (18.47%)	187 (21.44%)	203 (19.92%)	228 (19.91%)	253 (19.72%)	284 (19.14%)	360 (20.65%)
apremilast	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	11 (0.86%)	51 (3.44%)	93 (5.34%)
etanercept	10 (2.70%)	19 (3.67%)	22 (3.30%)	28 (3.21%)	35 (3.43%)	41 (3.58%)	44 (3.43%)	43 (2.90%)	43 (2.47%)
infliximab	5 (1.35%)	10 (1.93%)	14 (2.10%)	22 (2.52%)	24 (2.36%)	0 (0.00%)	1 (0.08%)	3 (0.20%)	3 (0.17%)
adalimumab	17 (4.58%)	25 (4.83%)	33 (4.95%)	45 (5.16%)	55 (5.40%)	61 (5.33%)	71 (5.53%)	86 (5.80%)	103 (5.91%)
certolizumab pegol	0 (0.00%)	1 (0.19%)	1 (0.15%)	1 (0.11%)	1 (0.10%)	5 (0.44%)	6 (0.47%)	6 (0.40%)	5 (0.29%)
ustekinumab	1 (0.27%)	6 (1.16%)	9 (1.35%)	13 (1.49%)	19 (1.86%)	28 (2.45%)	38 (2.96%)	49 (3.30%)	63 (3.61%)
secukinumab	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	11 (0.86%)	34 (2.29%)	42 (2.41%)
brodalumab	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
ixekizumab	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	5 (0.34%)	8 (0.46%)
guzelkumab	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
risankizumab	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
cyclosporin	4 (1.08%)	5 (0.97%)	5 (0.75%)	6 (0.69%)	13 (1.28%)	10 (0.87%)	8 (0.62%)	7 (0.47%)	7 (0.40%)
Topical corticosteroids	187 (50.40%)	221 (42.66%)	287 (43.09%)	356 (40.83%)	439 (43.08%)	468 (40.87%)	529 (41.23%)	629 (42.39%)	671 (38.50%)
Vitamin D analogues	203 (54.72%)	265 (51.16%)	332 (49.85%)	372 (42.66%)	428 (42.00%)	421 (36.77%)	453 (35.31%)	494 (33.29%)	643 (36.89%)

meaning potentially associated with another inflammatory disease than psoriasis, only 12% of patients had a biotherapy as a first-line psoriasis treatment. Around a third of patients switched biotherapies during the follow-up period.

Healthcare costs

Observed healthcare use is described in Supplement Results 1 and Supplement Figure 2.

The mean annual total healthcare cost in patients with moderate to severe psoriasis reimbursed by the NHI estimated with the GEE model increased from €4,088.43 per patient (95% Confidence Interval [CI] 3,302;4,876) in 2010 to €6,016.02 (95%CI 5,502;6,514) in 2017, then declined to €5,380.43 (95%CI 4,934;5,777) in 2018 (Figure 4). In 2018, three items represented 78% of the cost: drugs (34%;€1,834.37), hospital (hospital stays, at home hospitalization, and outpatient visits) (29%; €1,544.55) and sick leaves (15%;€784.83) (Supplement Figure 3a).

In controls, the mean annual total healthcare cost estimated with the GEE model also increased, from €1,205 per participant (95%CI 1,003;1,463) in 2010 to €2,695 in 2018 (95%CI 2,505;2,894). In 2018, three items represented 72% of the cost: drugs (20%;€545.94), hospital (34%;€918.67) and sick leaves (18%;€480.31) (Supplement Figure 3b). The total cost and the cost for each item were independently computed with the model. Hence there is a slight difference (€3, 0.11%) between the total cost and the sum of the cost of the items (shown on Figure 4).

In 2018, the total modelled healthcare cost potentially attributable to psoriasis was €2,685 per patient (95%CI €2,219; €3,117). It was 2.00 (95%CI 1.80;2.21) times higher than the total healthcare cost of control patients. The highest additional cost potentially attributable to psoriasis was incurred by drugs (€1,288 [95%CI €1,047; 1,468]). The gap between costs of patients with psoriasis and control patients for total healthcare and by item was stable over time, except for drug-related costs (gap reduction over 2014–2018).

Hospitalization for suicide attempt

Ten (0.54%) and twelve (0.22%) patients in the psoriasis and control cohorts were hospitalized at least once for a suicide attempt, respectively (odds ratio 1.58; p-value 0.0324).

Discussion

Based on a sample of the French NHI database, a variety of systemic drugs were administered to patients with moderate to severe psoriasis. However generally, patients only used one drug. Methotrexate represented around 20% of therapies at index date. In 2018, the mean total healthcare costs of patients with moderate to severe psoriasis reimbursed by the NHI was €5,365

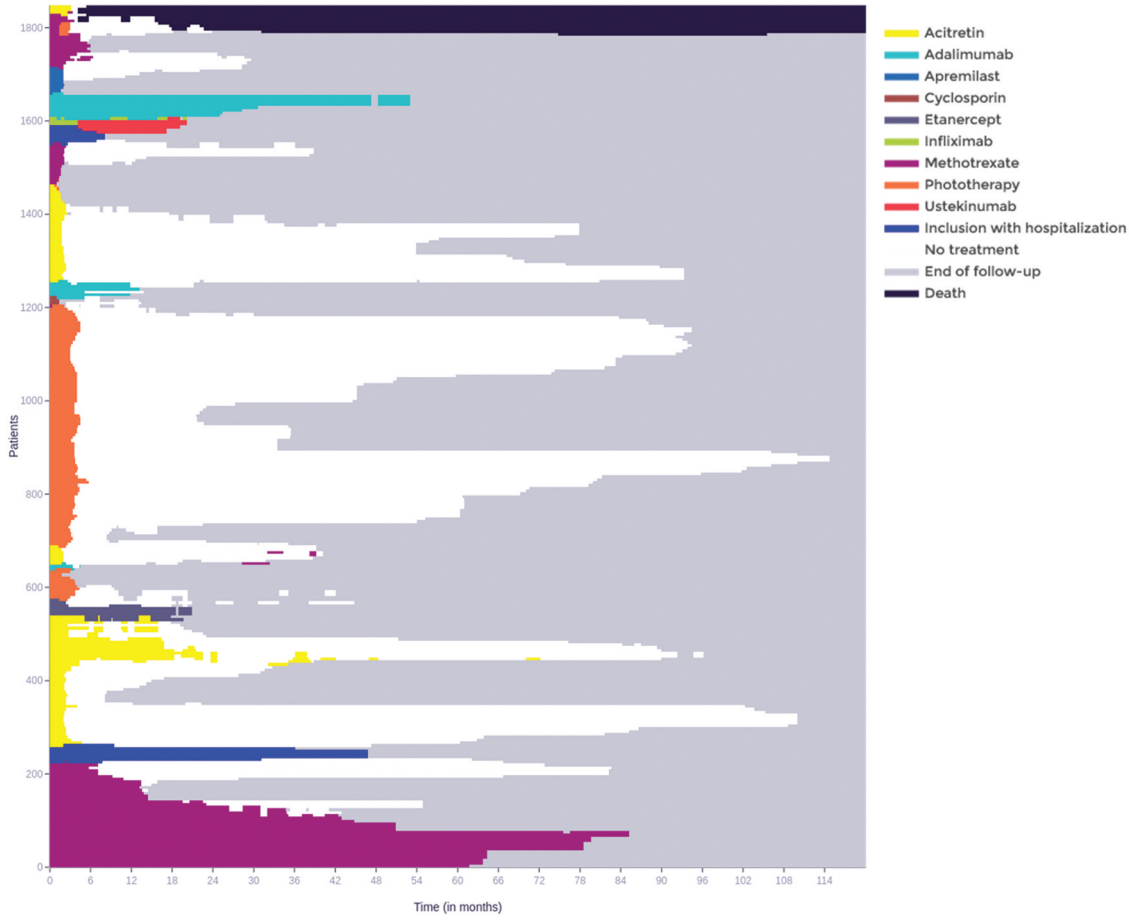

Figure 2. Systemic treatments and phototherapy sequences in patients with moderate to severe psoriasis after their index date (n = 1,848 patients).

The x-axis represents the time since the index date (reimbursement of the first systemic treatment, phototherapy, or hospital stay for psoriasis), in months (the index date is at x = 0). The 1,848 patients are stacked on the y-axis. Horizontal lines represent the treatment course of patients. Each color represents a treatment. Dark blue is time spent at the hospital, white represents absence of treatment, gray is the end of follow-up, and black is death. The large number of patients and the blurred display prevent seeing rapid alternating therapies.

per patient, of which €2,685 were potentially attributable to psoriasis. The mean total healthcare cost was twice as high in patients with psoriasis than in matched controls. Total healthcare costs increased during the study period, both in patients with moderate to severe psoriasis and in controls.

Psoriasis treatments appeared of short duration (except for methotrexate, adalimumab, and phototherapy) and few treatment switches occurred. This could indicate high treatment effectiveness or, conversely, raises the question of potential undertreatment in some patients. In particular, a large group of patients were on long-term methotrexate therapy. Patients with alternating periods of treatment (especially acitretin and methotrexate) and non-treatment were also detected, which could be a marker of early treatment discontinuation and successive relapses, or poor treatment compliance. In 2019, with the arrival of new, more effective biotherapies on the market, the number of switches may increase, however 2019 data were not available at the time of study. The percentage of treatment switch observed in this study seems to be low given that treatment effectiveness seems to decrease after two years [18] and treatment guidelines recommend 'rotational strategies'. Treatment switch was observed for only about 30% of patients in this study (who had ≥ 1 instance of another biotherapy within five years of follow-up). This proportion of switch has already been documented in a French study carried out over 2012–2019 on a register of patients with psoriasis treated with biotherapies and showed, using another method of calculation, that the cumulative incidence of switching from the first-prescribed biotherapy was 34% at three years and 44% at five years [19]. The main reason for switching was loss of efficacy (72%), followed by adverse events (11%).

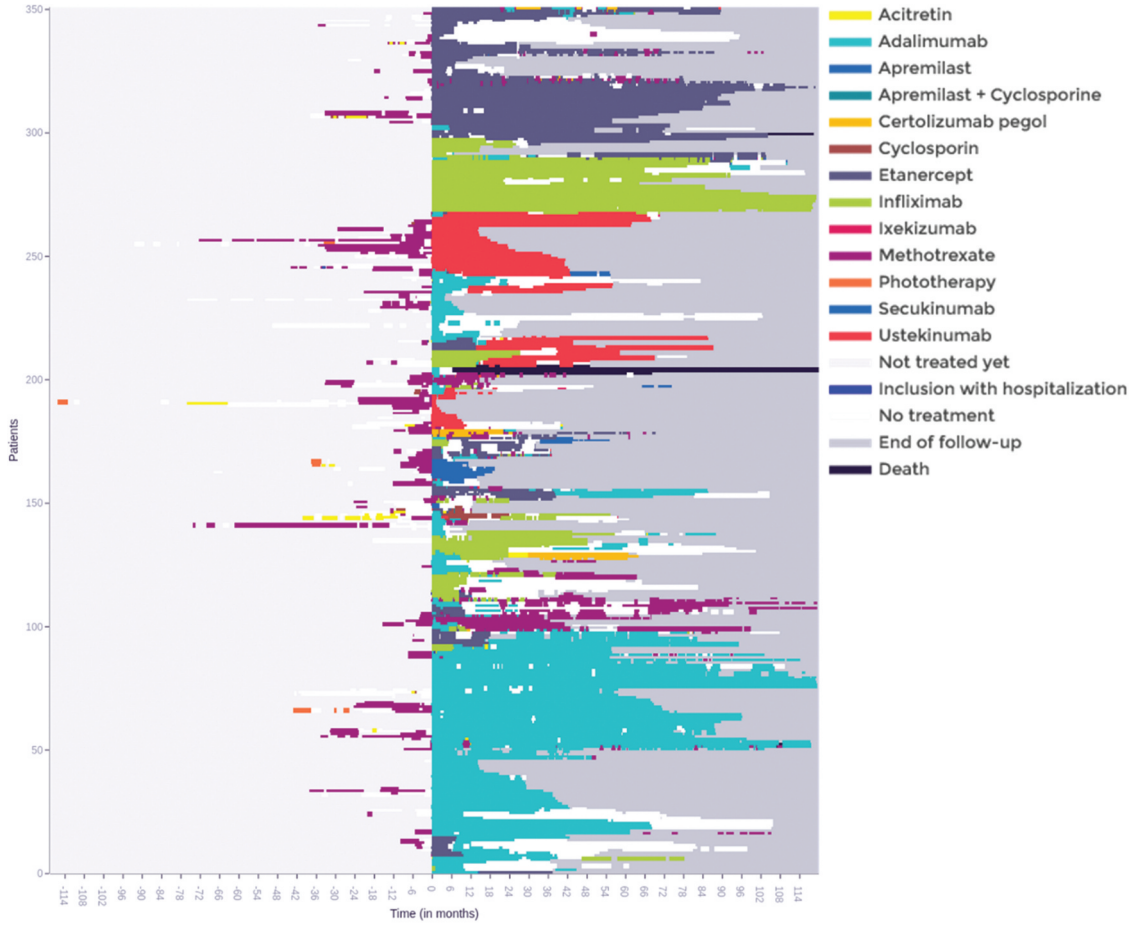

Figure 3. Systemic treatments and phototherapy sequences in patients treated with biotherapies before and after the index date (*n* = 351 patients).

The alternating treatment cessions sequences are visible on Figure 3 as well as association of treatments, for instance methotrexate (purple) used in association with adalimumab (light blue).

Contrary to the reimbursable indications of biotherapies, a high proportion of patients (40%) seemed to have a biotherapy as a first-line treatment. After excluding patients taking biotherapies prior to inclusion – possibly for inflammatory comorbidities, another indication for these treatments – this proportion fell to 12%. This was consistent with a French report showing that first-line biotherapies in patients with psoriasis varied between 11% and 17% [20].

A national French study, based on SNDS data, conducted by Sbidian et al. over 2012–2016 examined moderate to severe psoriatic patients [21]. Patients' characteristics (gender, age) and the preferred first-line treatments were consistent with those of patients in this study. The first- and second-line biotherapies identified in our study were consistent with results from a 2019 survey on dermatologists' prescription habits [22]. The most frequent biotherapies were adalimumab (39%) and ustekinumab (34%), which were also often administered in this study.

Psoriatic patient healthcare cost increased between 2010 and 2014 then stabilized until 2018 at approximately €5,500. This was mainly driven by the cost of treatment – a third of the total cost – which has progressively increased with the launch of more expensive biotherapies. Of note, between 2010 and 2018, the total healthcare cost in patients with psoriasis increased by about 50% while it doubled in control patients. Since this study was carried out, new French guidelines on the use of systemic treatments for moderate-to-severe psoriasis have been released [10]. Following the publication of these guidelines, dermatologists modified their prescriptions decisions: in particular, apremilast was less often prescribed and adalimumab biosimilar was more often prescribed [22].

The rate of hospitalized suicide attempts was higher in moderate to severe patients than in the control patients. However, the number of suicides and suicide attempts was underestimated due to the absence of data on patients who were not hospitalized. Indeed, a

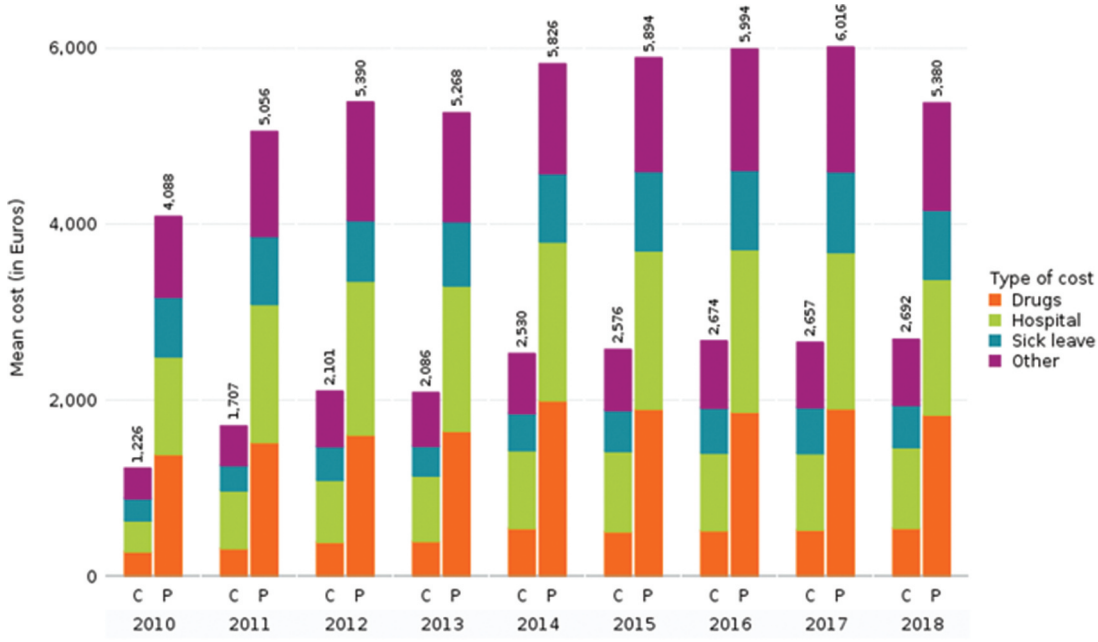

Figure 4. Estimated mean healthcare costs in patients with moderate to severe psoriasis (all diseases and injuries) and in control patients, computed with the GEE model.

C:Control patients. P: patients with moderate to severe psoriasis. Hospital costs: hospital stay, home hospitalization, outpatient visit. Other costs: doctors' visits (GP and specialists in the community setting), other healthcare professionals' visits (nurses, physiotherapists, etc.), medical procedures, biological tests, medical devices, transportation, other costs (spa treatment, dialysis, etc.).

meta-analysis on mental health in patients with psoriasis found that 0.8% committed suicide [7].

The main strength of this study was the use of a claims database representative of the French population, with exhaustive long-term care data (follow-up up to almost 10 years). The database allows a clear picture of the patient management in community setting. Finally, the identification of patients with psoriasis, as well as all comorbidities and medical events of interest, was performed using algorithms validated by the NIH or published in scientific articles.

The identification algorithm used in this study could select patients with mild or severe psoriasis (treated with topical drugs) and with inflammatory pathology (treated with biologic drugs). Reimbursed treatments were assumed to be used by patients. When two treatments were dispensed on the same day (<1% of all dispensing), only one was selected, in accordance with the clinicians. Also, treatments dispensed on different days were considered as treatment alternations while they could actually be taken together. For example, occasional associations with methotrexate could not be differentiated from a treatment alternation, and thus it was not possible to quantify patients treated with methotrexate in combination with another treatment and patients treated with methotrexate alternating with another treatment. The large number of patients and the high-level view prevent seeing rapid alternating therapies in the TAK® visualisation. The EGB only contains data on reimbursed drugs, hence no over-the-counter treatments could be studied, despite being an important health expenditure for patients with psoriasis [12]. To be comprehensive, the economic burden of psoriasis should include out-of-pocket treatments, as well as work-related productivity loss and indirect costs [23]. Therefore, the cost potentially attributable to psoriasis may be underestimated. Alternatively, despite matching the two cohorts, and given the potential unmeasured confounding factors between them, it is possible that some of the observed costs were not due to the presence of psoriasis. New drugs and new guidelines [10] have been released since the study was conducted; the results offer a picture of the therapeutic management and economic burden of moderate to severe psoriasis in France over 2009–2018 only.

The use of innovative data visualization methods made it possible to show that patients hardly use more than one treatment, raising the question of potential undertreatment in some patients and making the ongoing revision by the French Health Authorities of the therapeutic management

guidelines for patients with psoriasis timely. In 2018, the economic burden of moderate to severe psoriasis was high, with €2,685 of healthcare costs per patient potentially attributable to psoriasis.

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Disclosure statement

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Data availability statement

The data supporting the study findings are part of the National health data system (SNDS, Système national des Données de Santé) and are available from the HDH (Health Data Hub https://www.health-data-hub.fr/). Restrictions apply to the availability of these data, which were used with a special permission granted by the HDH (File No. 3358814) on 20 January 2021.

References

[1] Michalek IM, Loring B, John SM. A systematic review of worldwide epidemiology of psoriasis. J Eur Acad Dermatol Venereol. 2017;31(2):205–212. doi: 10.1111/jdv.13854

[2] Grodner C, Mezzarobba M, Weill A, et al. Evolution of topical steroids consumption before and after initiation of systemic treatment in psoriasis: epidemiologic study in a real-world analysis of the French national health insurance database. J Eur Acad Dermatol Venereol JEADV. 2020;34(6):e259–62. doi: 10.1111/jdv.16238

[3] Richard M-A, Corgibet F, Beylot-Barry M, et al. Sex- and age-adjusted prevalence estimates of five chronic inflammatory skin diseases in France: results of the OBJECTIFS PEAU study. J Eur Acad Dermatol Venereol JEADV. 2018;32(11):1967–1971. doi: 10.1111/jdv.14959

[4] Wilson FC, Icen M, Crowson CS, et al. Incidence and clinical predictors of psoriatic arthritis in patients with psoriasis: a population-based study. Arthritis Care Res. 2009;61(2):233–239. doi: 10.1002/art.24172

[5] Iskandar IYK. Disease burden and quality of life in patients with moderate-to-severe psoriasis stratified according to previous systemic treatment exposure. J Eur Acad Dermatol Venereol. 2020;34(11):2454–2455. doi: 10.1111/jdv.16971

[6] Singh S, Taylor C, Kornmehl H, et al. Psoriasis and suicidality: a systematic review and meta-analysis. J Am Acad Dermatol. 2017;77(3):425–440.e2. doi: 10.1016/j.jaad.2017.05.019

[7] Liu L, Lin N-X, Yu Y-T, et al. Epidemiology of mental health comorbidity in patients with psoriasis: an analysis of trends from 1986 to 2019. Psychiatry Res. 2023;321:115078. doi: 10.1016/j.psychres.2023.115078

[8] Van Beugen S, Schut C, Kupfer J, et al. Perceived stigmatization among dermatological outpatients compared with controls: an observational multicentre study in 17 European countries. Acta Derm Venereol. 2023;103:6485. doi: 10.2340/actadv.v103.6485

[9] Koo J, Marangell LB, Nakamura M, et al. Depression and suicidality in psoriasis: review of the literature including the cytokine theory of depression. J Eur Acad Dermatol Venereol JEADV. 2017;31(12):1999–2009. doi: 10.1111/jdv.14460

[10] Amatore F, Villani A-P, Tauber M, et al. French guidelines on the use of systemic treatments for moderate-to-severe psoriasis in adults. J Eur Acad Dermatol Venereol JEADV. 2019;33(3):464–483. doi: 10.1111/jdv.15340

[11] Meyer N, Paul C, Feneron D, et al. Psoriasis: an epidemiological evaluation of disease burden in 590 patients. J Eur Acad Dermatol Venereol JEADV. 2010;24:1075–1082. doi: 10.1111/j.1468-3083.2010.03600.x

[12] Richard M-, Paul C, De Pouvourville G, et al. Out-of-pocket expenditures in France to manage psoriasis in adult patients: results from an observational, cross-sectional, non-comparative, multicentre study. J Eur Acad Dermatol Venereol. 2021;35(4):912–918. doi: 10.1111/jdv.17000

[13] Le Moigne M, Sommet A, Lapeyre-Mestre M, et al. Healthcare cost impact of biological drugs compared with traditional systemic treatments in psoriasis: a cohort analysis in the French insurance database. J Eur Acad Dermatol Venereol JEADV. 2014;28(9):1235–1244. doi: 10.1111/jdv.12318

[14] Tuppin P, de Roquefeuil L, Weill A, et al. French national health insurance information system and the permanent beneficiaries sample. Revue d'Épidémiologie et de Santé Publique. 2010;58(4):286–290. doi: 10.1016/j.respe.2010.04.005

[15] Sbidian E, Mezzarobba M, Weill A, et al. Persistence of treatment with biologics for patients with psoriasis: a real-world analysis of 16 545 biologic-naïve patients

from the French National health Insurance database (SNIIRAM). Br J Dermatol. 2019;180(1):86–93. doi: 10.1111/bjd.16809

[16] INSEE. Indice des prix à la consommation - Base 2015 - Ensemble des ménages - France- Ensemble hors tabac. cited 2022 Mar 22. Available from: https://www.insee.fr/fr/statistiques/serie/001763852#Documentation

[17] Chouaïd C, Grumberg V, Batisse A, et al. Machine learning–based analysis of treatment sequences typology in advanced non–small-Cell lung Cancer long-term survivors treated with nivolumab. JCO Clin Cancer Inform. 2022;6(6):11. doi: 10.1200/CCI.21.00108

[18] Pina Vegas L, Penso L, Claudepierre P, et al. Long-term persistence of first-line biologics for patients with psoriasis and psoriatic arthritis in the French health Insurance database. JAMA Dermatol. 2022;158(5):513–522. doi: 10.1001/jamadermatol.2022.0364

[19] Curmin R, Guillo S, De Rycke Y, et al. Switches between biologics in patients with moderate-to-severe psoriasis: results from the French cohort PSOBIOTEQ. J Eur Acad Dermatol Venereol JEADV. 2022;36(11):2101–2112. doi: 10.1111/jdv.18409

[20] Haute autorité de santé. Rapport d'évaluation des médicaments biologiques du psoriasis en plaque de l'adulte inclus dans l'étude PSOBIOTEQ 1 - Résultats intermédiaires à 3 ans de l'étude PSOBIOTEQ 1. HAS; 2021.

[21] Sbidian E, Mezzarobba M, Shourick J, et al. Choice of systemic drugs for the management of moderate-to-severe psoriasis: a cross-country Comparison based on National health Insurance data. Acta Derm Venereol. 2021;101(6):adv00473. doi: 10.2340/00015555-3765

[22] Villani AP, Amatore F, Tauber M, et al. Impact of the French guidelines on the prescribing habits of systemic treatments for moderate-to-severe psoriasis. J Eur Acad Dermatol Venereol. 2020;34(11):e747–8. doi: 10.1111/jdv.16601

[23] Villacorta R, Teeple A, Lee S, et al. A multinational assessment of work-related productivity loss and indirect costs from a survey of patients with psoriasis. Br J Dermatol. 2020;183(3):548–558. doi: 10.1111/bjd.18798

[24] Tuppin P, Rudant J, Constantinou P, et al. Value of a national administrative database to guide public decisions: From the système national d'information interrégimes de l'Assurance Maladie (SNIIRAM) to the système national des données de santé (SNDS) in France. Rev DÉpidémiologie Santé Publique. 2017;65:S149–67. doi: 10.1016/j.respe.2017.05.004

[25] Dieleman J, Campbell M, Chapin A, et al. Evolution and patterns of global health financing 1995–2014: development assistance for health, and government, prepaid private, and out-of-pocket health spending in 184 countries. Lancet. 2017;389(10083):1981–2004. doi: 10.1016/S0140-6736(17)30874-7

[26] Centre des liaisons européennes et internationales de sécurité sociale, République Française. The French Social Security System. I-Health, maternity, paternity, disability, and death. Vous informer sur la protection sociale à l'international 2020. Accessed 2020 Oct 12. Availabe from: https://www.cleiss.fr/docs/regimes/regime_france/an_1.html

[27] Chevreul K, Berg Brigham K, Durand-Zaleski I, et al. France: health System review. Health Syst Transit. 2015;17(3): 1–218, xvii.

[28] Assurance Maladie. Tableaux récapitulatifs des taux de remboursement. Ameli.Fr. 2022 Mar 4. https://www.ameli.fr/rhone/assure/remboursements/rembourse/tableau-recapitulatif-taux-remboursement