Use of topical antipsoriatic drugs in Denmark
A nationwide drug utilization study
Svendsen, M T; Ernst, M T; Andersen, K E; Andersen, F; Johannessen, H; Pottegård, A

Published in:
British Journal of Dermatology

DOI:
10.1111/bjd.17074

Publication date:
2019

Document version
Accepted manuscript

Document license
Unspecified

Citation for published version (APA):

Terms of use
This work is brought to you by the University of Southern Denmark through the SDU Research Portal. Unless otherwise specified it has been shared according to the terms for self-archiving. If no other license is stated, these terms apply:

- You may download this work for personal use only.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying this open access version

If you believe that this document breaches copyright please contact us providing details and we will investigate your claim. Please direct all enquiries to puresupport@bib.sdu.dk

Download date: 09. Sep. 2019
Use of topical antipsoriatic drugs in Denmark: A nationwide drug utilization study

Running head Use of topical corticosteroid preparations among Danish psoriasis patients

M.T. Svendsen¹,²*, M.T. Ernst³*, K.E. Andersen¹,²,4, F. Andersen¹,4, H. Johannessen⁵, A. Pottegård³

¹) Dept. of Dermatology and Allergy Centre, Odense University Hospital, Odense, Denmark
²) Centre for Innovative Medical Technology (CIMT), Clinical Institute, University of Southern Denmark, Odense, Denmark
³) Clinical Pharmacology and Pharmacy, Dept. of Public Health, University of Southern Denmark, Odense, Denmark
⁴) Dermatological Investigations Scandinavia, University of Southern Denmark, Odense, Denmark
⁵) Research Unit of User Perspectives, Dept. of Public Health, University of Southern Denmark, Odense, Denmark

*These authors contributed equally to this work.

Correspondence: Mathias Tiedemann Svendsen
Email: mathias.tiedemann.svendsen@rsyd.dk

Funding: KEA and MTS were supported by a grant from LEO Pharma and a donation from Kirsten and Volmer Rask Nielsen’s Foundation.

Conflicts of interests: Part of MTS’ salary during the trial was paid by funding from LEO Pharma. LEO Pharma had no influence on the study.

AP and MTE report participation in unrelated projects with funds paid by LEO Pharma to their institution (no personal fees).

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/bjd.17074
This article is protected by copyright. All rights reserved.
What is already known about this topic?

• The use of topical drugs for treatment of psoriasis shows considerable heterogeneity worldwide
• Persistence to topical treatment in psoriasis patients is low
• Psoriasis is associated with several co-morbidities, such as hypertension, hyperlipidemia, congestive heart failure, ischemic heart disease, diabetes mellitus and depression

What does this study add?

• The use of topical antipsoriatic drugs has decreased, while the use of systemic drugs and biologics has increased
• The use of topical therapy increases at the time of diagnosis at the hospital clinic and decreases thereafter
• There is a skewness in the utilization of topical antipsoriatic treatments; 25% of patients consume 70% of the topical drugs

Summary

Background The reported real-life use of prescribed topical antipsoriatic drugs is conflicting and based on heterogeneous data sources.

Objective To describe the utilization of topical antipsoriatic drugs among psoriasis patients in Denmark.

Methods A drug utilization study was performed based on the nationwide Danish health registry data. We identified patients who received a first-time hospital diagnosis of psoriasis and redeemed at least one topical drug in the period 2005-2015 (n=7,743). Patients were followed for three years from the time of diagnosis. Utilization of topical and systemic antipsoriatic drugs was described, specified by the type of treatment.

Results The total use of topical drugs was divided between corticosteroids with calcipotriol (31%), calcipotriol (6.5%), very potent corticosteroids (24%), potent corticosteroids (30%), moderate corticosteroids (7.2%) and corticosteroids with antimicrobials (1.6%). There was a 19% reduction in
the overall use of topical drugs during the study period. Use increased around the time of diagnosis and the majority of patients redeemed more than 2 packages of topical drugs during the first year after being diagnosed. Regional differences in patients’ use of topical drugs varied considerably. The distribution of use of topical drugs was uneven, with a minority of all patients (25%) using 70% of the total amount of topical treatment. There was a 70% increase in the use of methotrexate over the study period. Biologics were used by up to 6%.

**Conclusion** The study provides further evidence that the use of topical antipsoriatic drugs shows considerable heterogeneity over time, regional practices and differences between patients.

**Keywords:** Calcipotriol, corticosteroids, Danish health registry data, drug utilization, nationwide study, psoriasis.

**Introduction**

Psoriasis is a chronic autoimmune T-cell-mediated inflammatory skin disease that affects about 2-4% of the adult population in Europe.\(^1\)\(^2\) The disease is heterogeneous in morphology, affected sites, age of onset and duration\(^3\) and presents with large variations in severity of disease, remissions and flare-ups.\(^4\) Psoriasis negatively affects quality of life\(^5\) and is a substantial social and economic burden both for the patient and for society.\(^6\) Co-morbidities linked to psoriasis include hypertension,\(^7\) hyperlipidemia,\(^8\) congestive heart failure,\(^9\) ischemic heart disease,\(^10\) diabetes mellitus type 2\(^11\) and depression.\(^12\)

Topical corticosteroids with and without calcipotriol are recommended as first-line treatments in mild-to-moderate psoriasis.\(^13\) Systemic drugs and subsequently biologics are prescribed for more severe psoriasis in which topical therapy and/or phototherapy are less effective.\(^13\) In a recent systematic literature review,\(^14\) the worldwide utilization of topical antipsoriatic drugs is described. While it included heterogeneous data sources and study designs,
corticosteroids were used by 16-79% and corticosteroid/calcipotriol combinations were used by 3.3-71% of patients. Another systematic literature review\textsuperscript{15} reported that non-adherence rates in psoriasis patients (measured by patient-reported adherence rates, weight of medication or by data on dispensed medication) to topical corticosteroids ranged from 8-88%. In addition, the use of systemic drugs and biologics increased over time after psoriasis diagnosis.\textsuperscript{16}

A report of patient’s real-life use of antipsoriatic treatments is needed, using nationwide register-based studies reporting from registers that clearly distinguish treatments for psoriasis and include data on the use of topical treatments as well as the use of concomitant treatments. This study aims to address the following five research objectives: 1) to investigate which antipsoriatic drugs are used and to what extent, both over time and, on an individual level, in relation to the time of psoriasis diagnosis, 2) to investigate the occurrence of treatments prescribed for co-morbidities associated with psoriasis among psoriasis patients, 3) to describe the regional variation in the use of topical antipsoriatic drugs, 4) to investigate skewness (i.e. a quantification of the extent to which some patients use more topical drugs than other patients) between patients in the use of topical antipsoriatic drugs, and 5) to describe the use of systemic drugs and biologics among psoriasis patients.

**Methods**

**Data sources**

National data on drug use in Denmark was extracted from the Danish National Prescription Database.\textsuperscript{17,18} The registry contains complete information, from 1 January 1995 onwards, on all prescriptions dispensed to Danish residents at outpatient pharmacies. For the dispensed prescription, the registry contains information on the following variables included in this study: drug type, quantity, date of purchase, person’s age, gender and region of residence. Registered drugs are categorized according to the Anatomic Therapeutical Chemical (ATC) classification, a hierarchical
classification developed by the World Health Organization (WHO) for purposes of drug use statistics. The registry is reported to have a high level of completeness and validity.

National data for coding diagnosis and use of systemic drugs, biologics and phototherapy treatments was extracted from the Danish National Patient Register, which contains nationwide data on all non-psychiatric hospital admissions since 1977 and outpatient contacts since 1995. Discharge/contact diagnoses have been coded according to International Classification of Diseases (ICD)-8 from 1977 to 1993 and ICD-10 since 1994. The register contains information on the following variables used in this study: personal identification number, diagnosis and treatment.

Population statistics were obtained and linked by Statistics Denmark, a governmental institution that collects and maintains electronic records from the Danish health registries for a broad spectrum of statistical and scientific purposes. Collected data was linked using a unique identifier assigned to all Danish residents since 1968, which codes gender and date of birth.

The study was approved by the Danish Data Protection Agency and Statistics Denmark’s Scientific Board. According to Danish law, purely register-based studies do not require approval from an ethics committee.

**Data selection, procedures and study drugs**

We obtained prescription data for all patients aged > 18 years consulting with psoriasis at a hospital dermatology clinic in Denmark during the period from 1 January 2005 to 31 December 2015. Data from each patient was used from one year prior to the date on which the patient was diagnosed with psoriasis at a hospital department through to three years after the time of diagnosis. To simplify the analyses, and to facilitate the analysis of changes over time, the study period was divided into three arbitrary time periods: 2005-2008, 2009-2012 and 2013-2015.
Several classification systems for topical corticosteroids exist, e.g. the American Stoughton-Cornell 7-point classification system and a 4-point system from the UK.\textsuperscript{23} For the purpose of this study, we divided topical antipsoriatic drugs into six groups: moderate corticosteroids, potent corticosteroids, very potent corticosteroids, corticosteroids in combination with antimicrobials, calcipotriol and corticosteroid/calcipotriol combinations (Table 1). All these drugs are only available via prescription in Denmark and thus captured by our data sources. To simplify the research questions, some topical drugs were excluded from the data extraction: topical corticosteroids combinations containing salicylic acid and milder corticosteroids (hydrocortisone) were excluded, mainly because these topical drugs are primarily bought over the counter.

We also describe the use of biologics (restricted to etanercept, adalimumab and ustekinumab), systemic drugs (restricted to methotrexate, ciclosporin and acitretin) and phototherapy. Several treatments were not considered: apremilast was not considered in this study, as it was first introduced to the Danish market in 2015; dimethyl fumarate has limited use and was therefore not considered relevant for this study; several biologics with marketing authorization for psoriasis in Denmark (i.e. brodalumab, infliximab, ixekizumab and secukinumab) were not included, since these agents did not have a code in the Danish National Patient Register at the time that the data was extracted for the study.

Co-morbidities defined by diagnosis or medications prescribed in the year prior to psoriasis diagnosis to treat the comorbidity were considered: hypertension (patients defined by having redeemed a prescription of either a calcium channel blocker, an angiotensin-converting-enzyme (ACE) inhibitor or a thiazide diuretic), hypercholesterolemia (patients defined by having redeemed a prescription for a statin), congestive heart failure (patients defined by the diagnosis), ischemic heart disease (patients defined by the diagnosis of acute myocardial infarction), diabetes mellitus type 2 (defined by the use of an oral antidiabetic drug) and depression/anxiety (patients defined as having redeemed a prescription for a selective serotonin reuptake inhibitor (SSRI)).
Data analysis

Data was analyzed by descriptive statistics. Analysis was divided into questions using data subsets (Supplementary Material 1) and analyzed for each of our five research questions. The study population was described by age, sex, Charlson Comorbidity Index classification and psoriasis comorbidity.

We investigated: the amount, distribution and formulation of use of topical drugs 1 year prior compared to 1 year after psoriasis diagnosis and in a 3-year period after psoriasis diagnosis; regional differences in the use of topical drugs compared to the national average; and inequality in the use of topical drugs by the use of Lorenz curves. In Lorenz curves, the x-axis represents a given proportion of the population ranked with respect to their use of medication, while the y-axis represents the equivalent proportion of the drug use that would be accounted for by the part of the population. By ranking the heavy users first, the depiction of the Lorenz curve returns a concave graph.25

Results

Study population

9,332 Danish patients were diagnosed with psoriasis at a hospital dermatology clinic, and during the study period 2005-2015, 7,743 Danish psoriasis patients redeemed at least one topical drug (Supplementary Material 1). Patients had a median age of 51 (interquartile range (IQR): 37-63) years and the majority were men (Table 2). Most patients (69-73%) had a low Charlson Comorbidity Index (Table 2), yet a non-negligible proportion of patients had a high Charlson Comorbidity Index (6.3-8.6%) and a considerable proportion (26%) had at least one psoriasis-associated comorbidity (Table 2).
Type of utilized topical antipsoriatic drugs

A total of 59,575 prescriptions of topical antipsoriatic drugs had been redeemed (Supplementary Material 1). The total use during the study period was divided between corticosteroids with calcipotriol (31%), calcipotriol (6.5%), very potent corticosteroids (24%), potent corticosteroids (30%), moderate corticosteroids (7.2%) and corticosteroids with antimicrobials (1.6%). There was a 19% reduction in the total use of all topical drugs during the study period (period 2005-2008 compared to 2013-2015), mainly caused by a 39% decrease in the use of calcipotriol-containing preparations (Fig. 1), while the remaining types of prescribed topical drugs only presented minor fluctuations (Fig. 1). Use the year before and after diagnosis was comparable (Fig. 1). Men 65 years consumed most topical drugs, while the distribution in use between sexes was comparable (Supplementary Material 2).

Many patients increased topical treatment prior to the first contact at the hospital, overall from 45% to 60%. Shortly after the first contact, there was a further 20% increase in use, but this decreased during the years following the first visit. During the following 3-year-period, a further decrease was observed leading to a use level similar to the time for referral to the hospital (Fig. 2). 10% did not redeem a second prescription the year after diagnosis, 23% redeemed 2 prescriptions the year after diagnosis, 39% redeemed 3-5 prescriptions the year after diagnosis and 28% redeemed more than 5 prescriptions the year after diagnosis.

During the study period, a change in the formulation of marketed topical antipsoriatic drugs was mainly observed for corticosteroid and calcipotriol combinations; the use of gel increased from 0.4% to 40% simultaneously with a drop from 100% to 60% in the use of ointment. Moderate corticosteroids were mainly prescribed as cream (84-86%), potent corticosteroids as cream (48-54%), very potent corticosteroids as ointment (46-51%), corticosteroids with antimicrobials as cream (92-97%) and calcipotriol as cream (58-100%) (Supplementary Material 3).
Regional differences in the use of topical antipsoriatic drugs

Considerable regional differences in the use of topical drugs between regions were registered compared to the national average in the 11-year study period. In the period 2012-2015, with regard to the relative difference (of regional compared to national average use), there was an 89% variation in the use of moderate corticosteroids, from highest use in the South region to lowest use in the Zealand region, and a 37% variation in the use of corticosteroids, with calcipotriol with highest use in the Zealand region and lowest use in the South region (Fig. 3). In the remaining period (2005-2012), similar patterns of use were observed, except for fluctuations in the pattern of use of calcipotriol with or without corticosteroids in the North region (Supplementary Material 4).

Inequality in the use of topical antipsoriatic drugs

The distribution of the use of topical drugs between patients was moderately skewed for all topical antipsoriatic drug classes, with 25% of patients using 70% of the total amount of the topical drugs (Fig. 4) (Supplementary Material 5).

Use of biologics, systemic drugs, and phototherapy

The majority of patients did not use other antipsoriatic treatments than topical drugs (Table 3). The biologic drug etanercept was used by 0.1% of patients in 2005, increasing to 1.5% in 2010 and then falling to 0.4% of patients in 2015. During the same period, the biologic drug adalimumab was used by 1.0% of patients in 2006, 4.4% in 2011 and 1.4% of patients in 2015. The biologic drug ustekinumab was introduced on the Danish market in 2009, when it was used by 0.3% of patients. Its use hereafter increased, with 1.1% of patients using it in 2014.

The use of systemic drugs increased over the study period for methotrexate (74% increase) and acitretin (260%), while ciclosporin use fell by 80% (Table 3). Phototherapy treatments fell by 44% (Table 3).

This article is protected by copyright. All rights reserved.
Discussion

Three-quarters of patients used only topical drugs to treat psoriasis, and corticosteroids with calcipotriol or calcipotriol were most frequently used. The variation in the use of topical drugs between regions and between individual patients is expected in accordance with the heterogeneous clinical expression of psoriasis. The use of topical therapies as well as phototherapy declined, while the use of systemic therapy increased, driven by a 70% increase in the use of methotrexate. 2.3-6% of patients used biologics during the study period.

The findings from this study are difficult to compare with the varying rates of use of topical corticosteroid-containing antipsoriatic treatments reported in a recent systematic literature review\textsuperscript{14} including publications from Western countries using register-based data from national medical care surveys (topical treatments used by 4-77%), claims databases (topical treatments used by 4-42%) and dispensed prescription databases (topical treatments used by 37%). These differences are likely attributable to the marked differences in study design and study settings, making it difficult to provide a reliable estimate of the real-life use of topical drugs in psoriasis patients.

The large heterogeneity in how patients use topical drugs\textsuperscript{26} does not allow for conclusions regarding adherence; many psoriasis patients with limited disease may use the same topical drug container for extended periods of time, so drug survival curves (where patients who did not redeem a new prescription within 6 or 12 months are considered non-adherent) must be interpreted with caution,\textsuperscript{27} and consequently, we refrained from providing a more exact estimate of adherence to topical antipsoriatic drugs.

The 45% increase in the use of topical antipsoriatic drugs around the time of diagnosis at the hospital aligns with previous literature.\textsuperscript{28} Patients were treated by a dermatologist in practice or general practitioner before referral to hospital, and the increase could reflect a higher adherence rate when referred to a hospital department or reflect that patients have more severe disease when they are admitted to hospital.
The same types of topical drugs are prescribed by the general practitioner or dermatologist in practice compared to the hospital. The use of topical drugs decreased over time after diagnosis, in accordance with a Nordic register-based study investigating adherence to prescribed topical drugs; within a year of diagnosis, 88% of patients were non-adherent to the topical drugs, but most patients were prescribed more than 1 type of topical drug within the first year. Furthermore, three-quarters of psoriasis patients were on topical therapy only; this either indicates that psoriasis patients treated at Danish hospitals have limited disease or may reflect that patients are undertreated and not treated according to the Danish national guidelines. The decrease in the use of topical drugs may reflect an increased use of methotrexate and a better control of disease. The reduced use of corticosteroids could also reflect increased corticophobia in the psoriasis population or prescribing physicians or a marked reduction in adherence to prescribed treatment.

The regional differences in the use of corticosteroids probably reflect local traditions and preferences among physicians and were generally found to be stable over time in the regions with larger populations of patients.

The use of methotrexate increased, in accordance with findings from another nationwide study, and complies with the expert recommendation in Denmark, where methotrexate is prescribed at hospitals as well as by dermatologists in private practice and monitored for adverse events according to national guidelines. Conversely, the use of phototherapy treatments decreased over time, a trend also seen in the US, perhaps due to an increasing awareness of potential side-effects and the development of more patient-friendly and less time-consuming treatment alternatives.

The fluctuations in the use of biologics may be related to a change in choice of biologic treatments in the individual patient due to decreased efficacy over time. Furthermore, in 2009 Denmark established the council for the use of expensive hospital medication RADS (Danish: Rådet for Anvendelse af Dyr Sygehusmedicin), and this led to guidelines to ensure that all patients,

This article is protected by copyright. All rights reserved.
including patients with moderate-to-severe psoriasis, have equal access to treatment with expensive hospital medications. RADS provided the first version of recommendations for psoriasis in 2012, where ustekinumab as well as adalimumab were recommended as first-line treatment, as reflected in this study. With the increasing cost of biologics and the introduction of biosimilars, treatment decisions are evidently becoming more centrally regulated and less physician-dependent.

The essential strength of this study is the use of real-life data from the Danish registries, with their high level of completeness and validity.

The study has limitations. A main limitation of this study is the lack of clinical data on scoring and monitoring the severity of psoriasis in the psoriasis patients included, which could have provided valuable information on the interplay between temporal changes in the severity of psoriasis and the use of medication. The data presented must be interpreted with the background information that Danish patients are reimbursed for drug expenses depending on annual consumption and choice of drug; e.g. topical corticosteroids with antimicrobials are not reimbursed, which may to some extent explain their limited use. Biologics are provided by the hospital free of charge. Some biologics not coded in the Danish National Patient Register, e.g. infliximab, have been used in the treatment of psoriasis. The high use of calcipotriol/corticosteroids preparations observed in the North region in 2009-2012 may reflect that only a few patients from the North region were included in the study, and only a few dermatologists in practice with a certain prescription pattern treated these patients. The study comprised only patients diagnosed at hospital clinics, including a majority of patients manageable on topical drugs, and also patients with more severe psoriasis not amenable to recommended first-line treatments.

Conclusion

The use of topical antipsoriatic drugs varies in individual patients and reflects that psoriasis is heterogeneous in severity and development over time. The use of topical drugs is influenced by traditions among physicians. However, prescription patterns in Denmark are similar among general practitioners.
practitioners, dermatologists in practice and hospital clinics. The largest amount of topical antipsoriatic drugs is used around the time of hospital diagnosis.

Acknowledgement

TranslatePlus proofread the manuscript.

References

Carrascosa JM, Rivera N, Garcia-Doval I et al. Does the treatment ladder for systemic therapy in moderate to severe psoriasis only go up? The percentage of patients with severe psoriasis on biologics increases over time. Actas Dermosifiliogr 2015; 106: 638-43.


Schmidt M, Pedersen L, Sørensen HT. The Danish Civil Registration System as a tool in epidemiology. European journal of epidemiology 2014; 29: 541.


Table 1. Topical antipsoriatic drugs selected for this study.

<table>
<thead>
<tr>
<th>Drug</th>
<th>ATC Class</th>
<th>Drug class description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clobetasone 17-butyrate</td>
<td>D07AB01</td>
<td>Moderate corticosteroids</td>
</tr>
<tr>
<td>Hydrocortisone 17-butyrate</td>
<td>D07AB02</td>
<td></td>
</tr>
<tr>
<td>Betamethasone 17-valerate / betamethasone</td>
<td>D07AC01</td>
<td>Potent corticosteroids</td>
</tr>
<tr>
<td>Mometasone furoate</td>
<td>D07AC13</td>
<td></td>
</tr>
<tr>
<td>Fluocinolone acetonide</td>
<td>D07AC04</td>
<td></td>
</tr>
<tr>
<td>Fluocinonide</td>
<td>D07AC08</td>
<td></td>
</tr>
<tr>
<td>Clobetasol propionate</td>
<td>D07AD01</td>
<td>Very potent corticosteroids</td>
</tr>
<tr>
<td>Betamethasone/clioquinol</td>
<td>D07BC01</td>
<td>Corticosteroid with antimicrobials</td>
</tr>
<tr>
<td>Betamethasone/fusidic acid</td>
<td>D07CC01</td>
<td></td>
</tr>
<tr>
<td>Fluocinolone acetonid/clioquinol</td>
<td>D07BC02</td>
<td></td>
</tr>
<tr>
<td>Calcipotriol</td>
<td>D05AX02</td>
<td>Calcipotriol</td>
</tr>
<tr>
<td>Betamethasone, calcipotriol</td>
<td>D05AX52</td>
<td>Corticosteroid with calcipotriol</td>
</tr>
</tbody>
</table>

*All drugs had a marketing authorization for psoriasis in Denmark in October 2015. Abbreviation: ATC, Anatomical Therapeutic Chemical.*
Table 2. Baseline characteristics for patients at the time of psoriasis diagnosis.

<table>
<thead>
<tr>
<th></th>
<th>North Region (n=348)</th>
<th>Mid region (n=1,734)</th>
<th>South Region (n=1,843)</th>
<th>Capital region (n=2,842)</th>
<th>Zealand region (n=966)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men</strong></td>
<td>201 (57.76%)</td>
<td>911 (52.54%)</td>
<td>983 (53.34%)</td>
<td>1,461 (51.41%)</td>
<td>531 (54.97%)</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td>147 (42.24%)</td>
<td>823 (47.46%)</td>
<td>860 (46.66%)</td>
<td>1,381 (48.59%)</td>
<td>435 (45.03%)</td>
</tr>
<tr>
<td><strong>Age (median, IQR), years</strong></td>
<td>51.6</td>
<td>50.5</td>
<td>50.8</td>
<td>52.1</td>
<td>52.2</td>
</tr>
<tr>
<td><strong>CCI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low (0)</td>
<td>252 (72.41%)</td>
<td>1,267 (73.07%)</td>
<td>1,305 (70.81%)</td>
<td>1,954 (68.75%)</td>
<td>680 (70.39%)</td>
</tr>
<tr>
<td>Medium (1)</td>
<td>52 (14.94%)</td>
<td>261 (15.05%)</td>
<td>264 (14.32%)</td>
<td>437 (15.38%)</td>
<td>145 (15.01%)</td>
</tr>
<tr>
<td>High (≥2)</td>
<td>22 (6.32%)</td>
<td>119 (6.86%)</td>
<td>158 (8.57%)</td>
<td>216 (7.60%)</td>
<td>64 (6.63%)</td>
</tr>
<tr>
<td><strong>Psoriasis-associated co-morbidities</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>aHypertension</td>
<td>90 (25.9%)</td>
<td>380 (21.9%)</td>
<td>399 (21.6%)</td>
<td>579 (20.4%)</td>
<td>194 (20.1%)</td>
</tr>
<tr>
<td>bHyperlipidemia</td>
<td>49 (14.1%)</td>
<td>224 (12.9%)</td>
<td>297 (16.1%)</td>
<td>394 (13.9%)</td>
<td>126 (13.0%)</td>
</tr>
<tr>
<td>cCongestive heart failure</td>
<td>(n&lt;5)</td>
<td>7 (0.4%)</td>
<td>9 (0.5%)</td>
<td>27 (1.0%)</td>
<td>10 (1.0%)</td>
</tr>
<tr>
<td>dIschemic heart disease</td>
<td>(n&lt;5)</td>
<td>9 (0.5%)</td>
<td>10 (0.5%)</td>
<td>8 (0.3%)</td>
<td>(n&lt;5)</td>
</tr>
<tr>
<td>eDiabetes mellitus type 2</td>
<td>25 (7.2%)</td>
<td>110 (6.3%)</td>
<td>165 (9.0%)</td>
<td>230 (8.1%)</td>
<td>79 (8.2%)</td>
</tr>
<tr>
<td>fDepression / anxiety</td>
<td>43 (12.4%)</td>
<td>182 (10.5%)</td>
<td>147 (8.0%)</td>
<td>239 (8.4%)</td>
<td>83 (8.6%)</td>
</tr>
</tbody>
</table>

Note: CCI based on diagnoses any time prior to index date. Abbreviations: CCI, Charlson Comorbidity Index; IQR, interquartile range. **a**Patients defined by having redeemed a prescription of either a calcium channel blocker, an angiotensin-converting-enzyme (ACE) inhibitor or a thiazide diuretic the year prior to psoriasis diagnosis. **b**Patients defined by having redeemed a prescription for a statin the year prior to psoriasis diagnosis. **c**Patients defined by the diagnosis the year prior to psoriasis diagnosis. **d**Patients defined by the diagnosis acute myocardial infarction the year prior to psoriasis diagnosis. **e**Patients defined by the diagnosis type 2-diabetes or having redeemed a prescription for an oral antidiabetic the year prior to psoriasis diagnosis. **f**Patients defined as having redeemed a prescription for a selective serotonin reuptake inhibitor (SSRI) the year prior to psoriasis diagnosis.
Table 3. Biologics, systemic drugs, and phototherapies prescribed for psoriasis patients.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>None of below treatments</td>
<td>77.6%</td>
<td>70.4%</td>
<td>75.0%</td>
</tr>
<tr>
<td><strong>Biologics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Etanercept</td>
<td>1.2%</td>
<td>2.0%</td>
<td>1.1%</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>1.1%</td>
<td>3.8%</td>
<td>2.0%</td>
</tr>
<tr>
<td>Ustekinumab</td>
<td>NA</td>
<td>0.2%</td>
<td>0.7%</td>
</tr>
<tr>
<td><strong>Systemic drugs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methotrexate</td>
<td>9.6%</td>
<td>17.3%</td>
<td>16.7%</td>
</tr>
<tr>
<td>Ciclosporin</td>
<td>2.0%</td>
<td>0.8%</td>
<td>0.4%</td>
</tr>
<tr>
<td>Acitretin</td>
<td>0.5%</td>
<td>1.9%</td>
<td>1.8%</td>
</tr>
<tr>
<td><strong>Phototherapy</strong></td>
<td>10.5%</td>
<td>9.0%</td>
<td>5.9%</td>
</tr>
</tbody>
</table>

Note: Treatments were initiated within 1 year of diagnosis. *Phototherapy includes: Psoralen combined with Ultraviolet A Phototherapy (PUVA) prescribed for feet, hands, and universal and Ultraviolet B (UVB) Phototherapy prescribed in small- and broadband. Abbreviation: NA, Not Applicable.