Prescribing Patterns of Systemic Immunomodulating Agents for Atopic Dermatitis

1. Milestones

Milestone	Planned/Estimated Date
Release of protocol to OHDSI community	**02/11/2021**
Deadline for feedback acceptance from OHDSI community	
Finalization of protocol and feedback from the OHDSI community	
Start of Analysis	
Presentation of Results	
Manuscript Submission	

2. Revision History – Amendments and Updates

Version	**Date**	**Author(s)**	**Comments**
0.0	7/1/20	Schilling Wetzel Dellavalle Sivesind Branda	Initial protocol

3. Objective

The primary objective of this study is to characterize prescribing patterns of systemic agents for atopic dermatitis and to describe variation by patient characteristics.

4. Specific Aims

The Specific Aims are to:

1. Describe prevalence of systemic immunomodulating agents prescribed for atopic dermatitis by patient characteristics.
2. Describe total number of courses of systemic steroids prescribed before initiating a nonsteroidal systemic immunomodulating agent by patient characteristics.
3. Describe total number of different systemic immunomodulating agents prescribed

before initiating dupilumab by patient characteristics and
4. Describe the time between start date of the first of first systemic immunomodulating agent and the start date of dupilumab

We hypothesize prevalence of systemic agent use will vary by patient characteristics, specifically race and age. We hypothesize the steroid sparing systemic immunomodulating agent first prescribed for treatment of atopic dermatitis will not vary by patient characteristics. We hypothesize black patients will be prescribed more courses of systemic steroids before a nonsteroidal systemic immunomodulating agent is prescribed. We hypothesize black patients will be prescribed more systemic immunomodulating agents before prescribing dupilumab.

5. Rationale:

Atopic dermatitis (AD) is a common chronic inflammatory disease. In the United States, the prevalence of AD in children is approximately 10-13% and in adults is approximately 7%.[1-4] Patients with severe disease experience a decrease in quality of life and worse mental health.[1,5] AD is associated with high healthcare resource utilization and healthcare costs from outpatient visits, pharmacy utilization, emergency department visits, and hospitalizations. These costs parallel disease severity.[6-8] Effectively treating patients with greater disease severity has both clinical and economic implications.

Treatment with a systemic immunomodulating agent is indicated when disease is considered moderate-to-severe or has significant psychosocial impact.[9] A variety of systemic agents including cyclosporine, azathioprine, methotrexate, mycophenolate mofetil, and systemic steroids are used in practice without strict guidelines or recommendations to guide treatment choice.[9,10] In March 2017, dupilumab became the first biologic drug approved for atopic dermatitis in adults; it now has indications for both pediatric and adult populations, having been approved for treatment of AD in children six years or older since May 2020. Compared with the aforementioned systemic immunomodulating agents, dupilumab may be more effective as a long-term/maintenance therapy and has the advantage of an overall better side effect profile, with no required drug-specific laboratory monitoring.[10] Access, however, may be limited by its novelty and cost.

The disease burden of AD disproportionately affects non-Hispanic black patients. In children with AD, the prevalence in black children is greater than 15%, versus approximately 10% in white children.[2] Environment, socioeconomic status, race, and genetics are associated with this disparity.[4,11] Loss of function mutations in the filaggrin gene are associated with an increased risk of developing AD and having persistent disease. Filaggrin mutations are less common in black patients compared to white patients.[12,13] However, regardless of filaggrin mutation status, black children with AD are more likely to have persistent disease than are white children.[12] Additionally, black patients have lower ceramide/cholesterol ratios, an attenuated Th1 and Th17 immunophenotype, and higher serum IgE levels.[14,15] Despite more severe disease and increased healthcare utilization, black patients are less likely to receive outpatient dermatology care.[3,16-18] Previous research has shown black patients with psoriasis are less likely than white patients to receive biologic treatment, independent of demographic/socioeconomic factors and comorbidities.[19,20] The use of systemic agents for AD has not been previously characterized by race or other patient demographics. Similar data on

prescribing patterns of systemic agents for AD are needed in order to ensure health equity and inform best practice guidelines.

6. Research methods

6.1 Study Design

This study was designed collectively by consensus among the authors following periodic conferencing between June 1, 2020 and January 31, 2021.

This study will be a retrospective, observational cohort study. By "retrospective" we mean the study will use data already collected before the start of the study. By "observational" we mean no intervention will take place in the course of this study. By "cohort study" we mean a collection of persons that meet certain criteria.

The analyses will be performed across a network of observational healthcare databases. All databases have been transformed into the OMOP Common Data Model, Version 5. The complete specification for the OMOP Common Data Model, Version 5 is available at: https://github.com/OHDSI/CommonDataModel. The following databases will be included in this analysis following successful feasibility and passing all study diagnostics.

6.2 Participating Organizations and their Data Sources

Information to be collected from participating entities (via form):
Data partners, please fill out the following form to provide institutional and data details:

- Owner (university, claims aggregator, etc.)
- Name of Database
- Type of data (claims, clinical data/electronic medical records)
- Medication information available (insurance claims, pharmacy fulfillments, prescriptions, clinical narrative documentation
- Geographic representation
- Study contact – Name and email

Participating Partners & Data Sources: TBD--Will be completed based on information completed on the form.

6.3 Data Collection

The University of Colorado will serve as the coordinating center (CC) for this study. The CC will share "study packages" (e.g., SQL queries and R code) that have been tested by the CC team prior to distribution to participating data partners. Partners will run the study packages on their own OMOP CDM data and return the extracted data sets to the CC Team. The CC team will complete the final data analysis.

6.4 Data Time Period

3/28/2017 to 9/27/2020

The data time period was chosen by consensus among the authors to capture prescribing patterns for the newest biologic agent, dupilumab, which received FDA approval on 3/28/2017 for the treatment of atopic dermatitis in adults. The data time period will therefore begin on the approval date and include three years and six months of data spanning 03/28/2017 – 09/27/2020.

6.5 Population Cohort Definitions

Study cohorts will be created using ATLAS parameters and code lists.

Target cohort – Patients with atopic dermatitis, age six to 85 years.

- Persons between six and 85 years of age during the study period of treatment that occurs between 3/28/2017 and 9/27/2020. This equates to an earliest birth date of 03/28/1932 and a latest birthdate of 03/28/11.
- The earliest potential start of inclusion for a person would be defined as the start of the 6th year of life (DOB + 6 years) within the data source time period.
- The latest potential end of a person's inclusion in the analysis would be defined as the start of the 85th year of life (DOB + 85 years) within the data source time period.
- Any two occurrences of a diagnosis of atopic dermatitis, as defined within the Atlas parameters, within study time period

Outcome cohort – Prescription for any systemic immunomodulating agent for treatment of atopic dermatitis.

6.5.1 Specific Aim 1: Addressing Prevalence of Drugs of Interest (DOI)

Aim 1 cohort inclusion criteria includes:

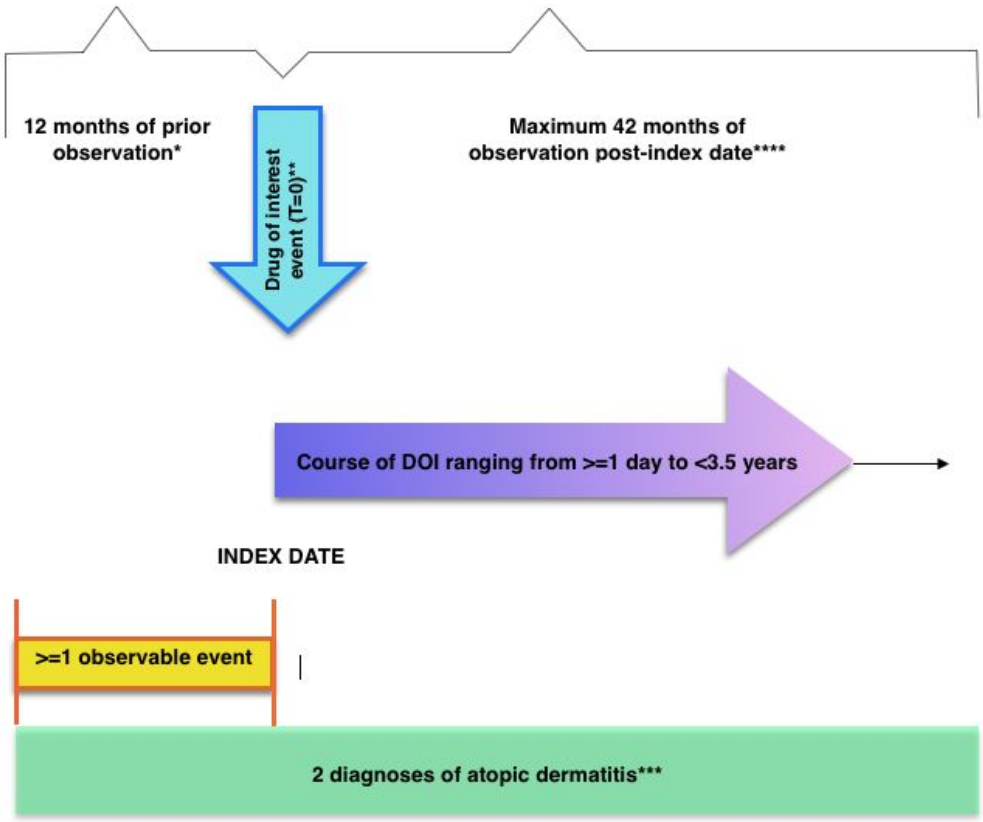
- Two diagnoses of atopic dermatitis with at least one diagnosis of atopic dermatitis occurring within the 3.5 year study period (= denominator) (see Figure 1).
- DOI Prescribing Prevalence - an eligible DOI prescribing event will be identified by the following:
    - A DOI must be a specified systemic immunomodulating agent.
    - DOI systemic immunomodulating agents include specific medications that are standard treatments for atopic dermatitis AND are prescribed for >= 1 day.
    - A DOI event must occur on or after the date of the 1st diagnosis of atopic dermatitis and until the end of the study period.

Potential Limitations:

- If the DOI prescribing event cannot be specifically associated with a diagnosis of atopic dermatitis, people who have AD but are on systemic immunomodulating agents for a reason other than AD may be included (numerator problem)
- We may miss people who have atopic dermatitis but are misclassified by diagnosis (e.g., “dermatitis unspecified,” “lichen simplex chronicus,” “prurigo nodularis”) (denominator problem).
- Without observation of patients’ full medical histories, it is possible that prior diagnoses of atopic dermatitis and associated courses of treatment for AD could be missed
- Over-the-counter topical steroids may be missed

6.5.2 Specific Aim 2

Figure 1. Prescribed drug of interest course



Inclusion Criteria

*A person should not be prescribed a DOI (type and days >=1) in this period

**T=0 is DOI prescribing date (clinical data) or fulfillment date (claims data)

***A person should have 2 diagnoses of atopic dermatitis with at least 1 diagnosis between the 12-month observation period and the 1st DOI date OR between the index date and the 3.5-year study period

****Observation will continue until the individual's observation period ends or the maximum observation period of 3.5 years is reached

Aim 2 cohort inclusion criteria include:

- Two diagnoses of AD, with at least one diagnosis occurring within the 12-month observation period or the 3.5-year study period.
- A non-steroidal DOI prescribing event –
  - DOI are systemic immunomodulating agents as defined for Aim 1 except corticosteroids (prednisolone, methylprednisolone, prednisone, triamcinolone acetonide, dexamethasone).
- Due to the fact we are attempting to capture the 1st non-steroidal systemic immunomodulating agent used we will require that a person not be prescribed a non-steroidal DOI (type) within the observation window prior to the index DOI prescription.

- At least 1 observable event (diagnosis, visit, procedure, any prescribing event or measurement) in the 12 months prior to the index 1st DOI event (T= -12 mo to T=0). This ensures that the person is observable during this window.

Potential limitations:

- We may consider a DOI event as the 1st even when it is not, as a person may have received DOI treatment prior to the observation window.
- We may miss people on maintenance therapy/active prescription for a DOI at the time of study start date.
- If the DOI prescribing event cannot be specifically associated with a diagnosis of atopic dermatitis, people who have AD but are on systemic immunomodulating agents for a reason other than AD may be included (numerator problem)

6.5.3 Specific Aims 3

Aim 3 cohort inclusion criteria include:

- Two diagnoses of AD within the study period with one DOI prescribing event defined as a prescription for dupilumab within the study period, with at least one diagnosis of atopic dermatitis within the observation period starting 12 months prior to- and ending at the 1st DOI event date, so T = -12 mo to T=0 days where T=0 is dupilumab prescribing (clinical data).
- A DOI prescribing event is any prescription for dupilumab.

Potential limitations:

- If the DOI prescribing event cannot be specifically associated with a diagnosis of atopic dermatitis, people who have AD but are prescribed dupilumab for a reason other than AD may be included (numerator problem).
- Patients who received dupilumab as a manufacturer sample may be missed.

Once a person is admitted to the cohort, the length of time of observation following the index date, and therefore information on subsequent DOI prescriptions, will continue until the period of the individual's observation (maximum 3.5 years) ends or the study period end date of 09/27/2020, whichever occurs first.
We will collect data on the latest date of an observable event (ie, visit, procedure, any prescribing event or measurement) so we can describe the length of each person's observable period.

6.5.4 Drugs of Interest

Drugs of Interest are defined as drug types, excluding topical formulations, that are known to be prescribed for atopic dermatitis >= 1 day [WM7] , they are represented

by the following concept sets:

- Systemic immunomodulating agents
  - A list of immunomodulating agents that might be prescribed for atopic dermatitis were determined by literature review and content expert (RD, MW, TS) consensus during protocol development and were identified by National Drug Code associated with generic names and Master Form Code.[9,10,21]
  - Cyclosporine, methotrexate (tablet, solution), azathioprine, mycophenolate mofetil, corticosteroids (prednisolone, methylprednisolone, prednisone, triamcinolone acetonide, dexamethasone), dupilumab,
  - Limitations:
    - Topical steroids purchased over-the-counter or given as manufacturer samples may be confounders
    - Investigational drugs at time of protocol development are not included.
    - Tumor necrosis factor-alpha inhibitors (etanercept, infliximab, adalimumab), omalizumab, intravenous immunoglobulin, Th17 inhibitors (ixekizumab, brodalumab, secukinumab), apremilast, JAK inhibitors will not be included as they are not frequently prescribed for atopic dermatitis. Rather, they are more often prescribed for psoriasis, urticaria, or other skin conditions.[9]
    - Dupilumab received as a manufacturer sample will not be captured.

6.5.5. Atopic Dermatitis Diagnosis

- The AD diagnoses used for the broad inclusion cohort are represented by the following concept set.
- Concept set to include ICD10 L20 (AD) and its descendant codes:
  - L20 Atopic Dermatitis
  - L20.0 Besnier's prurigo
  - L20.8 Other atopic dermatitis
  - L20.81 Atopic neurodermatitis
  - L20.82 Flexural eczema
  - L20.84 Intrinsic (allergic) eczema
  - L20.89 Other atopic dermatitis
  - L20.9 Atopic Dermatitis, unspecified

- Concept to exclude ICD10 L40 Psoriasis, L23 Allergic contact dermatitis, L24 Irritant contact dermatitis, L25 Unspecified contact dermatitis, L26 Exfoliative dermatitis, L27 Dermatitis due to substances taken internally, L28 Lichen simplex chronicus and prurigo, L29 Pruritus, L30 Other and unspecified dermatitis, R21 Rash and other nonspecific skin eruption, and their descendant codes

6.5.6 Other Variables of Interest

- Disease severity
    - Clinical data – disease grading by clinician (mild, moderate, severe); Eczema Area and Severity Index, SCORAD, if available
    - Patient Reported Outcomes (DLQI, Skindex, POEM), if available
    - Hospitalizations for primary diagnosis of AD during study time period
    - Hospital length of stay for primary diagnosis of AD during study time period
    - Concurrent use of systemic steroids with another systemic agent
- Other comorbid conditions/chronic disease (>=30 days prior to systemic agent initiation) that may affect treatment choice
    - Chronic liver disease
    - Hepatitis
    - Hypertension
    - Chronic kidney disease
    - Conjunctivitis
    - Diabetes mellitus
    - HIV/AIDS
    - Alcohol abuse/dependence
    - Pregnancy
- Information on select non-atopic dermatitis diagnoses for which a patient might be on dupilumab for >=14 days.
    - Asthma
    - Chronic rhinosinusitis
    - Allergic rhinitis
    - Nasal polyp/polyposis

- Date of last observable event (visit, prescribing event) for a given patient.
    - May be coded as days duration from index date to last observable event.
    - Limitations
        - Patients with malignancy are excluded (eliminate immunotherapy reactions, less likely to be offered immunosuppressive medication)

6.7 Outcomes

Reporting of results will adhere to STROBE guidelines for reporting observational studies.[22] Patient demographics will be reported using descriptive statistics with count and percentage for categorical characteristics or mean and standard deviation if normally distributed otherwise median and interquartile range for continuous characteristics.

For Aim 1: Patients with a diagnosis of AD will be categorized by demographic factors (age, gender, race and insurance) as well as the type of AD was first diagnosed. As race is a primary factor of interest (Denominator = # of persons with AD within each race category) we will be characterizing the distribution of immunomodulating agents within race. Within a race category, the prevalence of systemic immunomodulating agents will be captured by first showing the population counts with AD in each race category and the prevalence of those with a qualifying systemic immunomodulating agent prescription[WM12] . The race category will be

assigned as the most recent update of race within OMOP; we will not reassign the race category.

For Aim 2: Patients with a diagnosis of AD will be categorized by the total number of systemic steroids -- by: a) number of prescriptions, and b) total dose (mg/kg) -- prescribed before a non steroidal systemic immunomodulating agent. This will then be categorized within patient factors (age, race, ethnicity, and gender). For each of these patient factor categories, (Denominator = # of persons with AD within each category), the prevalence of nonsteroidal systemic immunomodulating agents will be captured by first showing the population counts with AD in each patient factor category and the prevalence of those with a qualifying nonsteroidal systemic immunomodulating agent prescription. We will characterize the first non-steroidal systemic immunomodulating agent by type and race.

For Aim 3: We will characterize previous treatments for AD by type and number of prescriptions/outpatient clinic orders by patient factor category (age, race, ethnicity, and gender). Within groupings, the mean number of prescriptions will be calculated by prescription type.

7. Limitations and Caveats

- Race may not be reported or captured by available categories.
- Atopic dermatitis may be coded differently. Broadening the diagnosis inclusion would run the risk of including patients who do not have atopic dermatitis.
  If the DOI prescribing event (e.g., prescription/order) is not directly associated with a diagnosis of atopic dermatitis, would run the risk of including patients who were prescribed systemic immunomodulating agents for diagnoses other than AD.

8. Protection of Human Subjects

- This study will use de-identified data.
- IRB approval: Each participating data site confirmed Institutional Review Board approval for the study or confirmed their analysis did not require approval because it was exempt or was deemed non-human subjects research (e.g., because the database had previously been de-identified).

9. Return of Data Query/Results

We seek deidentified row-level patient data so we may create aggregate overall results: For every patient meeting inclusion criteria, we would seek return of the following information:
Patient demographic table:

- Age at index visit (first prescription for a systemic immunomodulating agent for AD)
- Sex/gender -- biologic or other
- Race
- Ethnicity
- Zip code
- AD severity at beginning of study time period
- AD severity at index visit
- Encounter type for all encounters during study time frame [WM14]
- Systemic steroid prescription medication name, days supplied for prescription, unit of dose, quantity of dose
- Nonsteroidal systemic immunomodulating prescription medication name, days supplied for prescription, # of refills for prescription

10. Plans for disseminating and communicating study results

The study results will be posted on the OHDSI website after completion of the study and published in a peer-reviewed scientific journal.

Initial proposal date: TBD

Launch date: TBD

Study closure date: TBD

Results submission: Email

11. Example Text, Figures, and Table shells for eventual publication

This section illustrates example results text, tables and figures that will be generated:

Example results text:

"There were X systemic immunomodulating prescriptions among X patients. Median age was X and X% were male (Table 2). Fig 1 summarizes the most commonly prescribed systemic immunomodulating agents, which were x (%), followed by x (%), x (%). The mean duration of therapy was x days. The mean number of prescriptions as part of a course of therapy was x prescriptions."

"The number of courses of systemic steroids prescribed among X patients prior to prescription of a nonsteroidal systemic immunomodulating agent ranged from X to X, with a mean of X."

"The number of systemic immunomodulating agents prescribed prior to prescription of dupilumab ranged from X to X among X patients, with a median number of X. Median age was X and X% were male. X% of patients were Caucasian and X% Skin of Color."

Table 1: Concept sets (as defined and linked in Atlas)

Concept Set
CU-AMC Atopic dermatitis
CU-AMC Systemic Nonsteroidal Immunomodulators
CU-AMC Systemic steroids
CU-AMC TNF-alpha inhibitors
CU-AMC JAK inhibitors
CU-AMC Th17 inhibitors
CU-AMC Omalizumab
CU-AMC Apremilast
CU-AMC IVIG

Table 2: Atopic Dermatitis diagnosis concept set = CU-AMC Atopic Dermatitis; Table 2 lists the ICD-10 Included Source Codes that map to the included concept IDs for the purpose of face validity

Concept ID	**Concept Code**	**Concept Name**	**Class**	**Domain**	**Vocabulary**
1569765	L20	Atopic dermatitis	3-char nonbill code	Non-standard	Condition
35208449	L20.0	Besnier's prurigo	4-char billing code	Non-standard	Condition
1569766	L20.8	Other atopic dermatitis	4-char nonbill code	Non-standard	Condition
45543364	L20.81	Atopic neurodermatitis	5-char billing code	Non-standard	Condition
45552974	L20.82	Flexural eczema	5-char billing code	Non-standard	Condition

45601213	L20.84	Intrinsic (allergic) eczema	5-char billing code	Non-standard	Condition
45567351	L20.89	Other atopic dermatitis	5-char billing code	Non-standard	Condition
35208450	L20.9	Atopic dermatitis, unspecified	4-char billing code	Non-standard	Condition

Example Table 3: Databases included and their characteristics

Database	**Location**	**Years of data**	**Owner**

Example Table 4: Study population demographics by data source(s)

	Datasource #1	Datasource #2	Datasource #3, etc.
Age of first AD diagnosis between 6 - 85 years of age	Mean (std) N (%) within age groupings		
Race listed at first AD diagnosis	N (%) within age groupings		
Gender Male Female	N (%)		
Country(ies) of data source US UK Japan etc.	N (%)		
Atopic Dermatitis diagnosis X X X etc.	N (%)		

Insurance type Governmental Private None Other	N (%)		

Example Table 5a: Duration of systemic steroid course

Duration of steroid course (week range) **suggested breakdown of data	Number of steroid courses
<2 weeks	
>3-4 weeks	
>4-8 weeks	
>8-12 weeks	
>12 weeks - 1 year	
>1 year - 2 years	
> 2 years	

Example Table 5b: Duration of systemic nonsteroidal immunomodulating therapy

Duration of systemic nonsteroidal course (month range) **suggested breakdown of data	Number of systemic nonsteroidal courses
< 2 months	
>2-4 months	
>4-8 months	
>8-12 months	
>1-2 years	
>2 years	

Example Table 6a: User prevalence and prescription prevalence of qualifying systemic nonsteroidal immunomodulating agent prescriptions by database (prevalence per 1000 persons), ranked by the average user prevalence

	User prevalence						**Prescription prevalence**					
Systemic nonsteroidal agents	CPRD	JMDC	Optum	CCAE	Truven	Total	CPRD	JMDC	Optum	CCAE	Truven	Total
Overall												
Male												
Female												
Age 6-15												
16-25												
26-35												
36-45												
etc.												
Caucasian												
Skin of Color												

Example Table 6b: User prevalence and number of prescriptions of dupilumab by database (prevalence per 1000 persons), ranked by the average user prevalence

	User prevalence					**Prescription prevalence**				
Dupilumab	CPRD	JMDC	Optum	CCAE	Truven	CPRD	JMDC	Optum	CCAE	Truven
Overall										
Male										
Female										

Age 6-15										
16-25										
26-35										
36-45										
etc.										
Caucasian										
Skin of Color										

Example Table 7a: Number of systemic corticosteroid prescriptions by database

	Number of prescriptions				
Type of DOI	**Database #1**	**Database #2**	**Database #3**	**Database #4**	**Database #5**
Prednisone					
Prednisolone					
Methylprednisolone					
Triamcinolone acetonide					
Dexamethasone					

Example Table 7b: Number of qualifying systemic nonsteroidal immunomodulating agents and dupilumab by database

	Number of prescriptions				
Type of DOI	**Database #1**	**Database #2**	**Database #3**	**Database #4**	**Database #5**
Cyclosporine					
Methotrexate					

Azathioprine					
Mycophenolate Mofetil					
Interferon gamma					
dupilumab					

Example Table 8a: Description of duration of systemic corticosteroid courses

Sex	**Mean, standard deviation, median and interquartile range of course duration (weeks)**
Overall	
6-15	
16-25	
26-35	
36-45	
46-55	
56-65	
66-75	
76-85	
Male	
6-15	
16-25	
26-35	
36-45	
46-55	
56-65	
66-75	

76-85	
Female	
6-15	
16-25	
26-35	
36-45	
46-55	
56-65	
66-75	
76-85	
Caucasian	
6-15	
16-25	
26-35	
36-45	
46-55	
etc	
Skin of Color	
6-15	
16-25	
26-35	
36-45	
46-55	
etc	

Example Table 8b: Description of duration of nonsteroidal immunomodulating agent courses

Sex	Mean, standard deviation, median and interquartile range of course duration (weeks)
Overall	
6-15	
16-25	
26-35	
36-45	
46-55	
56-65	
66-75	
76-85	
Male	
6-15	
16-25	
26-35	
36-45	
46-55	
56-65	
66-75	
76-85	
Female	
6-15	
16-25	
26-35	

36-45	
46-55	
56-65	
66-75	
76-85	
Caucasian	
6-15	
16-25	
26-35	
36-45	
46-55	
56-65	
66-75	
76-85	
Skin of Color	
6-15	
16-25	
26-35	
36-45	
46-55	
56-65	
66-75	
76-85	

Example Table 9a: Variation in duration of corticosteroid therapy by country

Country	**Duration of therapy (days/months): Mean, standard deviation, median and interquartile range**
United States	
United Kingdom	
Japan	
France	
Germany	
Other	
Other	
Other	

Example Table 9b: Variation in duration of nonsteroidal immunomodulating systemic agents by country

Country	**Duration of therapy (days/months): Mean, standard deviation, median and interquartile range**
United States	
United Kingdom	
Japan	
France	
Germany	
Other	
Other	
Other	

Example of Figure 1: Courses of systemic nonsteroidal agents for atopic dermatitis

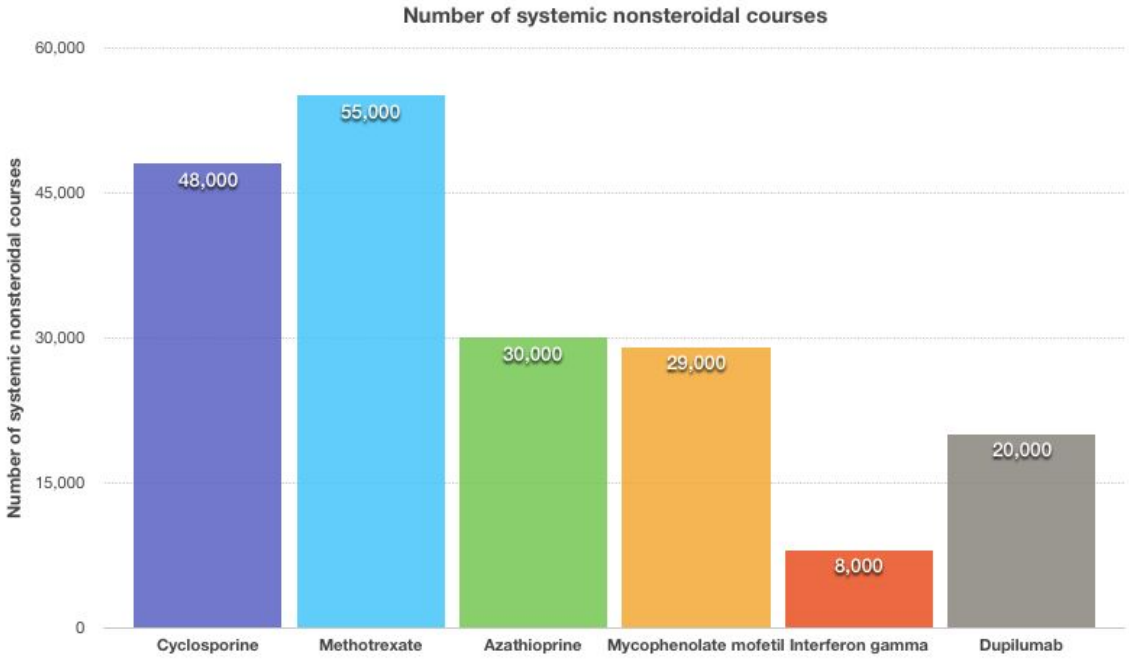


Fig. 1. Frequency and distribution of systemic nonsteroidal agents identified in the database

Example of Figure 2: Systemic nonsteroidal agents for atopic dermatitis by year for years 2017 to 2020

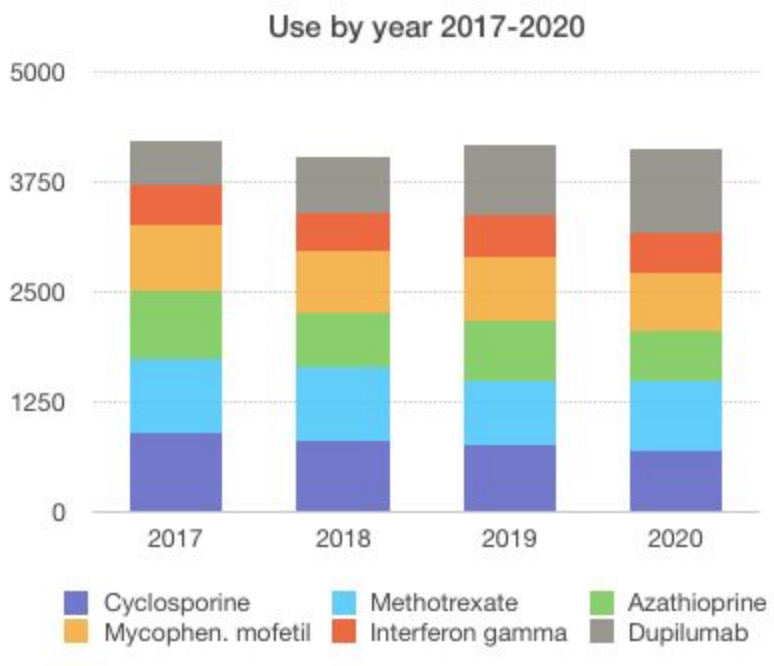
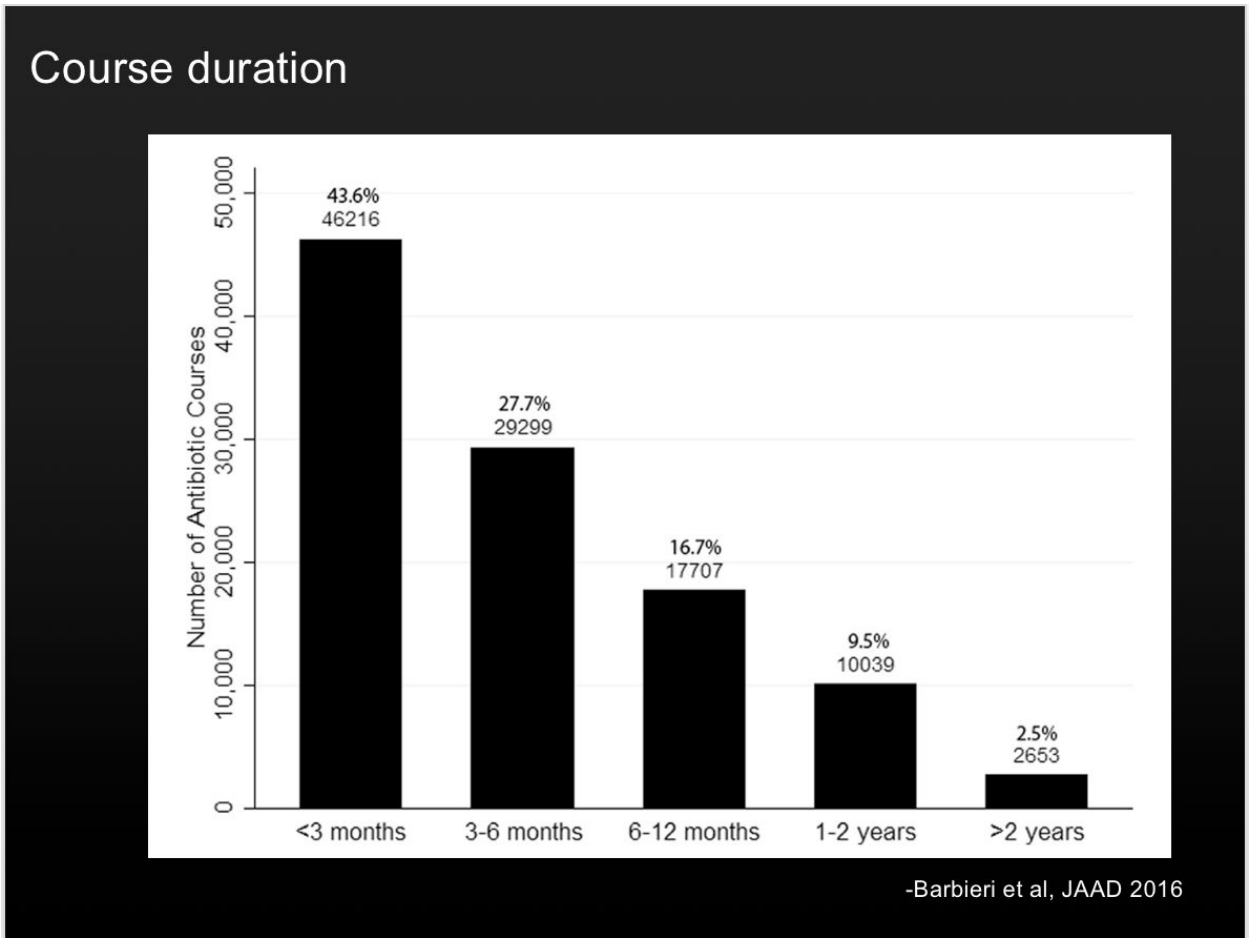


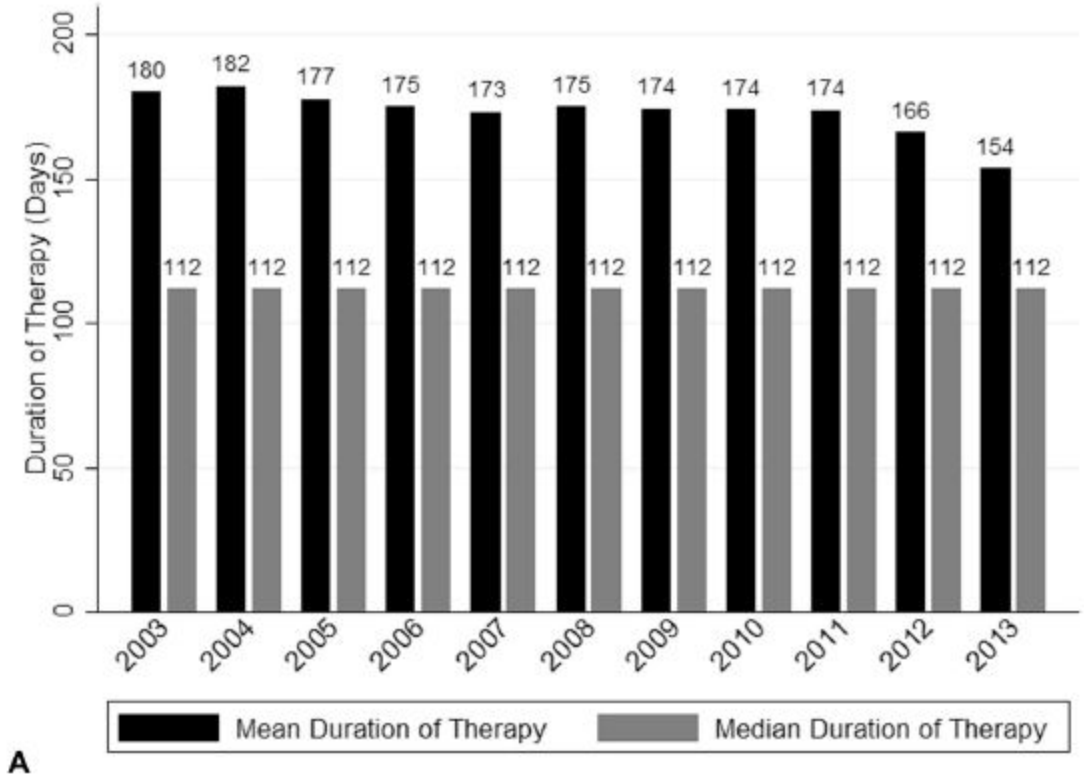
Fig. 2. Systemic nonsteroidal agents by year

Example of Figure 3: Duration of systemic nonsteroidal therapy for atopic dermatitis prior to prescription of dupilumab



*y-axis would be duration of systemic nonsteroidal therapy prior to dupilumab
*pictogram bars can be color-coded by database

Example of Figure 4: Nonsteroidal systemic agents for atopic dermatitis course duration per year (2017-2020)



*From Barbierie et al. JAAD 2016
*Our table would include years 2017-2020

Appendix 1

Please use the below format for adding your institution for this protocol

- Name of Database
- Owner (university, claims aggregator, etc)
- Type of data (claims, clinical data,electronic medical records)
- Medication information (insurance claims, pharmacy fulfillments, prescriptions, clinical narrative documentation)
- Geographic representation

References:

1. Chiesa Fuxench ZC, Block JK, Boguniewicz M, et al. Atopic Dermatitis in America Study: A Cross-Sectional Study Examining the Prevalence and Disease Burden of Atopic Dermatitis in the US Adult Population. *J Invest Dermatol.* 2019;139(3):583-590.
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