ACR Convergence
Where Rheumatology Meets
#ACR23

Influence of sex on the persistence of different classes of targeted therapies for psoriatic arthritis

a cohort study of 14,778 patients from the French health insurance database (SNDS)

Laura Pina Vegas, Laetitia Penso, Emilie Sbidian, Pascal Claudepierre
EpiDermE, Paris-Est Créteil University
Rheumatology Department, AP-HP, Henri Mondor Hospital (Créteil, France)

Disclosure

I have no relevant financial relationship with ineligible companies to disclose

Introduction

- Psoriatic arthritis (PsA) is a heterogeneous chronic inflammatory rheumatic disease
- Sex differences in phenotype presentation, disease trajectory, and treatment response in PsA have been reported[1]
- Several cohort studies and registries have reported sex-related disparities in the TNFi response in PsA but no formal conclusions can be drawn from these studies[2,3]
- Few studies have included the most recently marketed molecules, and the existing data on other targeted therapies in PsA is sparse[4]

[1]Tarannum S et al. Nat Rev Rheumatol. 2022 ; [2]Heiberg MS et al. Arthritis Rheum. 2008; [3]Højgaard P et al. Rheumatology (Oxford). 2018 ; [4]Roccuzzo G et al. Clin Exp Dermatol. 2023.

Objective

To evaluate the effect of sex on the long-term persistence of each targeted therapeutic class in PsA

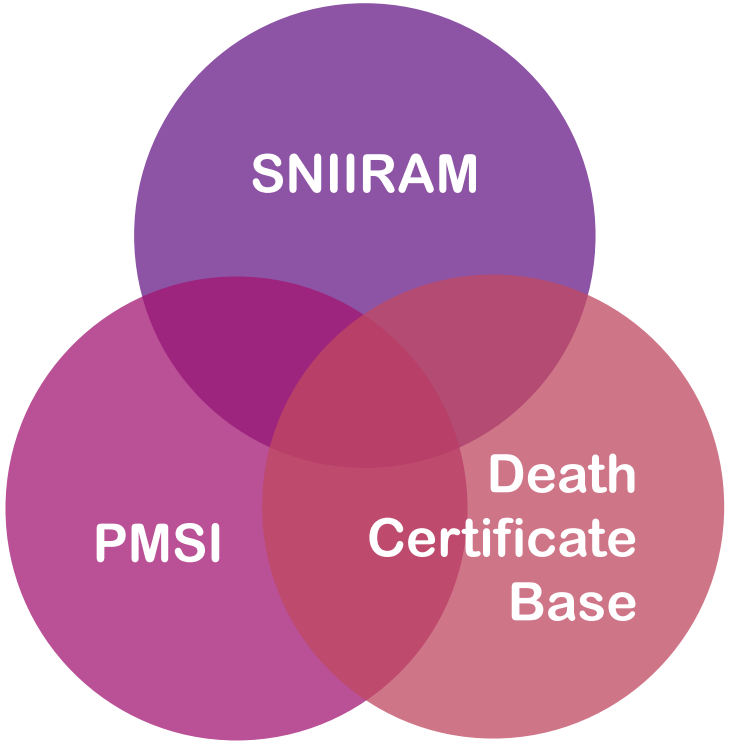
Data Sources

French National Health Insurance Database (SNDS)[1,2,3]

≈ 99% of the French population

National Health Insurance System (SNIIRAM)

Age, sex, social deprivation, reimbursed treatments dispensed in pharmacies, paramedical interventions, reimbursed care for long-term diseases



National Hospital Discharge System (PMSI)

Dates of hospital admission and discharge
Diagnosis codes for the main and accompanying diagnosis

Death Certificate Base

Dates of death
Diagnosis codes of death

[1]Tuppin P et al. Rev Epidémiol Sante Publique. 2017 ; [2]Meyer et al. Ann Intern Med. 2019; [3]Hoisnard L et al. Ann Rheum Dis. 2023.

Study Population

- **All adults identified with PsA**[1]

  ICD-10: M07 except M07.4 and M07.5
  - inpatients admitted with the ICD-10 diagnostic code for PsA
  - patients with fully reimbursed care procedures related to PsA

- **New users of a targeted therapy ("first line")**

  New users: no prescription of a targeted therapy the year before inclusion

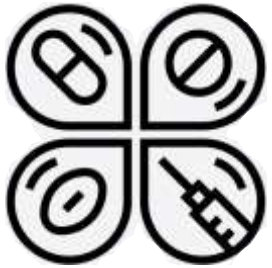
  Targeted therapies: **TNFi** (adalimumab, certolizumab, etanercept, golimumab, infliximab); **IL17i** (ixekizumab, secukinumab); **IL12/23i** (ustekinumab); **IL23i** (guselkumab, tildrakizumab, risankizumab) ; **JAKi** (tofacitinib, upadacitinib)

- **All treatment lines**

[1]Pina Vegas L, et al. Rheumatology (Oxford). 2021.

Main Outcome

Persistence of a targeted therapy



- Defined as the time between treatment initiation and discontinuation

Follow-up

- Inclusions: from January 1, 2015 to June 30, 2021
- Study end point: December 31, 2021
- Follow-up until:
  - Main outcome
  - Death
  - End of treatment exposure
  - Lost to follow-up
  - Study end point

Covariates

- **Sociodemographic:**
  Age, deprivation index (geographical indicator of social disadvantage)[1]
- **Associated inflammatory diseases:**
  Psoriasis, IBD, uveitis
- **Comorbidities:**
  Charlson index, obesity (proxy), tobacco use (proxy), alcohol use (proxy)
- **Other treatments of interest:**
  csDMARDs, NSAIDs, prednisone
- **Care consumption:**
  Hospitalizations for PsA, specialist consultations, corticosteroids injections, opioids use, work stoppages

[1]Rey G et al. BMC Public Health. 2009.

Statistical Analyses

- Changes in treatment persistence over time (for each sex and therapeutic class): Kaplan-Meier method
- Multivariate frailty models (non-independence of data)
- Adjusted for co-variates at baseline and time-dependent covariates (csDMARDs, NSAIDs, prednisone during follow-up)
- Bonferroni adjustment: $p \leq 0.01$ was considered significant, 99% CIs were estimated

Statistical Analyses

- **Subgroup analysis:**
  - Patients without active skin psoriasis
  - Patients <51 years old or ≥51 years (average age of menopause in France[1])
- **Sensitivity analysis:**
  - Modifying the date of censoring
  - Modifying the gap period to 90 days
  - Modifying the definition of new users

[1]https://www.inserm.fr/dossier/menopause/

Users of targeted therapies

Sex

Women (15,831 lines)

- **TNFi** : 9,462 (60%)
- **IL17i** : 3,762 (24%)
- **IL12/23i** : 1,639 (10%)
- **IL23i** : 392 (2%)
- **JAKi** : 576 (4%)

Men (10,488 lines)

- **TNFi** : 6,192 (59%)
- **IL17i** : 2,433 (23%)
- **IL12/23i** : 1,170 (11%)
- **IL23i** : 406 (4%)
- **JAKi** : 287 (4%)

Patients Characteristics

	Total n = 14,778	Women n = 8,475 (57%)	Men n = 6,303 (43%)
Age (mean ± SD ; years)	**50 ± 13**	**50 ± 13**	**51 ± 13**
Active psoriasis	5,357 (36%)	2,857 (34%)	2,500 (40%)
IBD	788 (5%)	533 (6%)	255 (4%)
Associated therapies at index date			
csDMARDs	6,659 (45%)	3,923 (46%)	2,736 (43%)
NSAIDs	6,170 (42%)	3,690 (43%)	2,480 (39%)
prednisone	2,991 (20%)	1,867 (22%)	1,124 (18%)
Associated therapies during follow-up			
csDMARDs	7,251 (49%)	4,358 (51%)	2,893 (46%)
NSAIDs (on at least 3 occasions)	7,411 (50%)	4,615 (54%)	2,796 (44%)
prednisone (on at least 3 occasions)	2,936 (20%)	1,910 (22%)	1,026 (16%)

Patients Characteristics

	Total	Women	Men
	n = 14,778	n = 8,475 (57%)	n = 6,303 (43%)
Age (mean ± SD ; years)	50 ± 13	50 ± 13	51 ± 13
Active psoriasis	5,357 (36%)	**2,857 (34%)**	**2,500 (40%)**
IBD	788 (5%)	533 (6%)	255 (4%)
Associated therapies at index date			
csDMARDs	6,659 (45%)	3,923 (46%)	2,736 (43%)
NSAIDs	6,170 (42%)	3,690 (43%)	2,480 (39%)
prednisone	2,991 (20%)	1,867 (22%)	1,124 (18%)
Associated therapies during follow-up			
csDMARDs	7,251 (49%)	4,358 (51%)	2,893 (46%)
NSAIDs (on at least 3 occasions)	7,411 (50%)	4,615 (54%)	2,796 (44%)
prednisone (on at least 3 occasions)	2,936 (20%)	1,910 (22%)	1,026 (16%)

Patients Characteristics

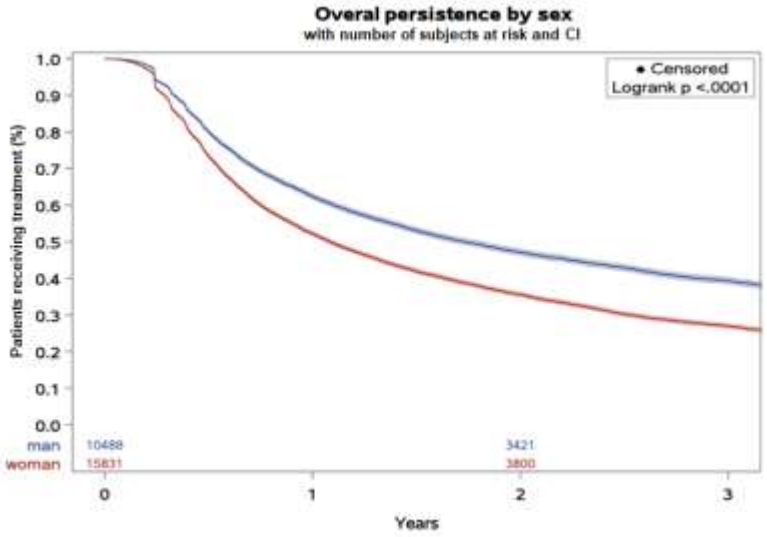
	Total	Women	Men
	n = 14,778	n = 8,475 (57%)	n = 6,303 (43%)
Age (mean ± SD ; years)	50 ± 13	50 ± 13	51 ± 13
Active psoriasis	5,357 (36%)	2,857 (34%)	2,500 (40%)
IBD	**788 (5%)**	**533 (6%)**	**255 (4%)**
Associated therapies at index date			
csDMARDs	6,659 (45%)	3,923 (46%)	2,736 (43%)
NSAIDs	6,170 (42%)	3,690 (43%)	2,480 (39%)
prednisone	2,991 (20%)	1,867 (22%)	1,124 (18%)
Associated therapies during follow-up			
csDMARDs	7,251 (49%)	4,358 (51%)	2,893 (46%)
NSAIDs (on at least 3 occasions)	7,411 (50%)	4,615 (54%)	2,796 (44%)
prednisone (on at least 3 occasions)	2,936 (20%)	1,910 (22%)	1,026 (16%)

Patients Characteristics

	Total	Women	Men
	n = 14,778	n = 8,475 (57%)	n = 6,303 (43%)
Age (mean ± SD ; years)	50 ± 13	50 ± 13	51 ± 13
Active psoriasis	5,357 (36%)	2,857 (34%)	2,500 (40%)
IBD	788 (5%)	533 (6%)	255 (4%)
Associated therapies at index date			
csDMARDs	6,659 (45%)	3,923 (46%)	2,736 (43%)
NSAIDs	6,170 (42%)	3,690 (43%)	2,480 (39%)
prednisone	2,991 (20%)	1,867 (22%)	1,124 (18%)
Associated therapies during follow-up			
csDMARDs	7,251 (49%)	4,358 (51%)	2,893 (46%)
NSAIDs (on at least 3 occasions)	7,411 (50%)	4,615 (54%)	2,796 (44%)
prednisone (on at least 3 occasions)	2,936 (20%)	1,910 (22%)	1,026 (16%)

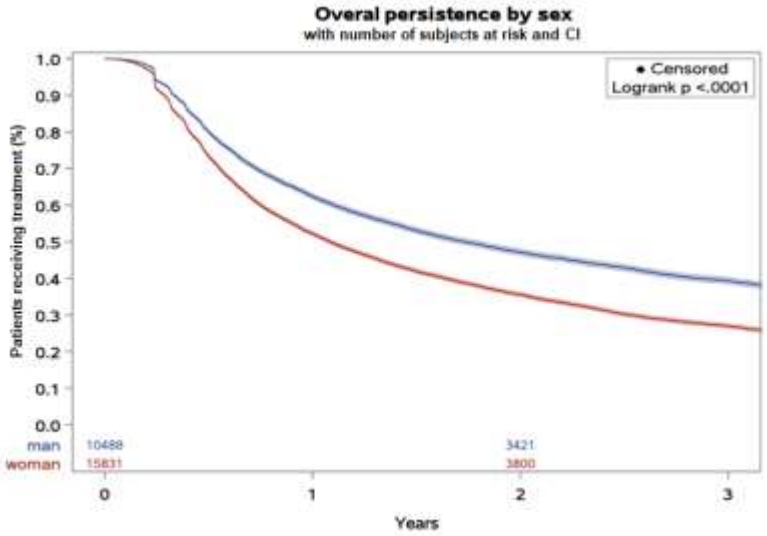
Results

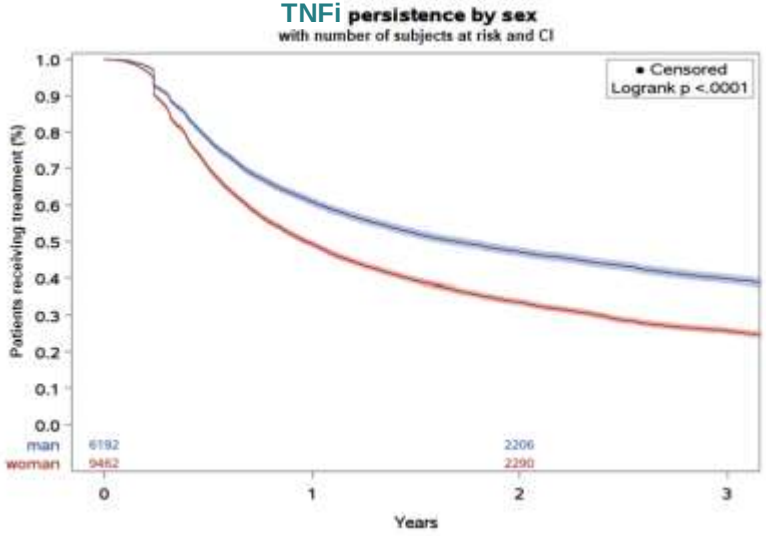
Kaplan Meier

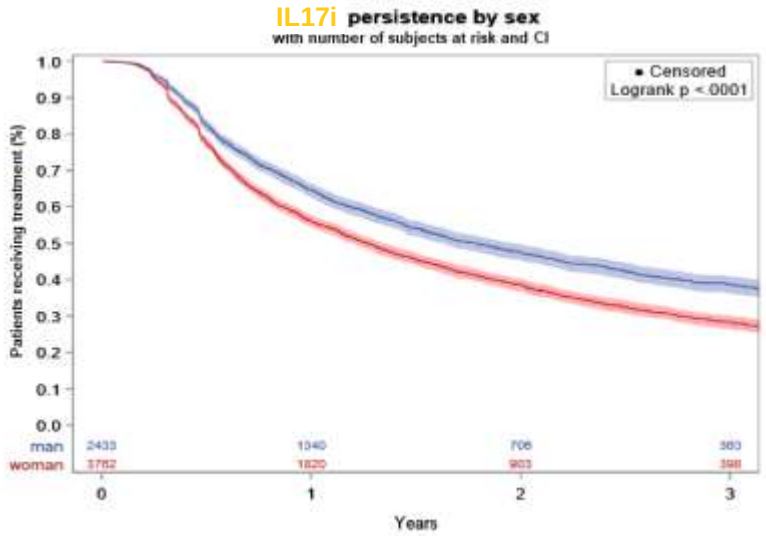


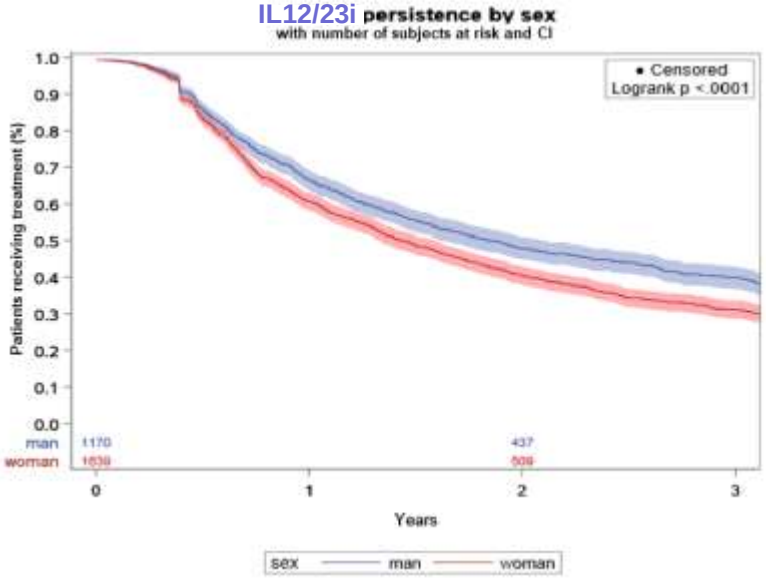
Results

Kaplan Meier









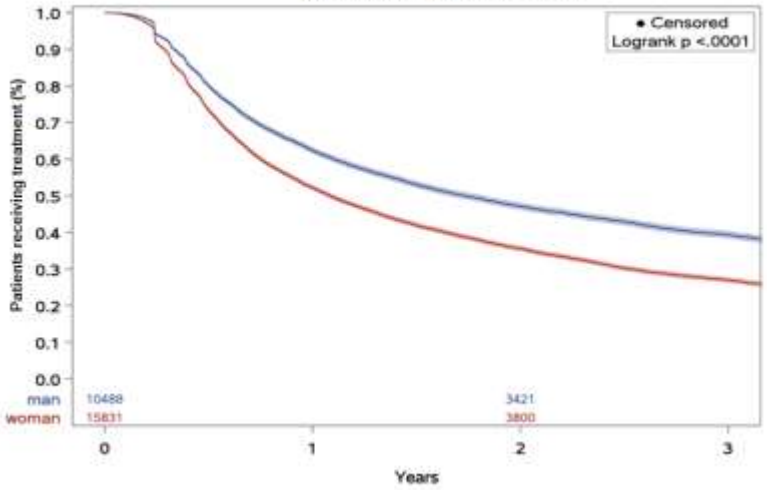
sex man woman

sex man woman

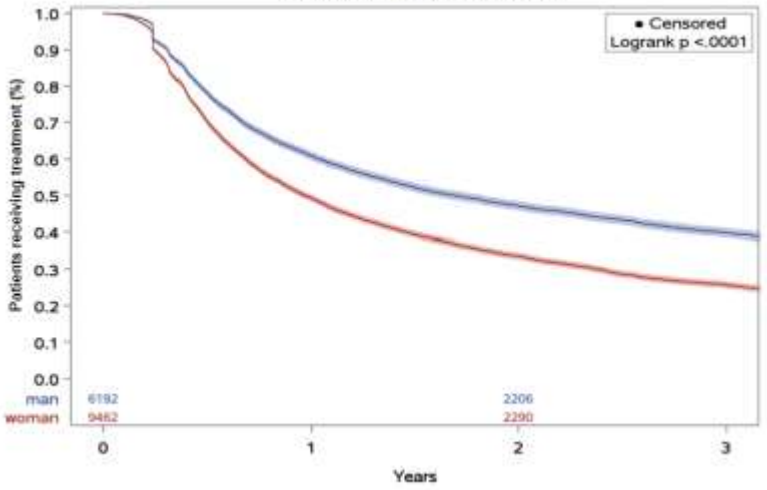
Results

Kaplan Meier

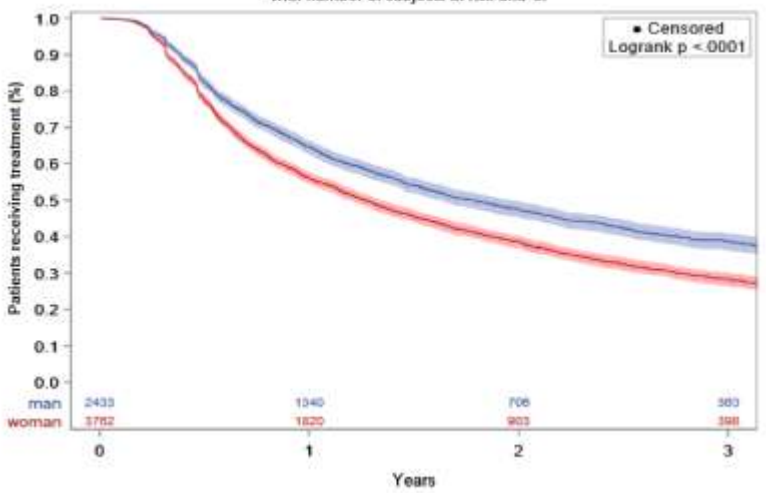
Overal persistence by sex
with number of subjects at risk and CI



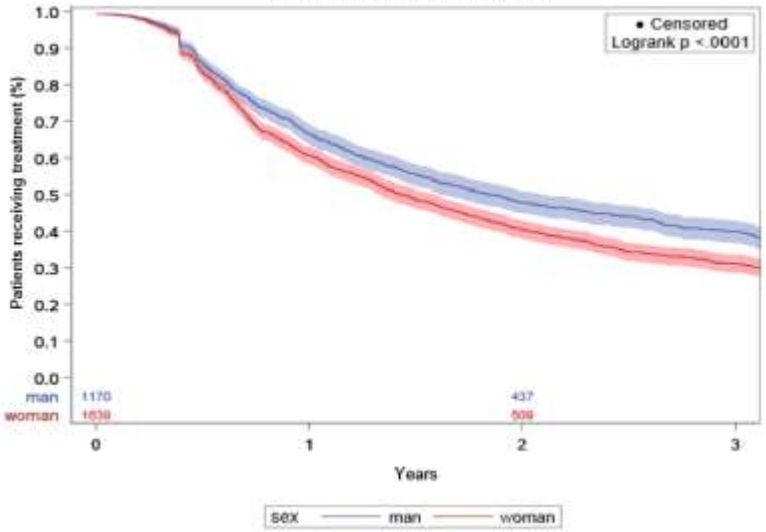
TNFi persistence by sex
with number of subjects at risk and CI



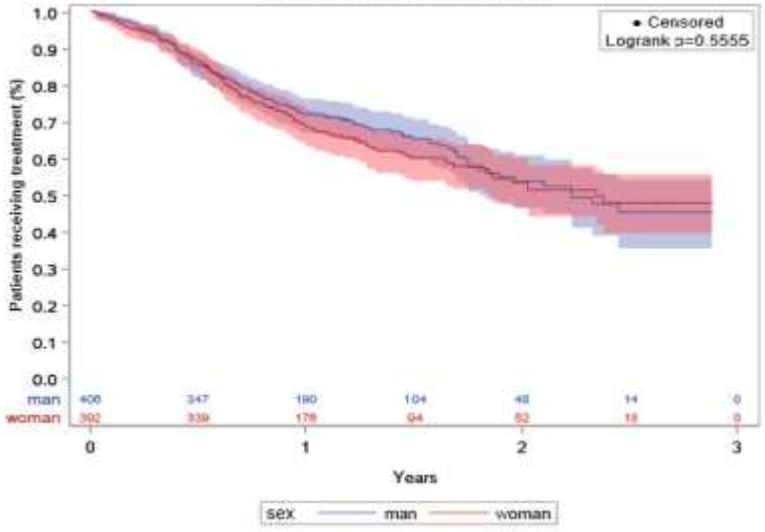
IL17i persistence by sex
with number of subjects at risk and CI



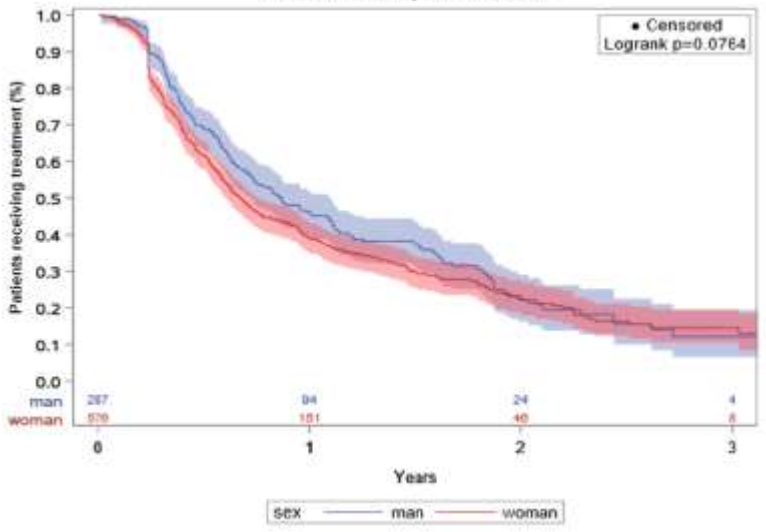
IL12/23i persistence by sex
with number of subjects at risk and CI



IL23i persistence by sex
with number of subjects at risk and CI



JAKi persistence by sex
with number of subjects at risk and CI



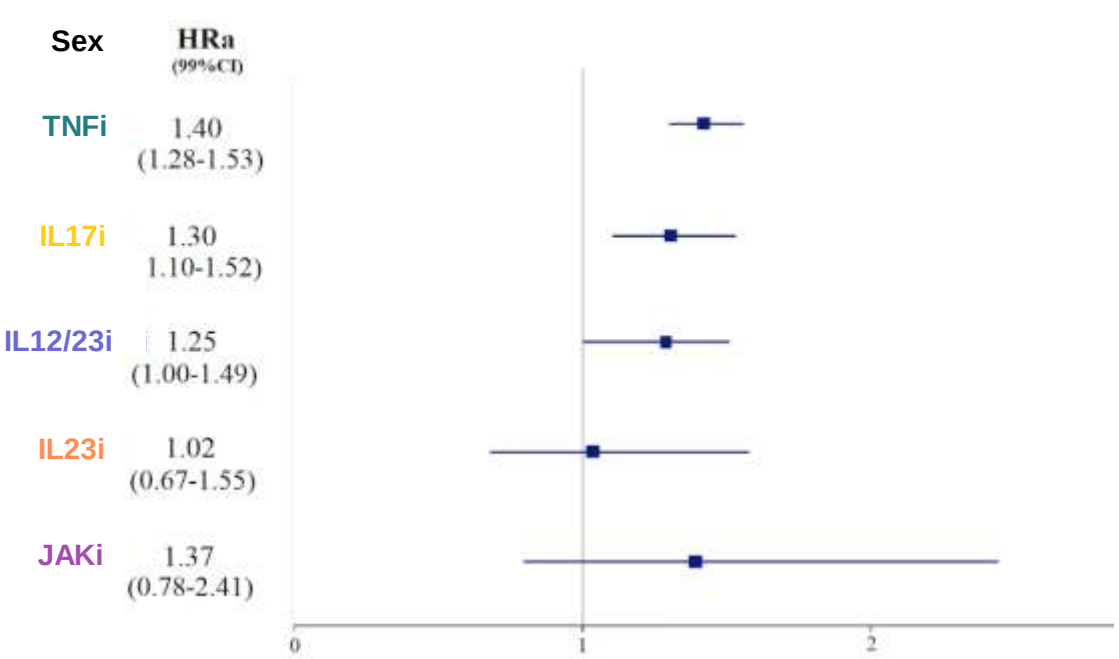
Main analysis

	Women vs Men			
	Crude		Ajusted	
	HR_c (99%CI)	*p-value*	HR_a (99%CI)	*p-value*
TNFi (n = 15,654)	1.46 (1.38-1.54)	$<10^{-4}$	**1.39 (1.32-1.47)**	$<10^{-4}$
IL17i (n = 6,195)	1.27 (1.16-1.38)	$<10^{-4}$	**1.18 (1.08-1.29)**	$<10^{-4}$
IL12/23i (n = 2,809)	1.23 (1.09-1.39)	$<10^{-4}$	1.14 (0.97-1.33)	0.03
IL23i (n = 798)	1.08 (0.79-1.47)	0.53	1.07 (0.75-1.52)	0.64
JAKi (n = 863)	1.17 (0.93-1.47)	0.07	1.21 (0.89-1.63)	0.11

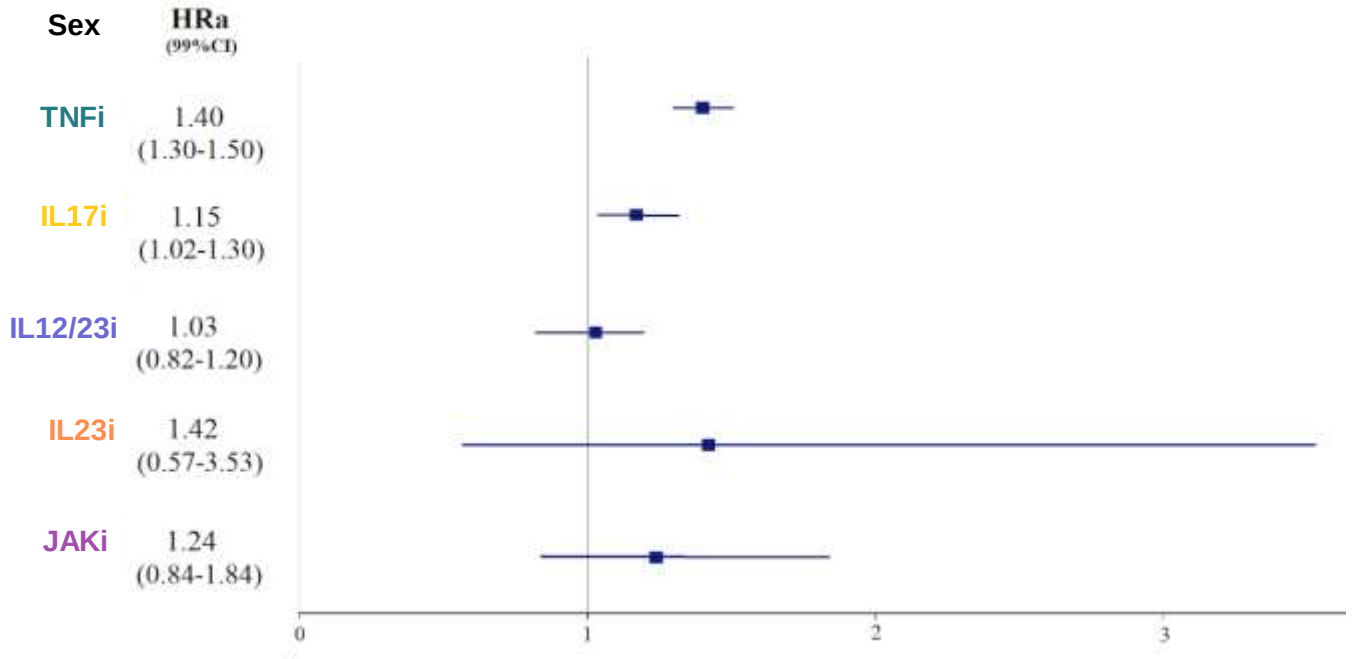
- Similar results among patients only in first line

Subgroup analysis

With psoriasis

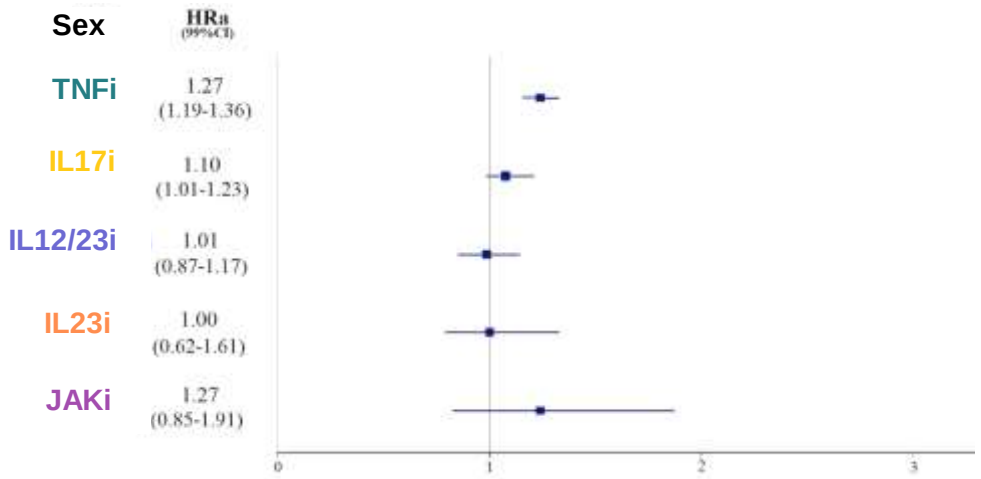


Without psoriasis

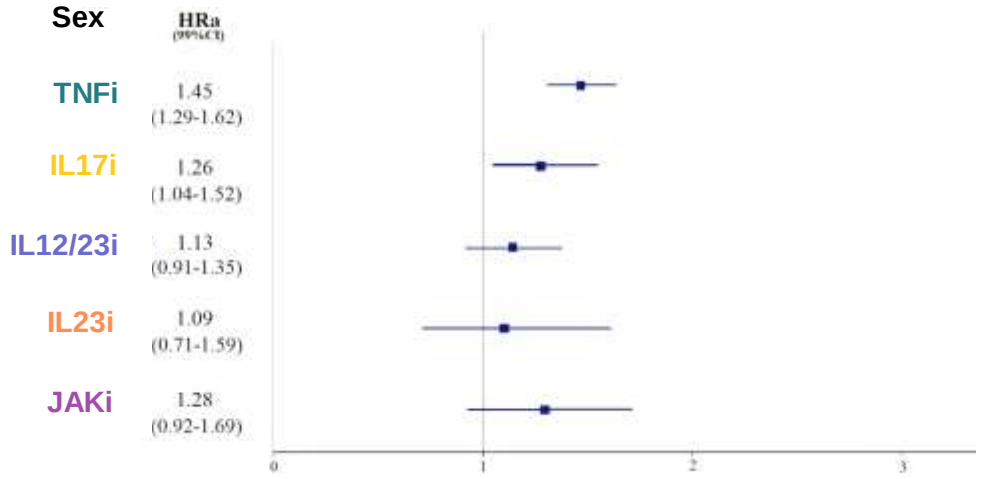


Sensitivity analysis

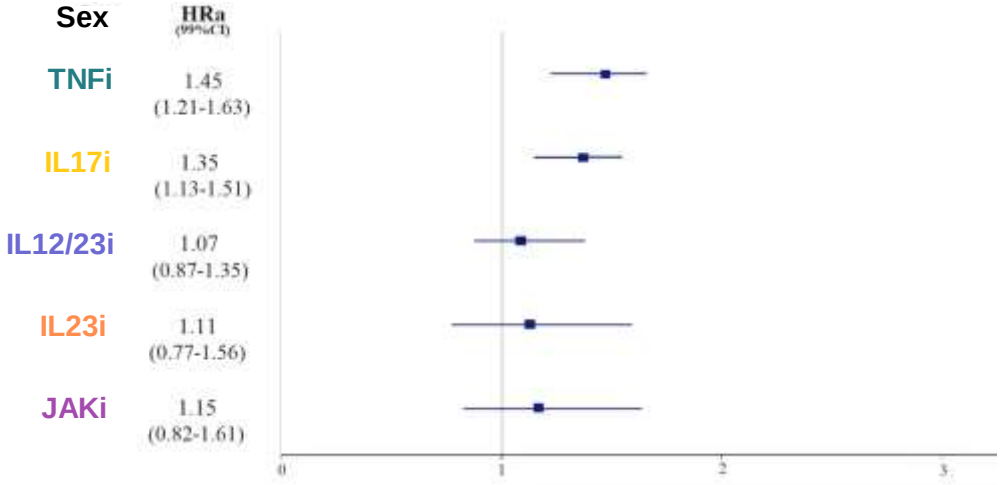
Intention to treat



Gap: 90 days



New users: 5 years



Discussion

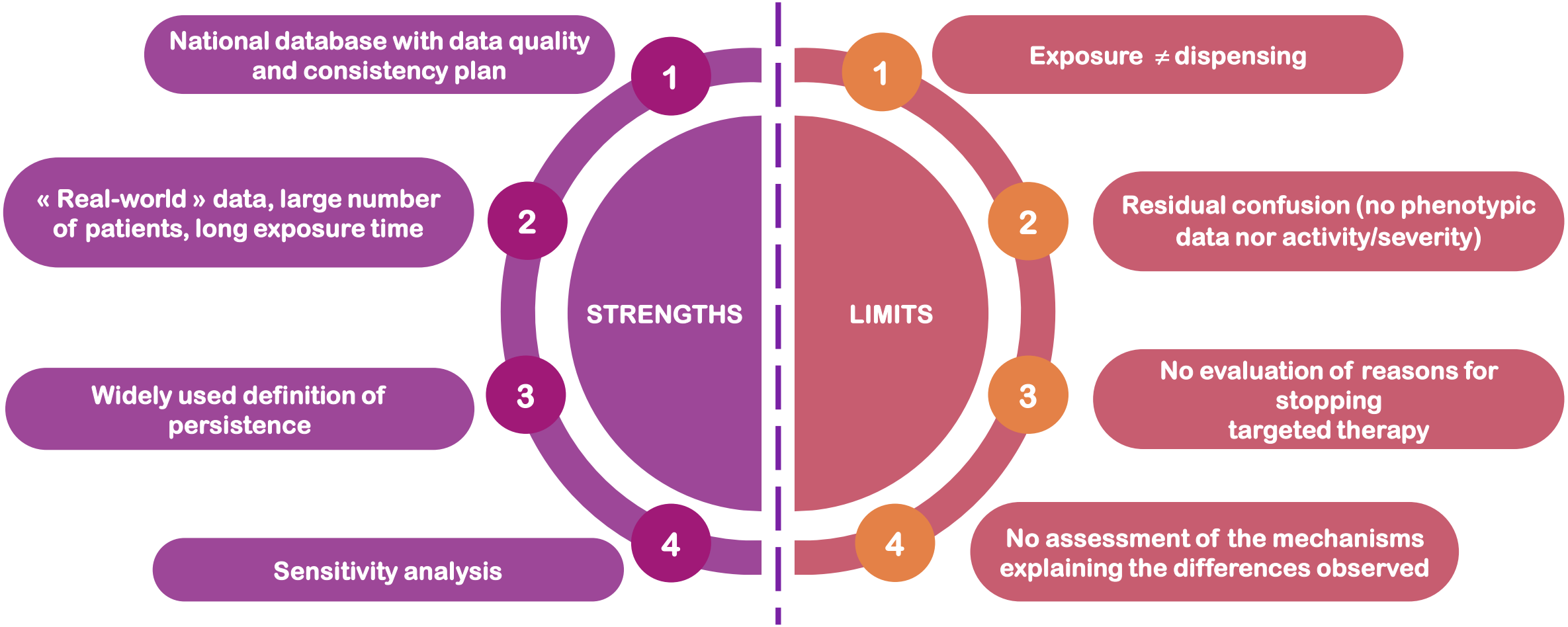
- **Confirmation of the lower persistence of TNFi in women compared to men in PsA[1,2]**

- **Few studies have specifically evaluated the impact of sex on responses to other therapies in PsA**
  - Sex difference with IL17i: result consistent with a recent observational study[3]
  - No statistically significant difference for IL12/23i[4], IL23i[5] or JAKi[6]: consistent with observational data in psoriatic patients

- **Hypotheses[7,8]: difference in phenotype, activity, severity of disease; different immune response; gender effect**

[1]Glintborg B et al. Arthritis Rheum. 2011 ; [2]Stober C et al. Rheumatology (Oxford). 2018 ; [3]Ramonda R et al. RMD Open. 2021 ;[4]Pogácsás L et al. J Dermatol Treat. 2017 ; [5]Roccuzzo G et al. Clin Exp Dermatol. 2023 ; [6]Eder L et al. RMD Open. 2023 ; [7]Eder L et al. Ann Rheum Dis. 2013 ; [8]Tarannum S et al. Nat Rev Rheumatol. 2022.

Strengths and limits

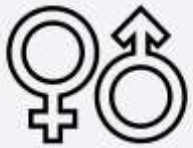


Tuppin P, et al. Rev Epidemiol Sante Publique. 2017 ; Glintborg et al. Arthritis Rheum. 2013 ; Lund J et al. Curr Epidemiol Rep. 2015.

Conclusions

Confirmation of lower persistence of TNFi in women than men with PsA

The sex difference in persistence also concerned IL17i, but is no longer significant for IL12/23i, IL23i and JAKi



Need for studies based on sex and gender

ACR Convergence
Where Rheumatology Meets
#ACR23

Influence of sex on the persistence of different classes of targeted therapies for psoriatic arthritis

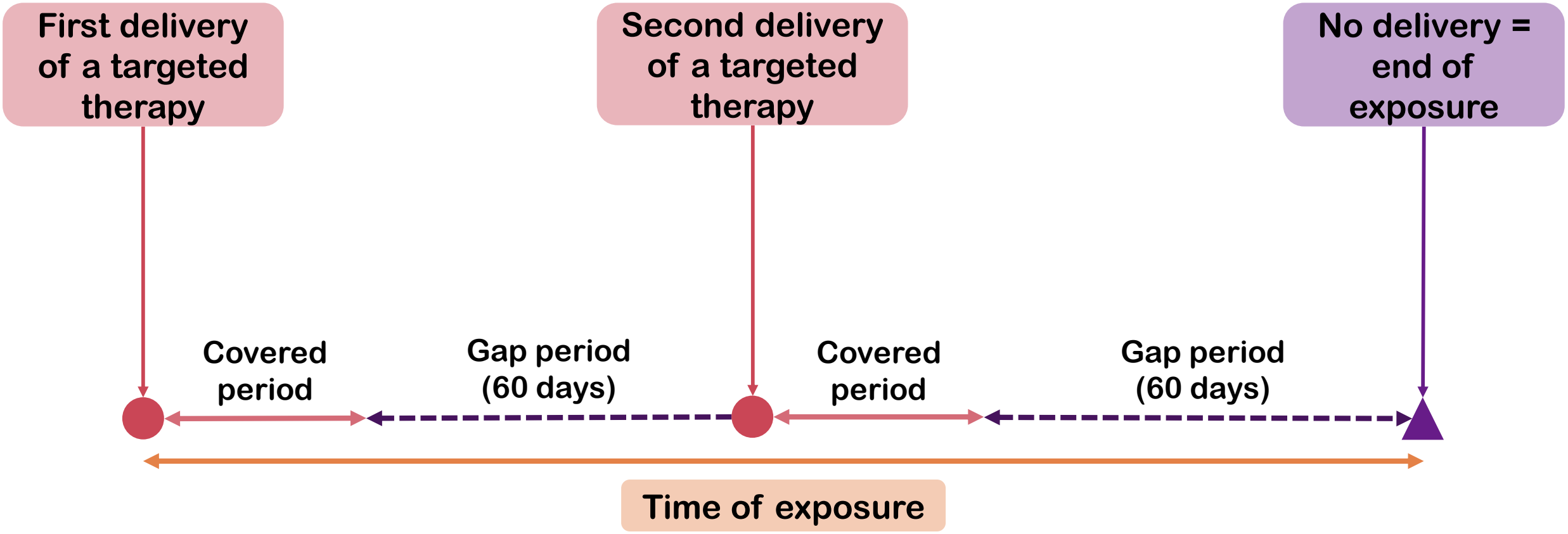
a cohort study of 14,778 patients from the French health insurance database (SNDS)

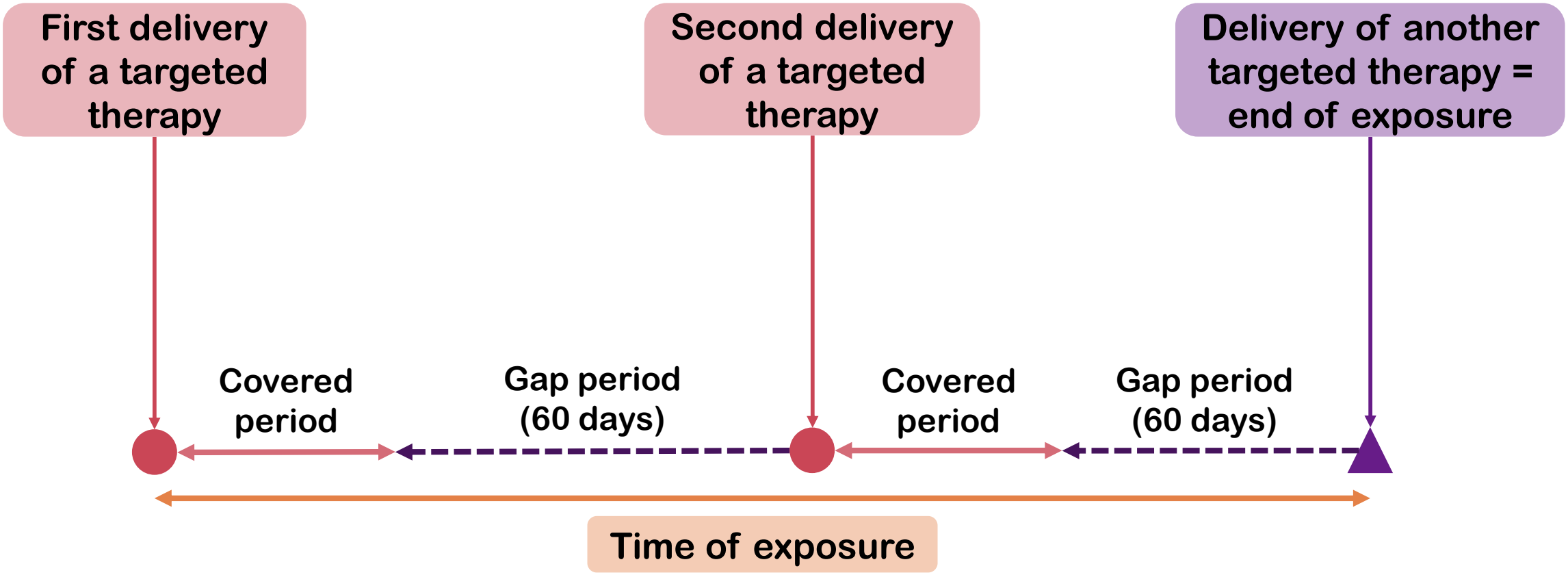
Laura Pina Vegas, Laetitia Penso, Emilie Sbidian, Pascal Claudepierre
EpiDermE, Paris-Est Créteil University
Rheumatology Department, AP-HP, Henri Mondor Hospital (Créteil, France)

Methods

Treatment Exposure

American College of Rheumatology
Empowering Rheumatology Professionals



Treatment Exposure

American College of Rheumatology
Empowering Rheumatology Professionals