

# **Tumor Necrosis Factor- $\alpha$ Inhibitor (TNFi) utilization among women with live birth pregnancies**

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# Disclosures

- Co-authors are employees of the US Food and Drug Administration and Harvard Pilgrim Health Care Institute
- No external funding to disclose

# Background

- Epidemiological data suggest chronic inflammatory conditions affect women of child-bearing age
  - Incidence of Inflammatory Bowel Disease\* is highest among 20-40 year olds
  - Rheumatoid Arthritis occurs later in life but affects women predominantly
  - Psoriatic Arthritis and Psoriasis affect men and women equally, presents primarily in 30-50 year olds
  - Ankylosing Spondylitis occurs more in men and peaks between ages 20 and 40 years old
- Tumor Necrosis Factor- $\alpha$  inhibitors (TNFis), important therapy for managing chronic inflammatory conditions (after/concurrent with corticosteroids, methotrexate)
- Data on the use and safety of TNFis during pregnancy is limited

\*Inflammatory Bowel Disease (UC: ulcerative colitis; CD: Crohn's Disease)

# Objective

To characterize TNFi use during pregnancy among women with a chronic inflammatory condition who delivered a live born infant by examining:

- What is the pattern of TNFi use among women with at least 1 chronic inflammatory condition (CID) who delivered a live born infant?
- Does the pattern of TNFi use during pregnancy differ from use among non-pregnant women of the same age with CID?

## Methods:

# Data & Pregnancy Cohort Identification

- Data: 01/01/2004 – 09/30/2015 from 16 data partners participating in Sentinel
- Pregnancy Cohort Eligibility Criteria:
  - Women 15-54 years old who delivered a liveborn infant
  - At least 480 days (approx. 16 months) of medical and drug coverage from delivery admission
  - Presence of at least 1 outpatient ICD-9 code for chronic inflammatory condition diagnosis: RA/JRA, AS, UC, CD, PsO, PsA during baseline period (183 days prior to pregnancy start)

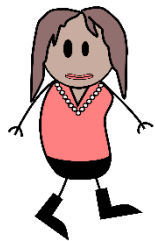
RA: rheumatoid arthritis, JRA: juvenile rheumatoid arthritis,

UC: ulcerative colitis, CD: Crohn's disease,

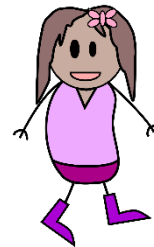
AS: ankylosing spondylitis, PsO: Psoriasis, PsA: psoriatic arthritis

# Create a Comparator Cohort of Non-pregnant women without Live-Birth

- Women with enrollment requirements relative to live-birth date were identified
  - Same Age and Duration of eligibility criteria
- Matched women without a live-birth episode on age, indication, site and calendar time period



Louisa  
Age: 22  
Condition: RA  
Live-Birth:  
4/21/2011 – 2/2/2012

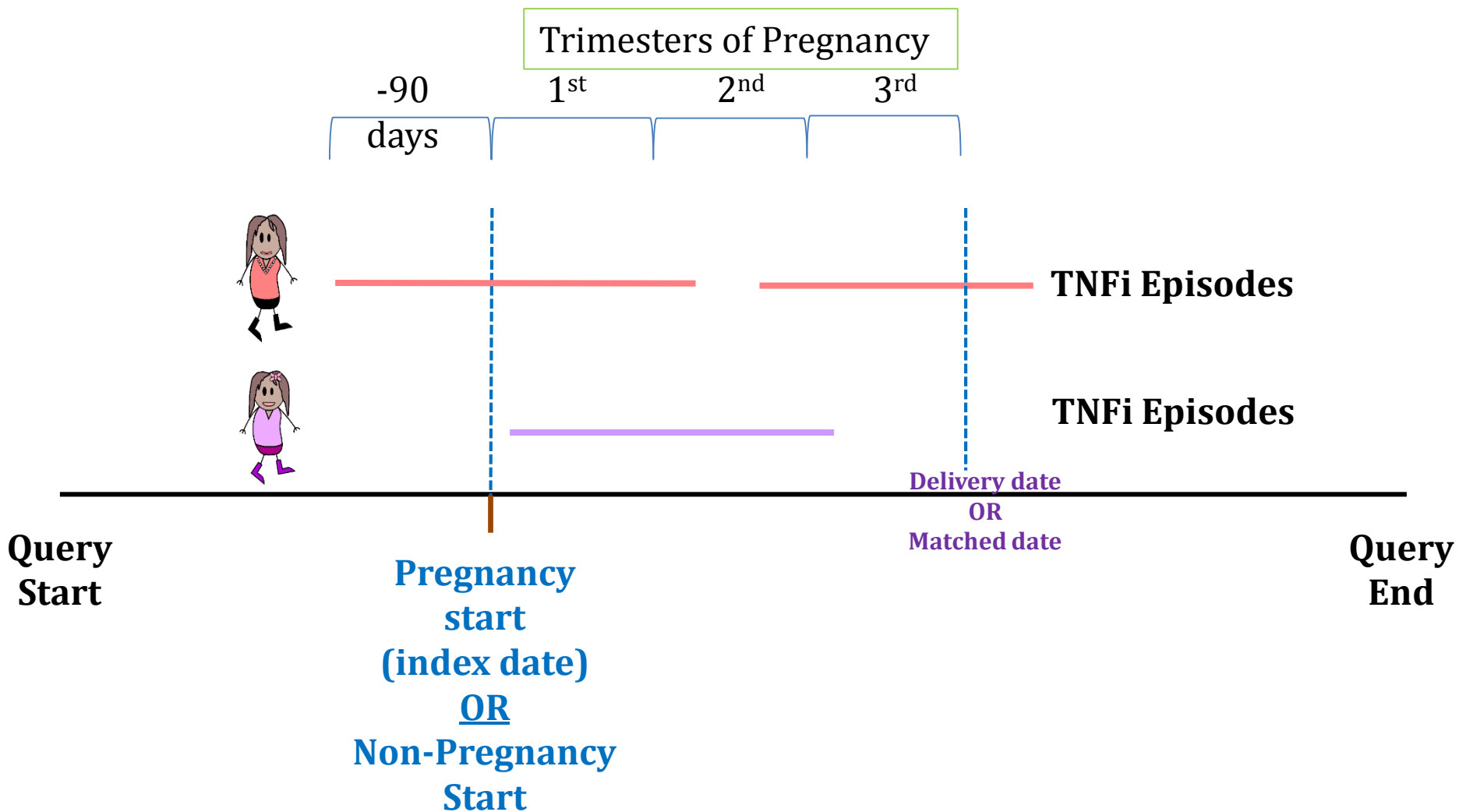


Gretl  
Age: 22  
Condition: RA  
Valid Enroll:  
4/21/2011-2/2/2012

# Exposure Episodes

- Using national drug codes (NDC) and procedure codes, identified these TNFi: etanercept, adalimumab, golimumab, certolizumab and infliximab
- Assigned the number of days on the maintenance dose for each TNFi, accounting for multiple injections per pack.
  - For example, etanercept prescribed weekly, will be assigned 14 days for a two-injection pack.

# TNFi Episodes during the study period





# Analyses

1. Prevalence of any TNFi use, stratified by inflammatory condition among pregnant and non-pregnant women
2. Prevalence of individual TNFi use, stratified by pregnancy trimester for each condition
3. Prevalence of any TNFi use, stratified by maternal age among pregnant and non-pregnant women
4. TNFi-specific annual prevalence of use from 2004 through 2015 among pregnant and non-pregnant women

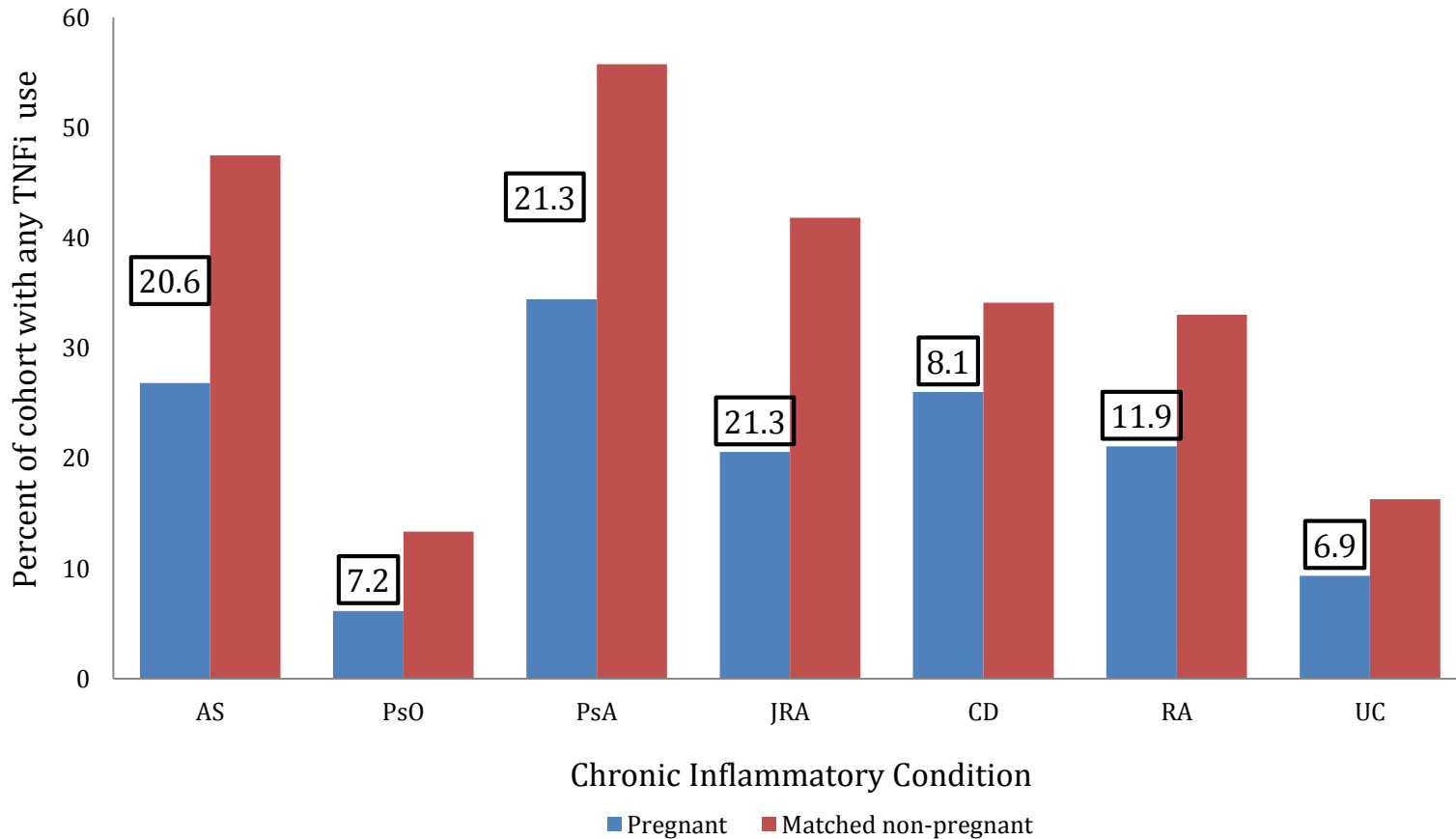
# RESULTS


# Cohort Characteristics for total cohort and women with pre-existing inflammatory condition, exposed to a TNFi during pregnancy

Characteristic		All pregnancies	RA Pregnancy	JRA Pregnancy	AS Pregnancy	PsO Pregnancy	PsA Pregnancy	CD Pregnancy	UC Pregnancy
Total unique pregnancy episode		2,220,332	4,047	418	354	6,791	633	3,748	3,690
Maternal age at delivery, years (%)	15-20	5.2	1.2	10.0	0.6	2.0	0.8	2.1	1.5
	20-24	13.0	6.5	16.7	6.2	6.8	4.9	8.9	6.0
	25-29	26.0	22.4	25.6	24.0	22.6	18.3	25.1	24.4
	30-34	33.4	37.1	33.5	35.6	38.9	37.9	39.6	39.8
	35-39	17.9	25.3	11.2	27.1	23.7	29.4	19.8	22.2
	40-44	4.1	6.2	2.9	5.4	5.5	7.9	3.8	5.6
	45-54	0.5	1.4	0.0	1.1	0.5	0.8	0.7	0.5
Any code for preterm birth (%)		7.4	10.1	9.6	9.6	6.9	11.7	9.8	10.5
Any code for post-term birth (%)		14.5	10.6	11.5	12.4	14.3	13.3	11.6	11.6

Data source: Sentinel Distributed Database  
Data years 2004-2015

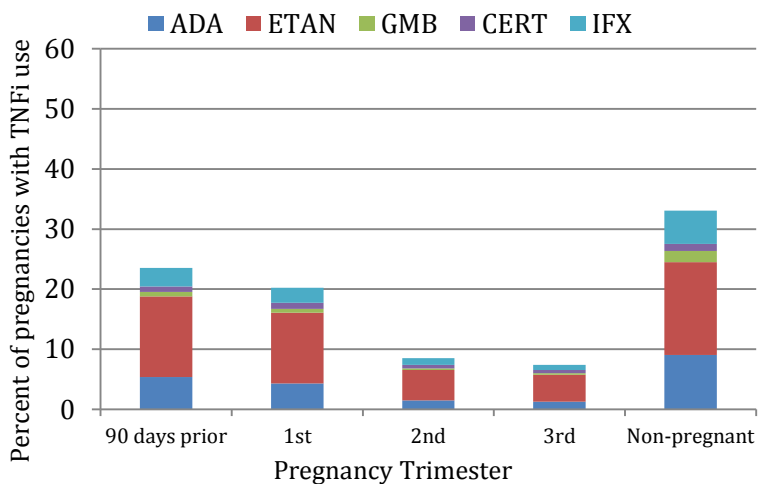
**Use of any TNF inhibitor in any pregnancy trimester for live birth pregnancies and among matched non-pregnant women (years 2004-2015 combined)**



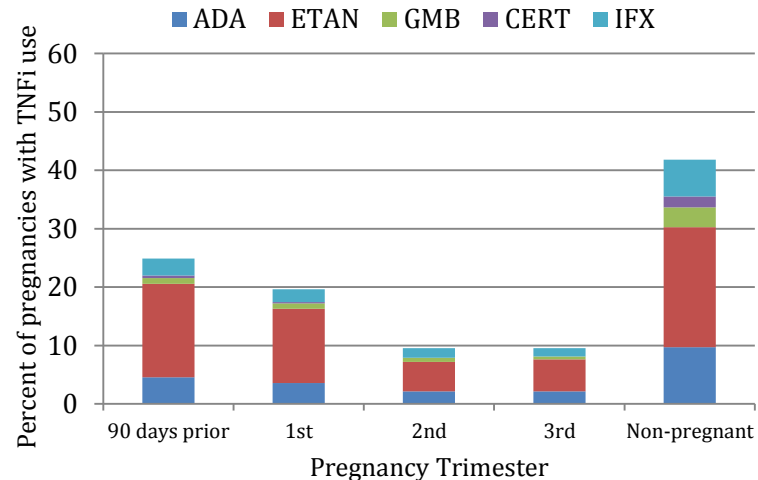
 Percent of TNFi use in non-pregnant population **minus** Percent of TNFi use in pregnant population

# TNF Inhibitor use by trimester, among women with a livebirth, stratified by indication (2004-2015)

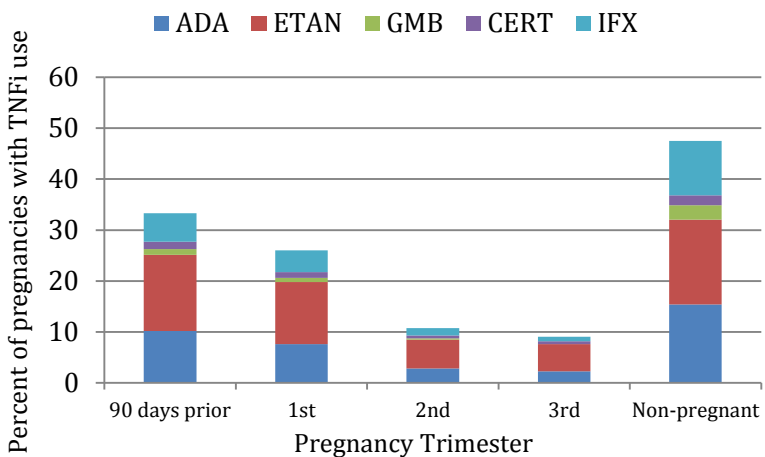
## Rheumatoid Arthritis



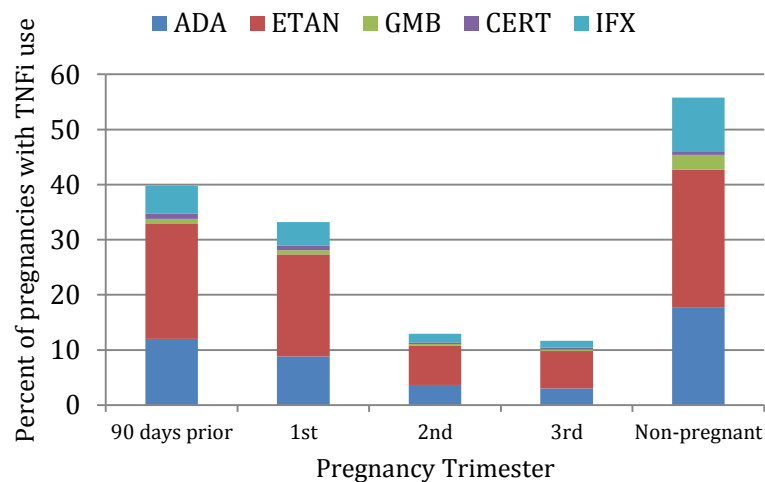
## Juvenile Rheumatoid Arthritis



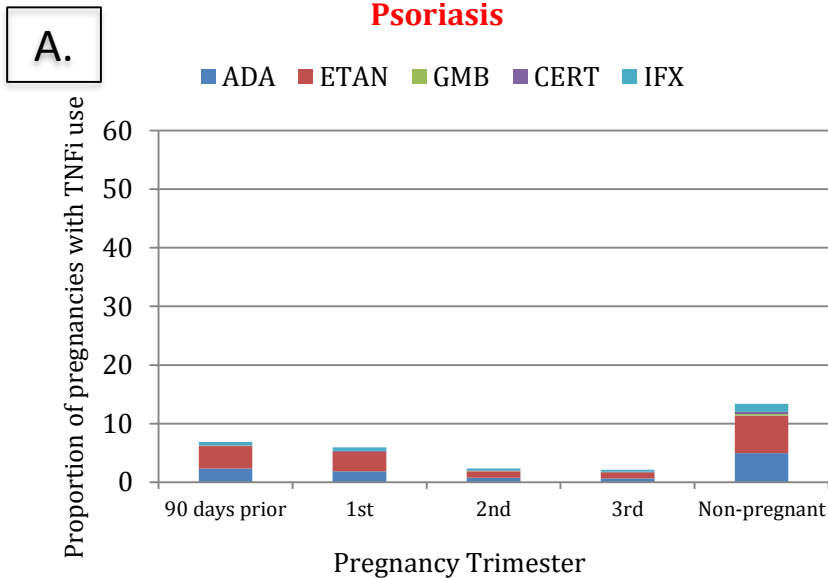
## Ankylosing Spondylitis



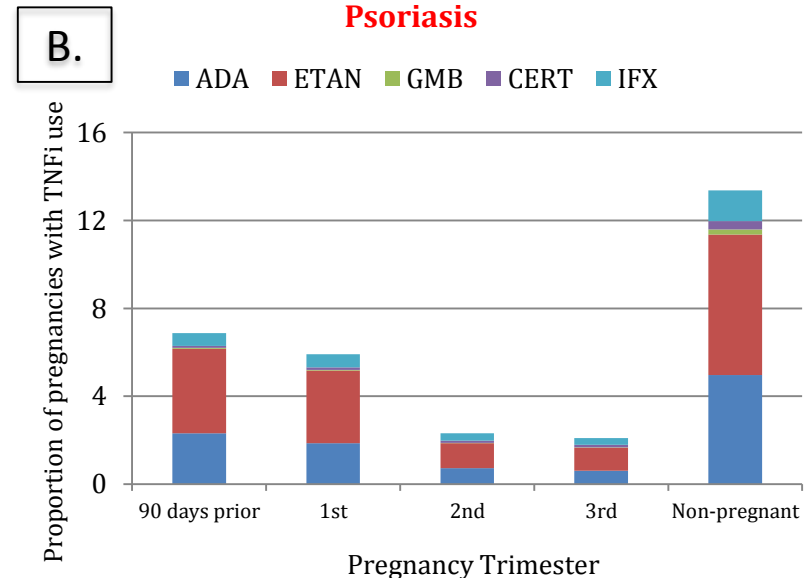
## Psoriatic Arthritis



# TNF Inhibitor use by trimester, among Psoriasis Patients with a livebirth, stratified by indication (2004-2015)



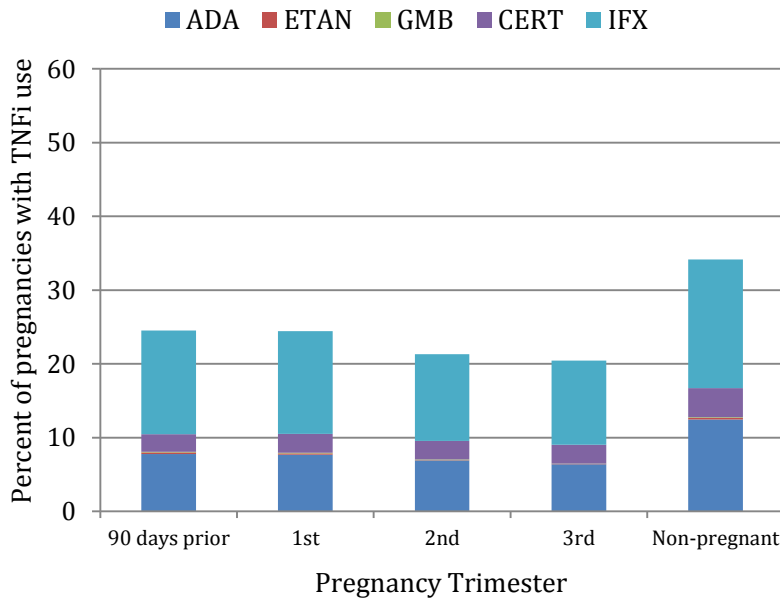
Using the same axis scale as in previous slide



Increased axis scale to examine trends

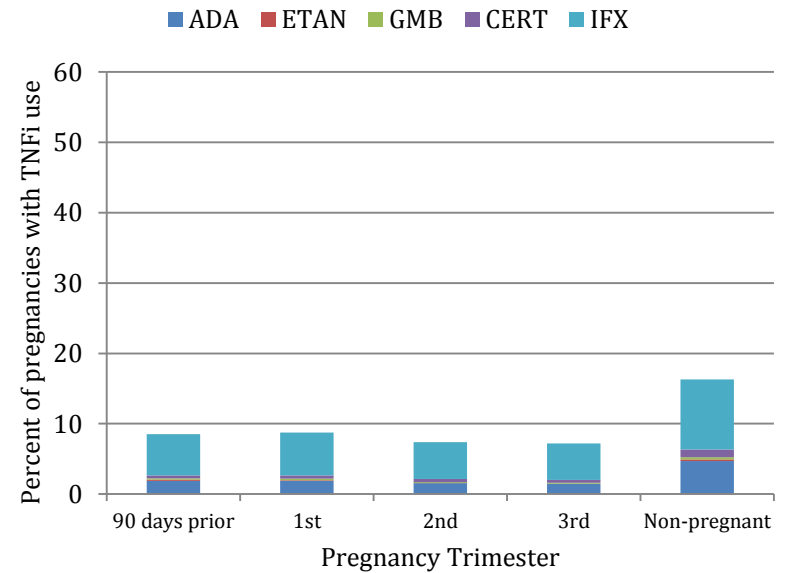
# TNF Inhibitor use by trimester, among women with a livebirth, stratified by indication (2004-2015)

## Crohn's Disease



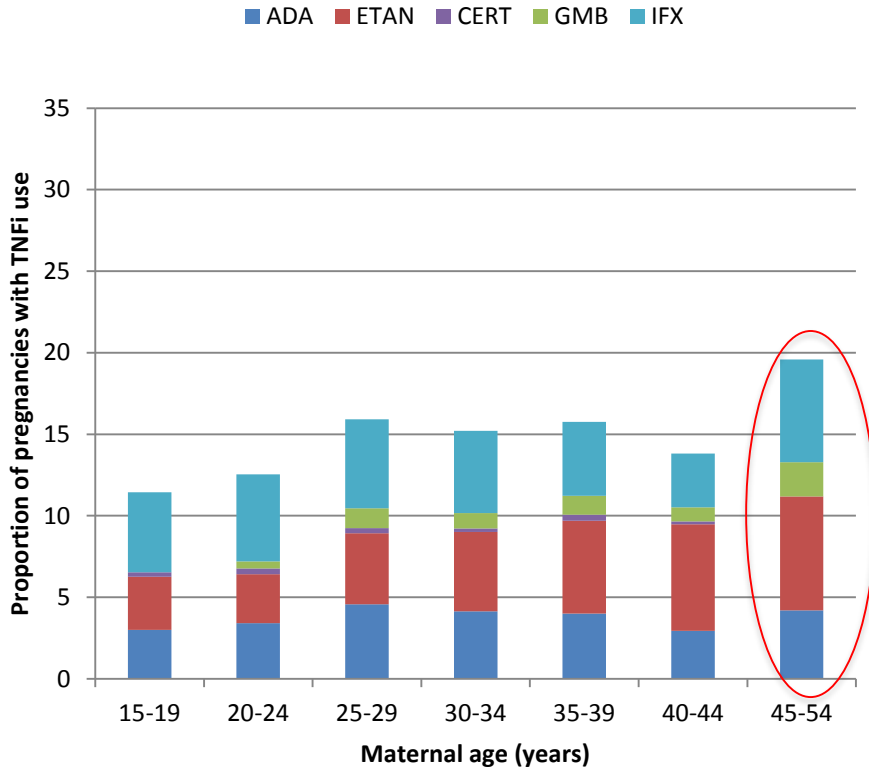
Approved TNFis: ADA, IFX, CERT

## Ulcerative Colitis

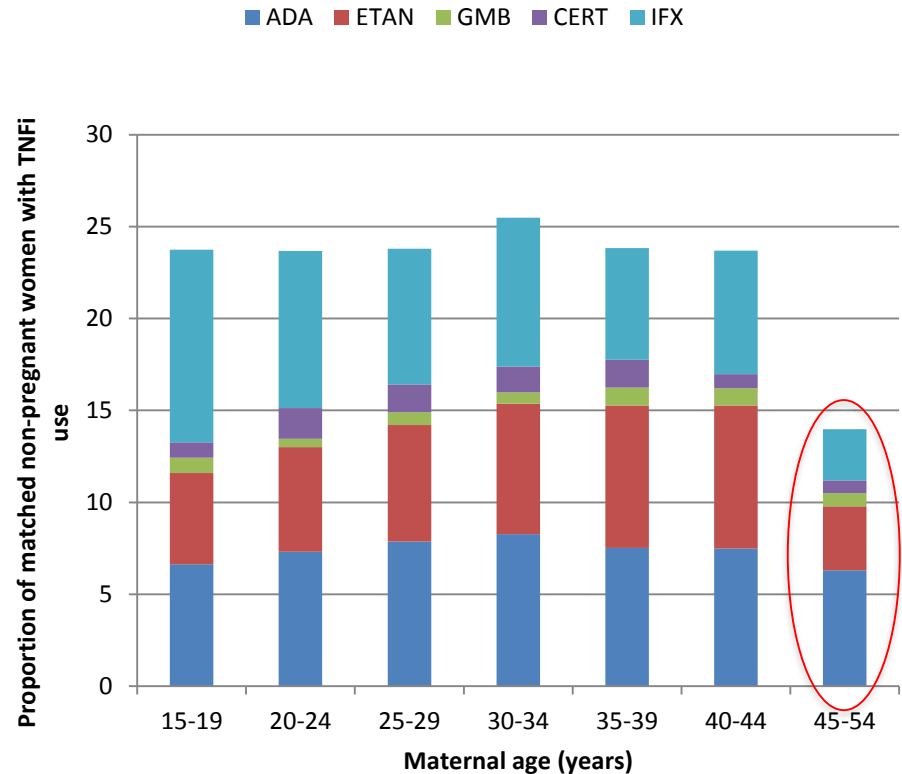


Approved TNFis: ADA, IFX, GMB

### Use of a specific TNF Inhibitor among pregnancies ending in live births with chronic inflammatory conditions, stratified by age (2004-2015)



### Use of a specific TNF Inhibitor among non-pregnant women with chronic inflammatory conditions, stratified by age (2004-2015)

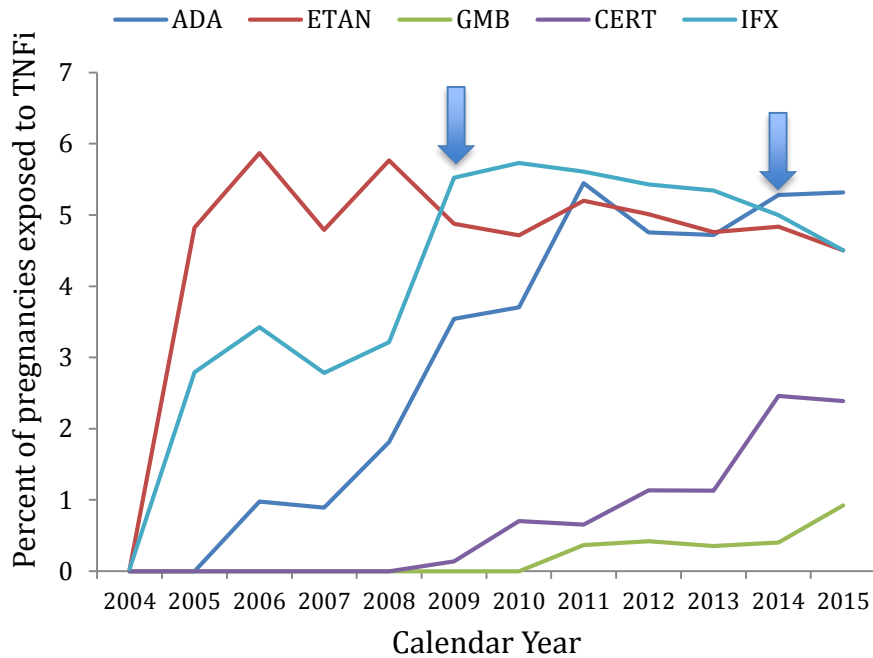


Sample size of pregnant and non-pregnant cohorts showing no differences in underlying disease distribution

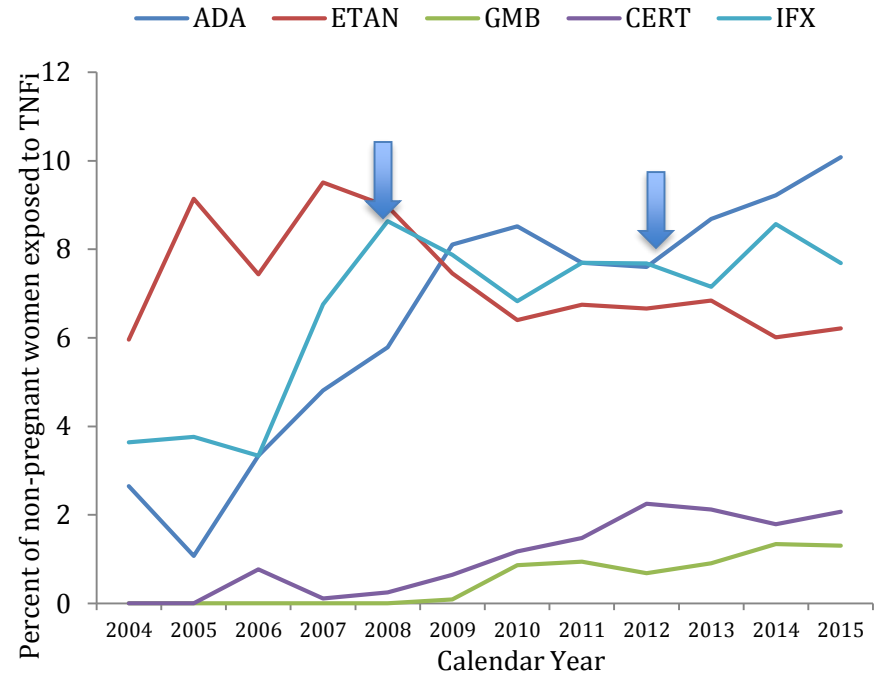
Cohort	AS	CD	PsA	RA	JRA	PsO	UC
Pregnant	367	1404	4588	7597	4526	1056	143
Not pregnant	362	1368	4514	7529	4494	1055	143



**Use of a specific TNF Inhibitor among pregnancies ending in live births with chronic inflammatory conditions (2004-2015)**



**Use of a specific TNF Inhibitor among non-pregnant women with chronic inflammatory conditions (2004-2015)**



\*Not all data partners contributed to all study years for the trend analysis

# Discussion of Key Findings

- TNFi selection and duration of use during pregnancy is specific to underlying inflammatory condition
  - Strong preference for Etanercept in RA, JRA, PsA, PsO and AS pregnancies despite availability of other approved TNFis
  - Preference for Infliximab in CD and UC pregnancies
  - Decreased use of any TNFi in 2<sup>nd</sup> and 3<sup>rd</sup> trimesters in RA, JRA, PsA, PsO and AS pregnancies not observed in IBD pregnancies
    - Patients with IBD are advised to continue medication during pregnancy
  
- Older pregnant women were more likely treated with TNFis compared to non-pregnant counterparts
  - Possibly due to differences in disease severity during pregnancy
  - Limited therapeutic options for older patients (poor control of blood glucose with corticosteroids)
  
- Annual trend analyses reflect dynamics between approvals for expanded indications and the decision to treat during pregnancy
  - Notable changes : Increase in infliximab use (2009: non-pregnant & 2014: pregnant) and Adalimumab use (2012: non-pregnant & 2014: pregnant) related to number of expanded indications between 2005 and 2006)

# Study Strengths

- Size of study cohort; large number of pregnancies suitable to assess a population with identified chronic inflammatory condition
- Age-, calendar year- and disease-matched non-pregnant cohort allows comparison to a reference population
- Use of dispensing data for exposure ascertainment minimizes recall bias

# Limitations

- Gestational age is not available in claims data, but derived from a validated algorithm
  - Possible misclassification of pregnancy duration and exposure timing relative to pregnancy timeline
  - Gestational age, estimated from ICD-9 codes from mother's claims, may have reduced sensitivity
- Comparator cohort may include women who were pregnant and had an outcome other than a liveborn delivery
- Disease severity measure not available in claims data

# Thanks to

Data Partners who provided data used in the analysis.



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TNF Inhibitor use by trimester, in the cohort women with pre-existing **Ulcerative Colitis** with a livebirth delivery during 2004-2015

