
The Corrona Registries

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Disclosures

- Consulting fees: Genentech, Novartis
- Employee Corrona
- Shares/options Corrona
- Faculty Columbia University, School of Medicine

Corrona USA rheumatologist network and RA registry

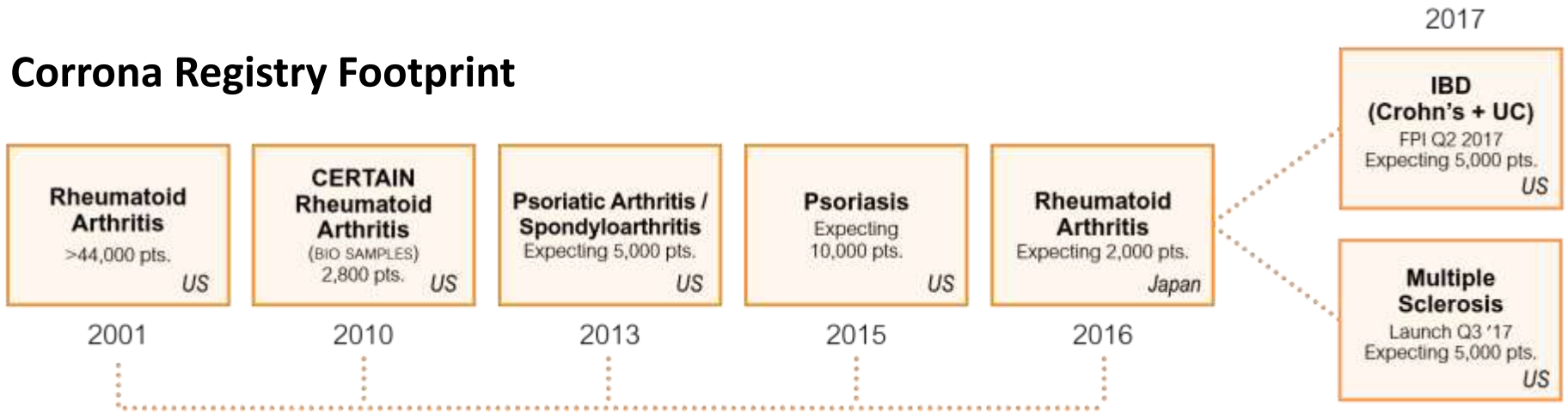
Corrona Network of Rheumatology Sites

- Network of 80 rheumatology sites
 - 12 academic/university sites
 - 68 private practice sites
 - 40 states
- Founded by Joel Kremer, MD
- Since 2001,
 - >45,000 RA patients
 - >150,000 person years



Corrona's expansion

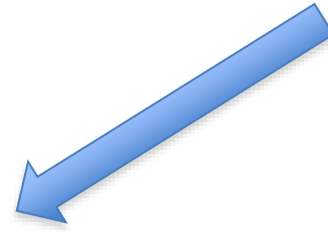
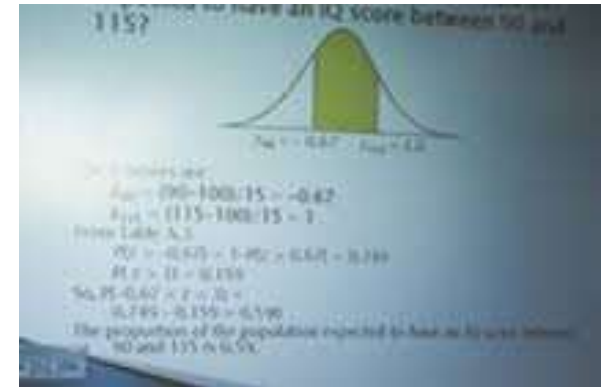
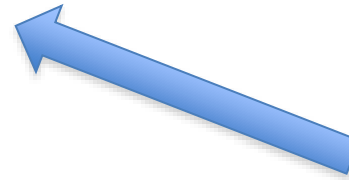
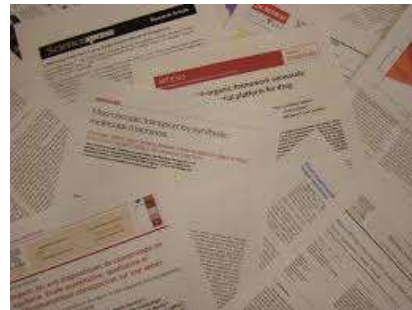
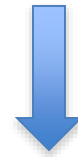
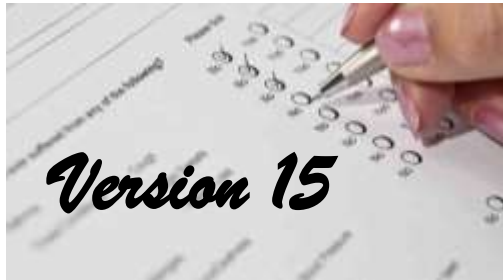
Corrona Registry Footprint



The goals of a registry

- 1. Flexible**, prospectively designed data collection tools, avoiding data gaps
- 2. Comprehensive**, by collecting information directly from physicians and patients
- 3. Credible** with the scientific community – over 100 full length manuscripts and over 300 abstracts using Corrona data in top tier journals

Data: Digitized, Datafied ...and... Clean?



2. Complete the following **at today's visit**:

28-Joint Counts:

Tender Swollen

Blood Pressure: /
(mm Hg)

Weight: lb

ACR Functional Class: I. II. III. IV.

Subcutaneous nodules: Yes No New

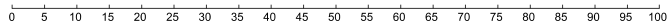
Clinical joint deformity: Yes No New
(hands, wrists, feet)

Secondary Sjogren's: Yes No New

3 PHYSICIAN GLOBAL ASSESSMENT OF CURRENT DISEASE ACTIVITY:

NOT ACTIVE

VERY ACTIVE



Disease Activity: Improved Unchanged Worsened

Today's disease prognosis: Good Poor Not assessed

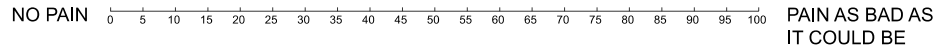
6. ADVERSE EVENTS, COMORBIDITIES, DRUG TOXICITIES (NEW since last visit) (check all that apply):
If any of the following have occurred since last visit, check the box and write the 3 letter month and 2 digit year of onset.

<input type="checkbox"/> Hypertension (HTN)	<input type="text"/> <input type="text"/>	<input type="checkbox"/> Lymphoma ^{1b}	<input type="text"/> <input type="text"/>
<input type="checkbox"/> HTN requiring hospitalization ^{1b}	<input type="text"/> <input type="text"/>	<input type="checkbox"/> Lung cancer ^{1b}	<input type="text"/> <input type="text"/>
<input type="checkbox"/> Hyperlipidemia	<input type="text"/> <input type="text"/>	<input type="checkbox"/> Breast cancer ^{1b}	<input type="text"/> <input type="text"/>
<input type="checkbox"/> Cardiac revascularization procedure ^{1b} (CABG, stent, angioplasty)	<input type="text"/> <input type="text"/>	<input type="checkbox"/> Skin cancer ^{1b} (melanoma)	<input type="text"/> <input type="text"/>
<input type="checkbox"/> Ventricular arrhythmia ^{1b}	<input type="text"/> <input type="text"/>	<input type="checkbox"/> Skin cancer ^{1b} (basal / squamous)	<input type="text"/> <input type="text"/>
<input type="checkbox"/> Cardiac arrest ^{1b}	<input type="text"/> <input type="text"/>	<input type="checkbox"/> Other cancer (specify below): ^{1b}	<input type="text"/> <input type="text"/>
<input type="checkbox"/> Myocardial infarction ^{1b}	<input type="text"/> <input type="text"/>		

	Start Date ^a		Current user ^b		Past but not current user ^b		Changes planned today			Reason ^c Code(s) ^d Since last visit
	MM	YY	Dose	Frequency	Most recent dose	Most recent date	Start Drug	Change Drug	Dose	
<input type="checkbox"/> Investigational Agent	<input type="text"/>	<input type="text"/>	N/A	N/A	N/A	<input type="text"/>	<input type="text"/>	<input type="radio"/>	<input type="radio"/>	N/A
<input type="checkbox"/> abatacept (Orencia)	<input type="text"/>	<input type="text"/>	○ 500 mg/IV ○ 1000 mg/IV	○ q ○ 125 mg/sq	○ q ○ 125 mg/sq	○ 500 mg/IV ○ 1000 mg/IV	<input type="text"/>	<input type="radio"/>	<input type="radio"/>	

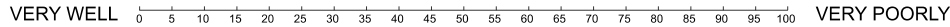
5. Pain:

How much pain have you had because of your arthritis IN THE PAST WEEK?
Put a single line (|) on the scale to show how severe your pain has been.



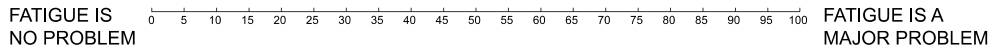
6. Disease Activity:

Considering all the ways arthritis affects you, put a single line (|) on the scale to show how well you are doing.



7. Fatigue:

How much of a problem has unusual fatigue or tiredness been for you IN THE PAST WEEK? Put a single line (|) on the scale to show how well you are doing.



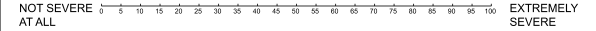
2.

A. When you get up in the morning do you feel stiff? Yes No, (if NO, Go to letter D)

B. If you have morning stiffness, how long does it take until you are as limber as you will be for the day?

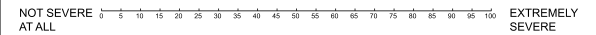
Enter the number of hours and/or minutes: hours: minutes:

C. If you have morning stiffness, please indicate the severity of the morning stiffness, by marking a single vertical line (|) across the severity scale.



D. When you get up in the morning do you have pain? Yes No, (if NO, go to #3)

E. If you have morning pain, please assess the intensity of your pain when you woke up over the last week, by marking a line (|) on the scale:



3. Have you been to the emergency room or had an emergent visit to your health care provider since you last filled out this questionnaire? Yes No

4. Health Assessment Questionnaire

Please check the response which best describes your usual abilities OVER THE PAST WEEK:

Are you able to:	Without ANY Difficulty	With SOME Difficulty	With MUCH Difficulty	UNABLE To Do
Dressing & Grooming				
Dress yourself, including tying shoelaces and doing buttons?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Shampoo your hair?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Arising				
Stand up from a straight chair?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Get in and out of bed?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

1. **LABORATORY RESULTS** (Most recent lab including results from today's visit *if new*):

i. Date of results
(DD/MMM/YYYY)

--	--	--	--	--	--

WBC	<input type="text"/>	thou/uL	Total	<input type="text"/>	mg/dL
Neutrophils	<input type="text"/>	%	Bilirubin	<input type="text"/>	mg/dL
Hematocrit	<input type="text"/>	%	Albumin	<input type="text"/>	g/dL
Hgb	<input type="text"/>	g/dL	Creatinine	<input type="text"/>	mg/dL
Platelets	<input type="text"/>	thou/uL	ESR	<input type="text"/>	mm/hr
AST (SGOT)	<input type="text"/>	IU/L	CRP	<input type="text"/>	<input type="radio"/> mg/L <input type="radio"/> mg/dL
ALT (SGPT)	<input type="text"/>	IU/L	CRP (Upper Limit Normal)	<input type="text"/>	
			CPK	<input type="text"/>	IU/L

ii. Date of results
(DD/MMM/YYYY)

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CCP Abs	<input type="text"/>	U/ml	CCP Abs	<input type="text"/>	U/ml
			(Upper Limit Normal)		

iii. Date of results
(DD/MMM/YYYY)

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Total	<input type="text"/>	Cholesterol	<input type="text"/>
HDL	<input type="text"/>	LDL	<input type="text"/>
Triglycerides	<input type="text"/>		
<input type="radio"/> Fasting	<input type="radio"/> Non-fasting		
On lipid lowering medication at the time of testing. <input type="radio"/> Yes <input type="radio"/> No			

iv. Date of results
(DD/MMM/YYYY)

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25-OH	<input type="text"/>	ng/mL
Vitamin D	<input type="text"/>	

v. Date of results
(DD/MMM/YYYY)

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Vectra™ DA	<input type="text"/>
Score	<input type="text"/>

7. **BONE DENSITOMETRY**(most recent): Date of most recent bone density value:

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Lumbar spine T-score: or Not Available
BMD (g/cm²):

Femoral neck T-score: or Not Available
BMD (g/cm²):

1/3 Radius: or Not Available
BMD (g/cm²):

Type of machine:
 Hologic Lunar Norland

Bone density test not ordered.

2. **JOINT RADIOGRAPHS** (each finding requires a response): Date of most recent radiograph:

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	Not Present	Present	New*
Erosions:	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Joint space narrowing:	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Deformity:	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Radiographs not ordered.
*If prior imaging available for comparison

4. **JOINT MRI**

	Not Present	Present	New*
Synovitis:	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Erosions:	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Osteitis:	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Bone Marrow Edema:	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Date of most recent MRI:

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MRI Field Strength:
 high field (≥1.0T) low field (<1.0T)

MRI test not ordered.
*If prior imaging available for comparison

5. **ULTRASOUND**

	Not Present	Present	New*
Synovitis:	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Erosions:	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Doppler signal:	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Date of most recent Ultrasound:

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Ultrasound not performed.
*If prior imaging available for comparison

8. What was the primary site/organ system of the cancer? (i.e. breast, lung, prostate)

9. Was a tissue diagnosis made? Yes No
What was the cancer type/histology? (i.e. adenocarcinoma, small cell, etc.)

 Unknown

10. Was this the first cancer/malignancy in this patient? Yes No
If there was a prior cancer(s), what was (were) the organ system(s) previously involved?
1 2 3
 Unknown
Was this a recurrence of a specific malignancy (same site/organ system) in this patient? Yes No

11. Was there spread to distant sites (organs other than lymph nodes) at the time of diagnosis?
 Yes No Unknown

12. What is the outcome/status of event?
 Patient Deceased* Patient Recovered Patient lost to follow-up/Unknown* Ongoing event
If ongoing event is the patient: Improving Stable Deteriorating
If patient recovered, was this a full recovery to previous health status? Yes No
***If deceased, or lost to follow-up, please complete a CORRONA Final Exit**

13. Did the investigator attribute the current event to a specific **biologic, small molecule, or non-biologic DMARD**? Yes No
If yes, name of drug dose at the time frequency
of the event
When was the medication started?

D	D	M	M	M	Y	Y	

Did this event result in any of the following changes to the responsible medication? (Check all that apply.)
 Temporary interruption of treatment Permanent discontinuation of treatment
 Modification of dose
Date of discontinuation

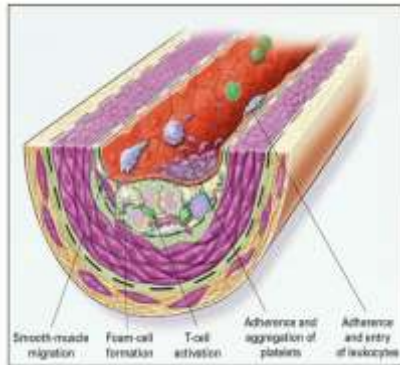
D	D	M	M	M	Y	Y	

Date of modification

D	D	M	M	M	Y	Y	

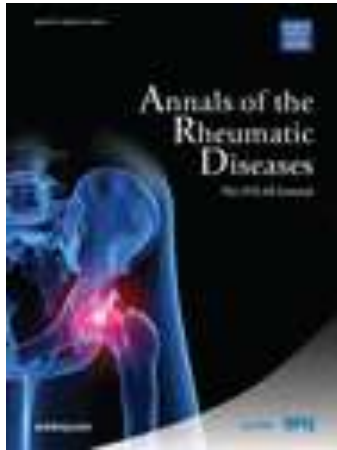
Did the investigator attribute the event to a specific drug **other than a biologic, small molecule, or non-biologic DMARD**?
 Yes No (Include medications not used for the treatment of arthritis)
If yes, what was the drug name(s)?
(List in order of importance)

Clinical insights on CVD risk factors, drug effects and risk prediction models



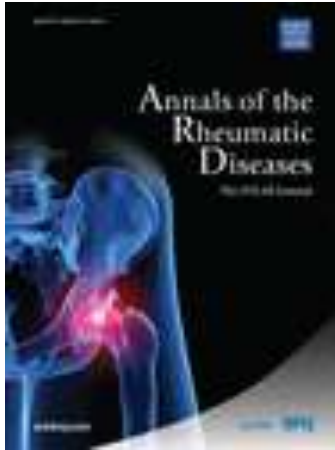
- Solomon DH et al. **Explaining the cardiovascular risk associated with rheumatoid arthritis: traditional risk factors versus markers of rheumatoid arthritis severity.** *Ann Rheum Dis.* 2010;69(11):1920-5.
- Greenberg JD et al. **Tumour necrosis factor antagonist use and associated risk reduction of cardiovascular events among patients with rheumatoid arthritis.** *Ann Rheum Dis.* 2011;70(4):576-82.
- Solomon DH et al. **Disease activity in rheumatoid arthritis and the risk of cardiovascular events.** *Arthritis Rheumatol.* 2015 ;67(6):1449-55.
- Solomon et al. **Derivation and Internal Validation of an Expanded Cardiovascular Risk Prediction Score for Rheumatoid Arthritis: A Consortium of Rheumatology Researchers of North America Registry Study.** *Arthritis Rheumatol.* 2015;67(8):1995-2003.

Examples of Comparative Drug Safety Publications



- Greenberg JD et al. **Association of methotrexate and tumour necrosis factor antagonists with risk of infectious outcomes including opportunistic infections in the CORRONA registry.** *Ann Rheum Dis.* 2010;69(2):380-6
- Greenberg JD et al. **Tumour necrosis factor antagonist use and associated risk reduction of cardiovascular events among patients with rheumatoid arthritis.** *Ann Rheum Dis.* 2011;70(4):576-82
- Pappas DA et al. **Herpes zoster reactivation in patients with rheumatoid arthritis: Analysis of disease characteristics and disease modifying anti-rheumatic drugs.** *Arthritis Care Res (Hoboken).* 2015 May 27. . [Epub ahead of print]
- Solomon DH et al. **Comparative cancer risk associated with methotrexate, other non-biologic and biologic disease-modifying anti-rheumatic drugs.** *Semin Arthritis Rheum.* 2014 Feb;43(4):489-97
- Harrold LR et al. **Risk of infection associated with subsequent biologic use after rituximab: Results from a national rheumatoid arthritis patient registry.** *Arthritis Care Res (Hoboken).* 2016 Apr 25. [Epub ahead of print]

Examples of Comparative Effectiveness Research Publications



- Dewitt EM et al. **Comparative effectiveness of nonbiologic versus biologic disease-modifying antirheumatic drugs for rheumatoid arthritis.** J Rheumatol. 2013 Feb;40(2):127-36.
- Greenberg JD et al. **A comparative effectiveness study of adalimumab, etanercept and infliximab in biologically naive and switched rheumatoid arthritis patients: results from the US CORRONA registry.** Ann Rheum Dis. 2012 Jul;71(7):1134-42
- Harrold LR et al. **The comparative effectiveness of abatacept versus anti-tumor necrosis factor switching for rheumatoid arthritis patients previously treated with an anti-tumor necrosis factor.** Ann Rheum Dis 2015 Feb;74(2):430-6
- Harrold LR et al. **Comparative effectiveness and safety of rituximab versus subsequent anti-tumor necrosis factor therapy in patients with rheumatoid arthritis with prior exposure to anti-tumor necrosis factor therapies in the United States Corrona registry.** Arthritis Res Ther. 2015 Sep 18;17(1):256



RCT vs registry data

A Small Minority (5%–19%) of RA Patients Prescribed TNF Antagonists Would Meet Eligibility Criteria From Pivotal Trials

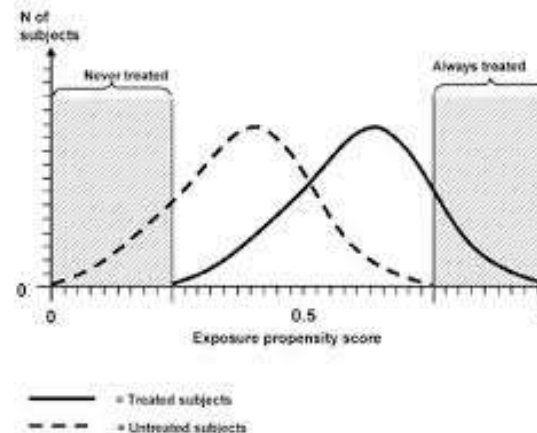
	Cohort A (n=336)	Cohort B (n=129)
Pivotal TNF antagonist RCT		
Infliximab ATTRACT	65 (19.4%)	7 (5.4%)
Etanercept monotherapy	38 (11.3%)	13 (10.1%)
Adalimumab ARMADA	22 (6.6%)	12 (9.3%)

.....the majority would not receive biologics in the U.K., etc.

Greenberg JD et al. *Am J Med.* 2008;121:532-538.

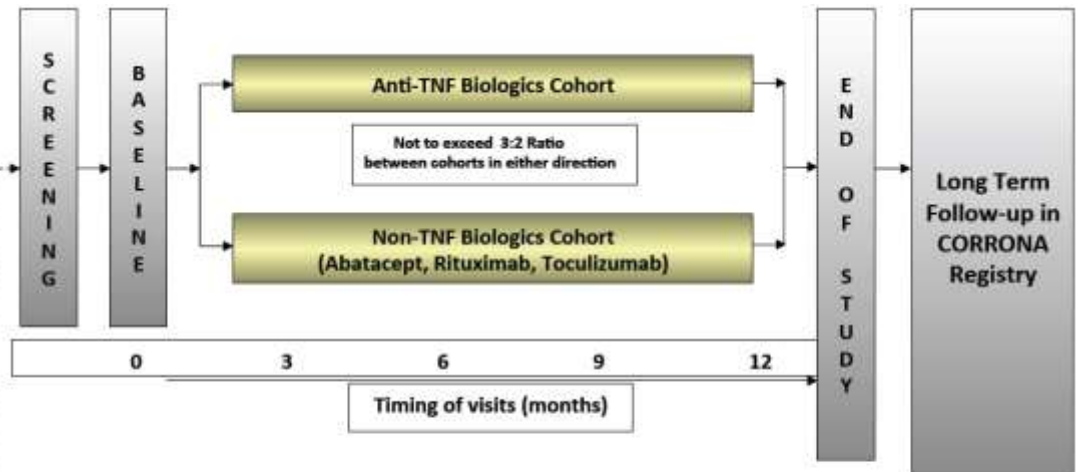
Propensity Score Matching (PSM)

- Employs a predicted probability of group membership
 - E.g. treatment vs. control group
 - Based on observed predictors, usually obtained from logistic regression to create counterfactual group (Rosenbaum & Rubin, 1983)
 - Dependent variable: $T=1$, if participate; $T=0$, otherwise
 - $T=f(\text{age, gender, pre-cci, etc.})$
- Allows “quasi-randomized” experiment
 - Two subjects, one in treated group and one in the control, with the same (or similar) propensity score, can be seen as “randomly assigned” to either group



CORRONA CERTAIN Sub-study: nesting comparative effectiveness studies in registries

- Comparative Effectiveness of biologic agents used in RA
- Comparative safety of biologic agents used in RA
- Biomarkers, genomics, genetics; correlations with effectiveness and safety across classes of biologics
- CV safety; hsCRP, lipid levels, metabolic markers, with time



CERTAIN: Comparative Effectiveness Registry to Study Therapies for Arthritis and Inflammatory Conditions (CERTAIN)

Pappas, DA et al. The CORRONA-CERTAIN sub-study. Presented at the ACR Clinical Trials/Registry Poster Exhibit at the ACR Annual Scientific Meeting in Washington, DC, 2012.

- Eligible patients: adult patients with RA **starting** or **switching** to a new biologic agent
- Enrollment period: 3 years, 2711 patients
- Number of subjects: approx 3000


**CORRONA - RA Registry Protocol 02-021
PHI Collection**

 Site ID:
To be completed by site staff

 Subject ID:

 Date form completed:

 Year of Birth:
To be completed by the participant
Directions: Once completed, the data contained in this form and the accompanying Medical Release Form should be submitted by the site directly to the honest broker following the instructions provided.

 1. Last Name: Middle Initial: First Name:

 2. Date of Birth: Example: 01-Jan-2000

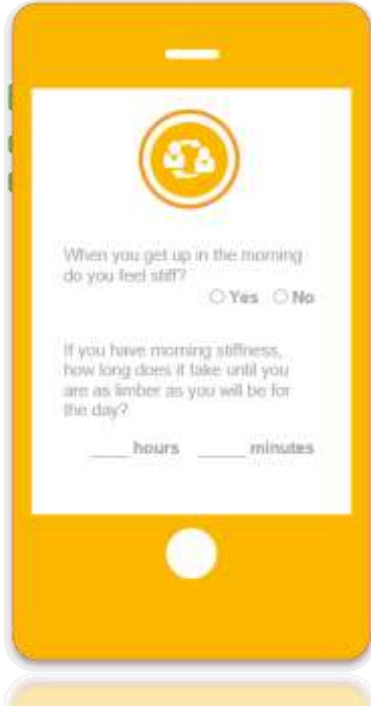
 3. Social Security Number:

 4. Preferred method of contact: (Check all that apply)
 Phone E-mail Mail
 Best Phone: Alternate Phone:
 E-mail:
 Street 1:
 Street 2:
 City: State: Zip:

 5. Alternate contact person in case we are unable to reach you:
 Last Name: Middle Initial: First Name:
 Best Phone:
 E-mail:
 Street 1:
 Street 2:
 City: State: Zip:

Smart-phones and wearable devices

Data to capture could include:



- ✓ **Activity levels, sleep**
- ✓ **PROMIS-CAT** Instruments (e.g. Pain, Fatigue, Sleep)
- ✓ RAPID3
- ✓ **Pain Visual Analog Scale (VAS)**
- ✓ Fatigue VAS
- ✓ **Patient Global**
- ✓ Belief about medications
- ✓ **Medication-related information**
- ✓ Compliance
- ✓ **Reasons for non-compliance**
- ✓ Cognition and applied cognition
- ✓ **Depression / mood**
- ✓ Social activity participation
- ✓ **Fear / motivation from DTC ads**



The NEW ENGLAND JOURNAL *of* MEDICINE

Perspective
FEBRUARY 22, 2018

The Psychology of Clinical Decision Making — Implications for Medication Use

Jerry Avorn, M.D.

Thank you !