



# MSKAI: Musculoskeletal Adverse Events associated with Hormonal Treatment for Breast Cancer

Jenny Lane

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Seojeong Shin, Jose Posada, Thomas Falconer, Talita Duarte Salles, Marc Suchard, Patrick  
Ryan and Dani Prieto-Alhambra



# Background

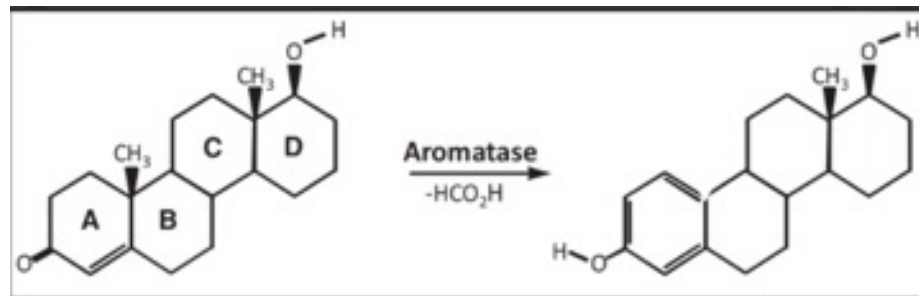
2/3 Breast ca= hormone receptor +ve

Centrally: tamoxifen

Peripherally:

Non steroidal reversible (competitive) inhibitors= letrozole, anastrozole

Steroidal irreversible inhibitors= exemestane





# Background

ATAC (2005; 2009)

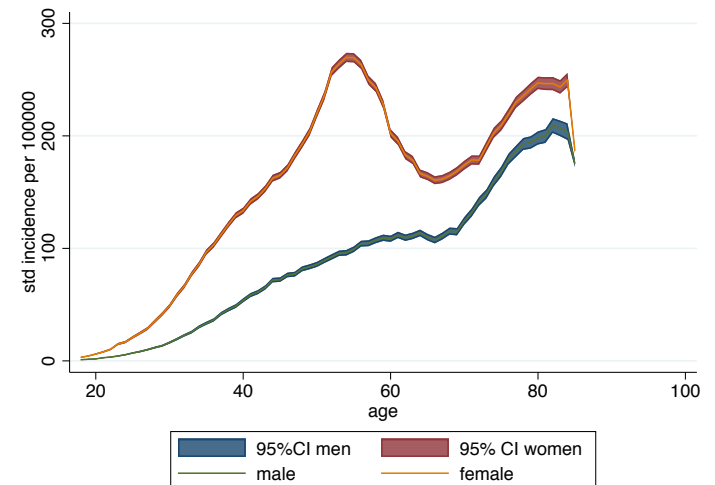
IBIS II (2013)

IES (2004)

Laboratory science: Aromatase in OA

Clinically: Arthralgia

Data: Perimenopausal peak CTS



Lancet Rheum 2021; 3(1) E49-57



# Research Question

## Association of MSK events in New Users Tamoxifen versus Aromatase Inhibitors?

- Carpal Tunnel Syndrome
- Tendinopathies
- Osteoarthritis

Steroidal vs Non-steroidal  
Anatomical location



<https://github.com/ohdsi-studies/MusculoskeletalAEsAfterAIs>



# Protocol registration



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**Status:** Planned

**First registered on:** 01/12/2020

**Last updated on:** 09/12/2020

## 1. Study identification

EU PAS Register Number

EUPAS38362

Official title

The risk of musculoskeletal adverse outcomes after treatment with endocrine blocking treatments for breast cancer



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# New User Study Design, Comparative cohorts

Target = Aromatase Inhibitor

Comparator = Tamoxifen

$\geq 55$ y at index

with breast cancer (LEGEND)  $< 365$ d prior

Female sex

No prior use of other drug

365d continuous observation prior

*Secondary Cohorts:*

*Steroidal/ NonSteroidal vs TMX; NSAID vs SAI*

*Excluding Bisphosphonate users*



# Incident Outcomes

**OA** (All + hip, knee, shoulder, hand, thumb)

**Tendinopathy** (All + shoulder, hand&wrist, knee, foot&ankle)

**Carpal Tunnel Syndrome**

1. Medical condition occurrence
2. Surgery occurrence

= 26 in total 😊; no prior outcome in 365d



# Cohort Diagnostics & Collaborators



Cohort Diagnostics							
Cohort Counts	Show 10 entries	Search: <input type="text"/>					
Incidence Rate	Cohort	ajou_CDMPv532		CUIMC		CPRD	
Time Distributions		Entries	Subjects	Entries	Subjects	Entries	Subjects
Included (Source) Concepts	[MSK_AI] target_ai_drugduration	584	584	23,102	23,102	3,741	3,741
Orphan (Source) Concepts	[MSK_AI] target_ai_nonsteroidal_drugduration	579	579	22,994	22,994	3,460	3,460
Inclusion Rule Statistics	[MSK_AI] target_ai_steroidal_drugduration	69	69	1,127	1,127	946	946
Index Event Breakdown	[MSK_AI] comparator_tamoxifen_drugduration	174	174	18,478	18,478	659	659
Visit Context	[MSK_AI] outcome_cts_condition_agesex	1,540	1,540	63,410	63,410	12,346	12,346
Cohort Characterization	[MSK_AI] outcome_cts_surgery_agesex			31,896	31,896	2,790	2,790
Temporal Characterization	[MSK_AI] outcome_cts_surgery_agesex_nonstandard			31,896	31,896	2,790	2,790
Cohort Overlap	[MSK_AI] outcome_oa_all_conditionANDsurg_agesex_nonstandard	2,206	2,206	57,977	57,977	19,405	19,405
Compare Cohort Char.	[MSK_AI] outcome_oa_all_conditiononly_agesex	8,046	8,046	469,726	469,726	131,691	131,691
	[MSK_AI] outcome_oa_hand_condition_agesex			5,823	5,823	7,290	7,290
	All	All	All	All	All	All	All
Showing 1 to 10 of 31 entries		Previous 1 2 3 4 Next					







# Datasets

Source	Population	Patients	Type
AUSOM	Ajou University Tertiary Hospital	2M	EHR
CIUMC	Columbia University Irving Medical Center/NY-Presbyterian Hospital	6.6M	EHR
CPRD	UK (primary care general popn)	13M	EHR
IBM CCAE	US (commercially insured <65y)	142M	Claims
IBM MDCD	US (Medicaid enrollees)	26M	Claims
IBM MDCR	US (commercially insured >=65y)	10M	Claims
IQVIA LPD Australia	Australia (primary care general popn)	3.1M	EHR
IQVIA DA France	France (primary care general popn)	7.8M	EHR
IQVIA DA Germany	Germany (general popn)	34M	EHR
IQVIA Hospital Chargemaster	US (Administrative billing data)	>86M	Claims
IQVIA LPD Belgium	Belgium (primary care/ outpatient general popn)	2M	EHR
IQVIA Openclaims	US (commercial claims)	>200M	EHR
JMDC	Japan (insured general popn 18-65y)	5.5M	EHR
Optum PanTher EHR	US (general population)	>95M	EHR
Optum Clinformatics SES	US (commercially insured)	85M	Claims
Pharmetrics	US (medical and pharmacy claims)		Claims
SIDIAP	Catalonia (primary care general popn)	7.7M	EHR
STARROMOP	Stanford (hospital)	>2.7M	EHR

*Adapted from work by  
Jamie Weaver, Kristin  
Kostka & Talita Duarte  
Salles*



# Cohort Diagnostics- things to think about

3 iterative rounds 😊

Time: Introduction of AIs into practice

Outcome: condition vs surgery occurrence

Surgery in US: conversion of ICD9-10PCS

Inclusion: *Apriori* determination of which datasets contribute to which analyses





# MSKAI analysis plan

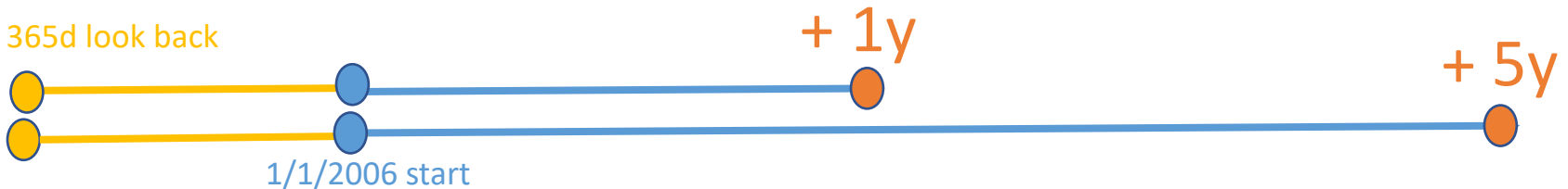
## On Treatment

365d look back



## Intention to Treat:

365d look back



No outcome prior 365d; TAR = 1 day

Propensity Score 5:1 matched observed confounding = demographics/condition/drugs

Calibration outcomes for unobserved confounding = 73 negative controls

Cox PH outcome; Meta-analysis if  $I^2 < 40\%$

Sensitivity: 1/1/2015 start

Development of a Fine & Gray Model- UCLA



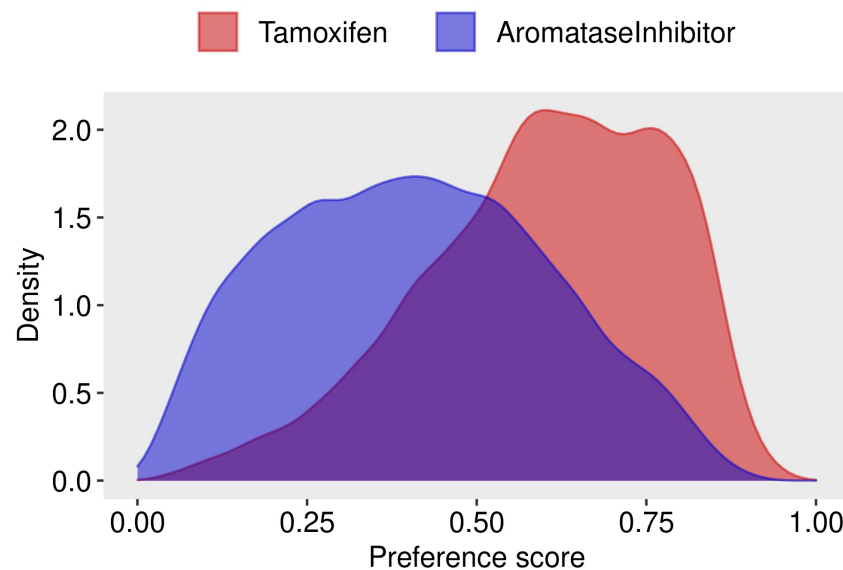
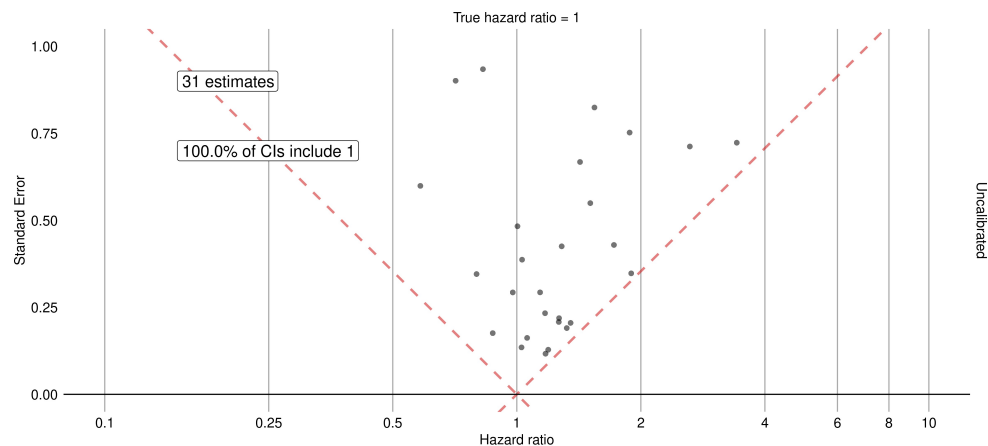
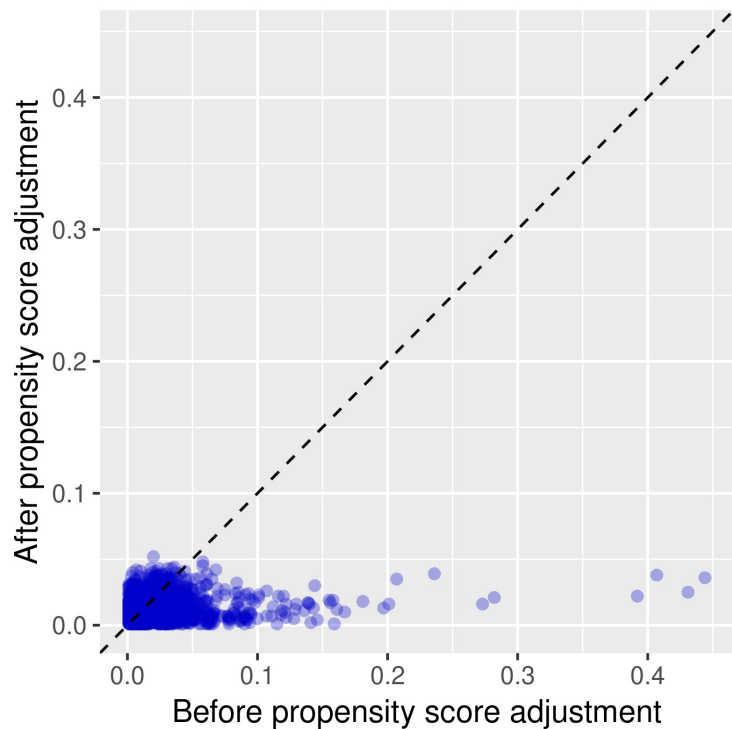
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*Infographic inspired by work from Jamie Weaver*



# Results- some CPRD diagnostics





# Thank you

Edward Burn

Kristin Kostka

Joshua Ide

Stephen Fortin

Alan Andryc

Seng Chan You

Seojeong Shin

Talita Duarte Salles

Jose Posada

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