The Influence of Time-Dependent Drug Exposures on Joint Surgeries in Rheumatoid Arthritis Patients

Cross-Provincial Comparisons

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Disclosures

- None of the authors have any commercial relationships relevant to this study.

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Background

- **JOINT DAMAGE OCCURS EARLY IN RA**
  - **Early and aggressive treatment with DMARDs can:**
    - **help reduce joint inflammation**
    - **prevent or delay joint damage**
    - **reduce the need for joint surgery**

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Hypothesis

- **Early & greater cumulative use of DMARDs, soon after RA diagnosis, are associated with longer time to joint surgeries**

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Background

- **To study the effects of early and aggressive treatment on time to joint surgeries**
  - **Statistical analyses must account for TIMING of drug use:**
    - **Drug use and dose varies across users and over time**
    - **Benefits (and risks) associated with a specific drug depend on dose, duration, and time of treatment.**

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Objective

- **To evaluate joint surgeries, and the influence of early exposure & cumulative use of DMARDs on time to surgery, comparing incident RA populations from Ontario and Quebec.**

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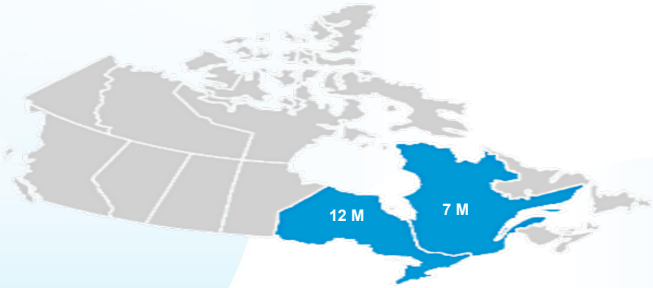
Setting

BACKGROUND | METHODS | RESULTS | DISCUSSION | CONCLUSION

- **Ontario and Quebec**
  - **Health administrative databases**
    - Universal comprehensive health care data on physician visits, hospitalizations, and drugs (dose, duration, and dates)



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Study Population

BACKGROUND | METHODS | RESULTS | DISCUSSION | CONCLUSION

- **Incident RA patients (2000-2013)**
- **Recipients of public drug coverage**
  - **all seniors ages 66 years and older.**

Cohort Entry Criteria:

- **3 ICD codes (714) with ≥ 1 code by a specialist over 2 years**

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Study Design

- **Population-based cohort study:**
  - Using a standard protocol, incident RA patients were followed from cohort entry until their first joint surgery, or were censored at death or end of study period.
- **New drug user study design**:
  - Analyses were confined to patients who were a "new user" for the drug of interest.
- **Outcome:**
  - Time from cohort entry to the first joint surgery (any joint) defined by procedure codes.

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Analysis

COX PROPORTIONAL HAZARDS REGRESSION

- **Time-dependent variables (in the first year of follow-up):**
  - **time-varying cumulative use of methotrexate, other DMARDs**
- **Time-dependent variables (over duration of follow-up):**
  - **time-varying cumulative use of anti-TNFs, COXIBs, NSAIDs, steroids**
  - **time-varying number of physician visits**
- **Time-independent variables (baseline covariates):**
  - **Demographics (age, sex, residence, SES)**
  - **Risk factors for joint surgeries (prior joint surgeries, OA, past use of NSAIDs/COXIBs and steroids, and comorbidities, EAFs)**
- **Adjusted hazard ratios (HRs) along with 95% CIs were estimated.**

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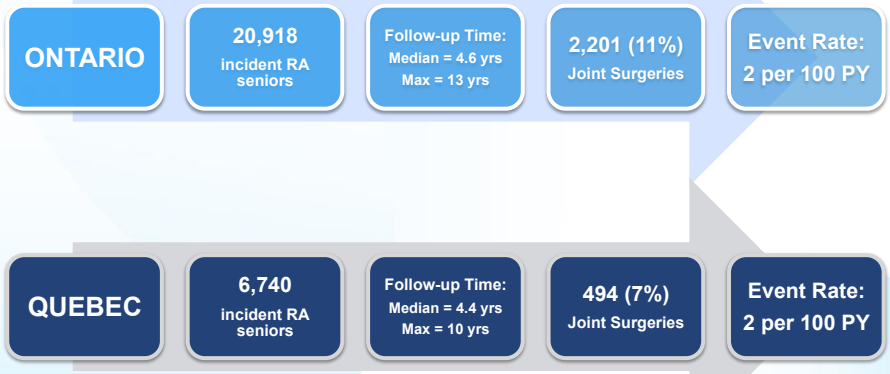
Study Flow Diagram

BACKGROUND METHODS **RESULTS** DISCUSSION CONCLUSION



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Baseline Characteristics

BACKGROUND METHODS **RESULTS** DISCUSSION CONCLUSION

	ONTARIO n=20,918	QUEBEC n=6,740
Age, mean (SD)	75 (6)	75 (6)
Female	68%	68%
Urban residence	85%	81%
Pre-existing OA	51%	38%

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Drug Exposures During Follow-up

BACKGROUND METHODS RESULTS DISCUSSION CONCLUSION

	ONTARIO n=20,918	QUEBEC n=6,740
MTX	58%	53%
Other DMARDs*	65%	61%
Anti-TNF	10%	5%
Glucocorticosteroids	74%	78%
NSAIDs	58%	38%
COXIBs	31%	49%

*Other DMARDs: sulfasalazine, chloroquine, hydroxychloroquine, leflunomide, cyclosporine, minocycline, penicillamine, and cyclophosphamide

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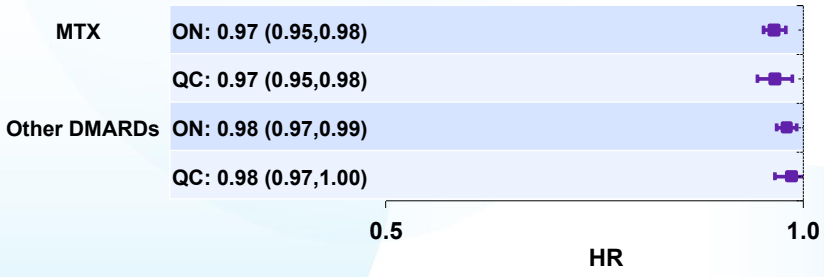
Multivariable Analyses

BACKGROUND METHODS RESULTS DISCUSSION CONCLUSION

Greater exposure to MTX and other DMARDs within the first year were associated with longer time to joint surgeries



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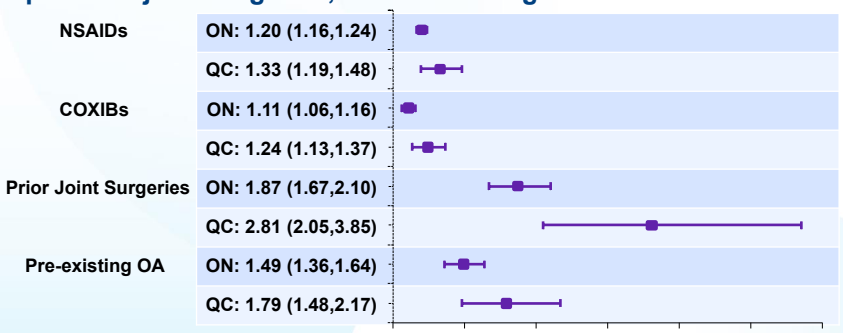
Multivariable Analyses

BACKGROUND METHODS **RESULTS** DISCUSSION CONCLUSION

Strongest independent associations with shorter time to joint surgeries included greater exposure to NSAIDs and COXIBs, previous joint surgeries, and co-existing OA



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Strengths & Limitations

BACKGROUND METHODS RESULTS **DISCUSSION** CONCLUSION

- **Large population-based cohorts:**
  - Wide geographic population representation
  - Long follow-up time
- **Analytic approach:**
  - Incident RA + New user drug design
  - We assessed time-varying (daily exposures over follow-up) rather than classifying drug exposures into Never/Ever/ Average use etc

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Strengths & Limitations

BACKGROUND METHODS RESULTS DISCUSSION CONCLUSION

- Administrative data preclude confirmation of diagnosis
  - we used a validated case definition
  - high prevalence of RA drug use during follow-up
- Lack of data on potential confounders
  - clinical measures (symptom onset, disease activity)
- Some RA may not have been truly incident
  - damage may have already been present
- Relationship between RA and OA (pre-existing, or secondary to RA) and need for joint surgery may be complex

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Conclusions

BACKGROUND METHODS RESULTS DISCUSSION CONCLUSION

- Greater cumulative exposures to MTX and other DMARDs, within 1 year after RA diagnosis, were associated with longer time to joint surgeries in both ON and QC.
  - This could be related to the joint-sparing effects of DMARDs, but alternative explanations should be considered
- Our coordinated approach across provincial data sources identified highly comparable and consistent findings.

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