

Canadian Real-World Evidence on Epidemiology, Outcomes and Economics of Moderate-to-Severe Osteoarthritis: a Systematic Literature Review

Larkin-Kaiser KA¹, Waters-Banker C¹, Cowling T¹, Snow L-A², Hasani I², Fernet M²
¹Medlior Health Outcomes Research Ltd. Calgary, Alberta, Canada; ²Pfizer Canada, Montreal, QC, Canada

INTRODUCTION

- Approximately 3.6 million Canadians (2010 population: 33.7 million) are living with any type of osteoarthritis (OA).^{1,2}
- Quality of life is greatly impacted among patients with moderate-to-severe OA.
- Limited Canadian Real-World Evidence (RWE) is available to understand the burden of disease of OA.
- Capturing the burden of disease of OA in Canada utilizing Real-World Evidence (RWE) is important for the development and effective implementation of novel treatment strategies.

OBJECTIVE

- This systematic literature review identified RWE on the clinical and economic burden of moderate-to-severe OA in Canada.

METHODS

Data Sources and Search Strategy

- OA Studies published between January 1, 2013 to November 5, 2018 were searched in: MEDLINE® In-Process; MEDLINE® Daily, MEDLINE®; Embase; and the Cochrane® Library, including Cochrane Reviews; the Database of Abstracts of Reviews of Effects (DARE); and the Central Register of Controlled Trials Library (CENTRAL).
- Conference abstracts published between 2015-2018 were searched for: Opioid Summit, Canadian Musculoskeletal Conference, Canadian Chiropractic Association National Convention and Tradeshow, Pain Society of Alberta Conference annual scientific conference, Canadian Society of Anesthesiology Annual Meeting, International Society for Pharmacoeconomic Research (ISPOR), Canadian Pain Network, Canadian Rheumatology Association and Arthritis Alliance of Canada.

Eligibility Criteria

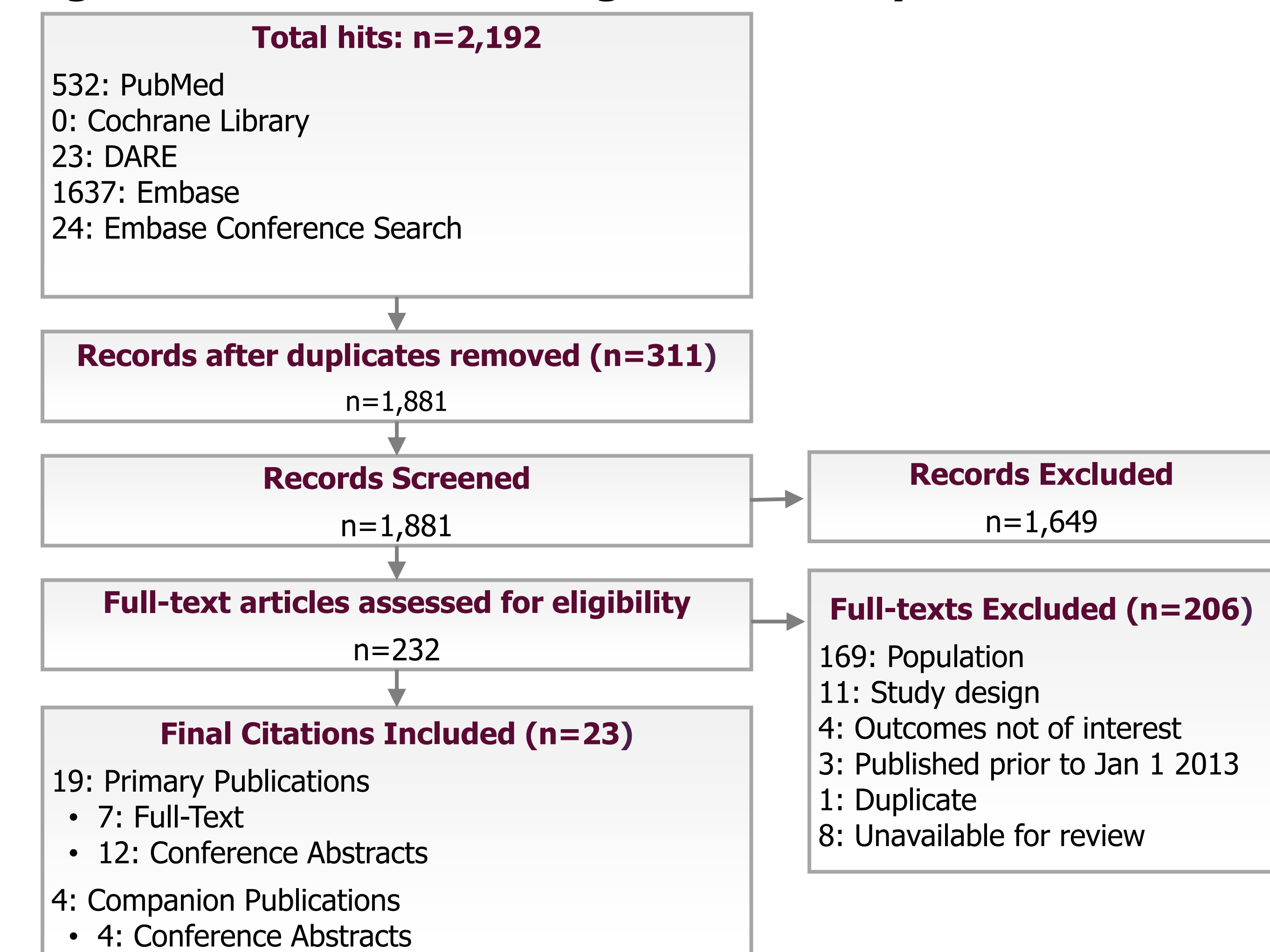
- Population:** Canadian patients 18 years and older with clinically or radiologically confirmed OA. Inclusion was restricted to studies including Canadian patients with OA severity defined by the study author as moderate-to-severe.
- Outcomes:** Epidemiological, clinical, pain/functional, treatment patterns, healthcare utilization/costs, mental health, opioid abuse/dependence.
- Study Design:** Real-world evidence studies (excludes clinical trials).

Study Selection and Data Extraction

- Two reviewers independently assessed the eligibility of identified citations via title/abstract and full-text screening using predefined selection criteria.
- Two reviewers independently extracted data from the included studies.
- Limitations of the included studies are noted in the discussion.

RESULTS

Figure 1. PRISMA Flow Diagram for Study Selection



Prevalence of moderate-to-severe OA in Canada

- Prevalence rates of moderate-to-severe OA in Canada were not reported.
- Two studies reported population estimates from large study cohorts (Table 1).

Table 1. Proportional Population Data of Moderate-to-Severe OA

Population	N (%)
Ravi, 2013 ^{3, a}	
Individuals 55+ in Ontario Canada with clinically and radiographically confirmed OA identified from individuals reporting moderately severe hip or knee problems (N= 48,218)	2200 (4.5)
Females	1585 (72.0)
Sharif, 2017 ⁴	
General Population 2010 (in Canada, ≥20 years of age)	26,260,862
Individuals with OA who visited an orthopaedic surgeon ^b	340,505 (1.3)
Individuals with OA who have had first TJA surgery ^c	308,708 (1.2)

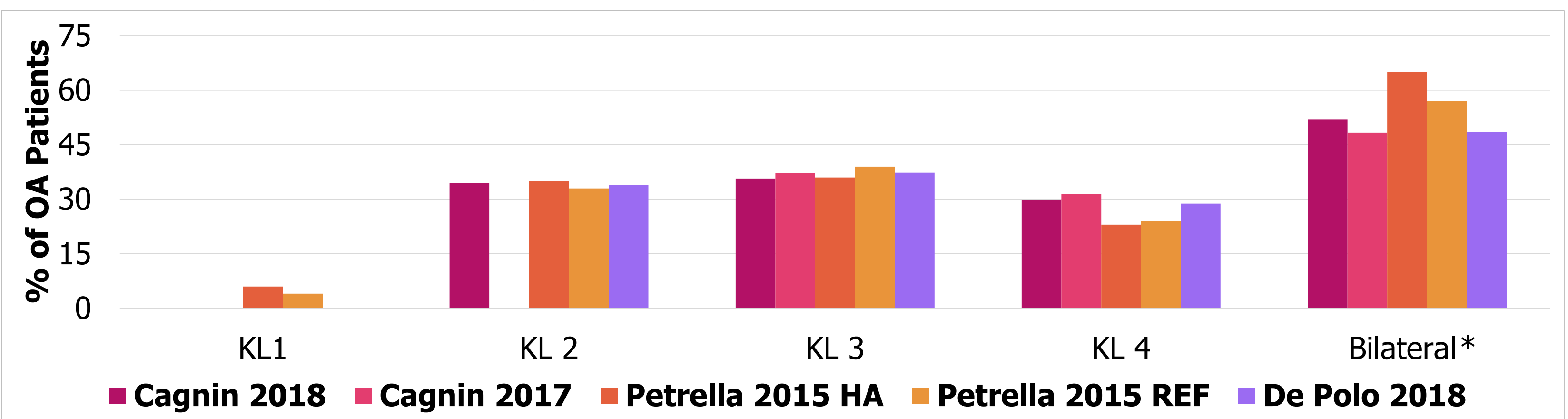
^aFrom survey of 100% of the Ontario population 55+ from 1996-1998. Captured patients with radiographic confirmed OA excluding RA (rheumatoid arthritis) and IA (inflammatory arthritis); ^bDefined as Stage 2 by the study author: Diagnosed OA and have visited an orthopaedic surgeon; ^cDefined as Stage 3 by the study author: Primary TJA surgery (no revision). Abbreviations: N: Population number; OA: Osteoarthritis; TJA: Total Joint Arthroplasty

Patient Characteristics

- Study populations were predominately female (44-83%) and 57-74 years old
- Limited outcomes were reported:
 - 7 studies = joint characteristics of the hip or knee (Figure 2/Table 2)^{7-8, 11-14}
 - 6 studies = pain scores^{3, 5, 6, 11, 12, 15}
 - 3 studies = average of 3-6 symptomatic joints^{8, 13, 14} (Table 2)
 - 2 studies = hypertension as most common comorbidity (Figure 3)^{3, 7}
 - 2 studies = NSAIDs as most frequent treatment^{3, 7}
 - 3 studies = opioid use^{3, 7, 9}

ACKNOWLEDGEMENTS: The authors would like to acknowledge Eileen Shaw for her assistance in screening and data extraction for this systematic literature review and Drs. Jacek Kopec, John Esdaile and Jolanda Cibere for their expert review of the Research Study. **FUNDING SOURCES:** This work was supported by Pfizer Canada Inc (Pfizer), Montreal, Quebec, Canada. Pfizer collaborated with Medlior Health Outcomes Research Ltd. (Medlior) in the study design of the project. Medlior was responsible for the gathering, analyzing, and reporting of data. Medlior and Pfizer Canada Inc. collaborated in the decision to submit this manuscript for publication. **DISCLOSURES:** Kelly Larkin-Kaiser, Christine Waters-Banker, and Tara Cowling are employed by Medlior Health Outcomes Research Ltd. who received funding for the study from Pfizer Canada Inc. Lori-Ann Snow and Mireille Fernet are employed by Pfizer Canada Inc., who funded this study. Ina Hasani is a former Pfizer Canada Inc. employee.

Figure 2. Joint Characteristics Reported Among Individuals Reported to Suffer from Moderate-to-Severe OA^{7, 11, 12, 15}



*Individuals who report bilateral knee pain, not mutually exclusive to KL grade as disparity exists between clinical and radiographic severity. Abbreviations: OA: Osteoarthritis; KL: Kellgren-Lawrence Grading Scale (0-4); HA: Hyaluronic Acid Injection group; REF: Reference group

Table 2. Number of Symptomatic Joints Reported Among Individuals with Moderate-to-Severe OA^{8, 13, 14*}

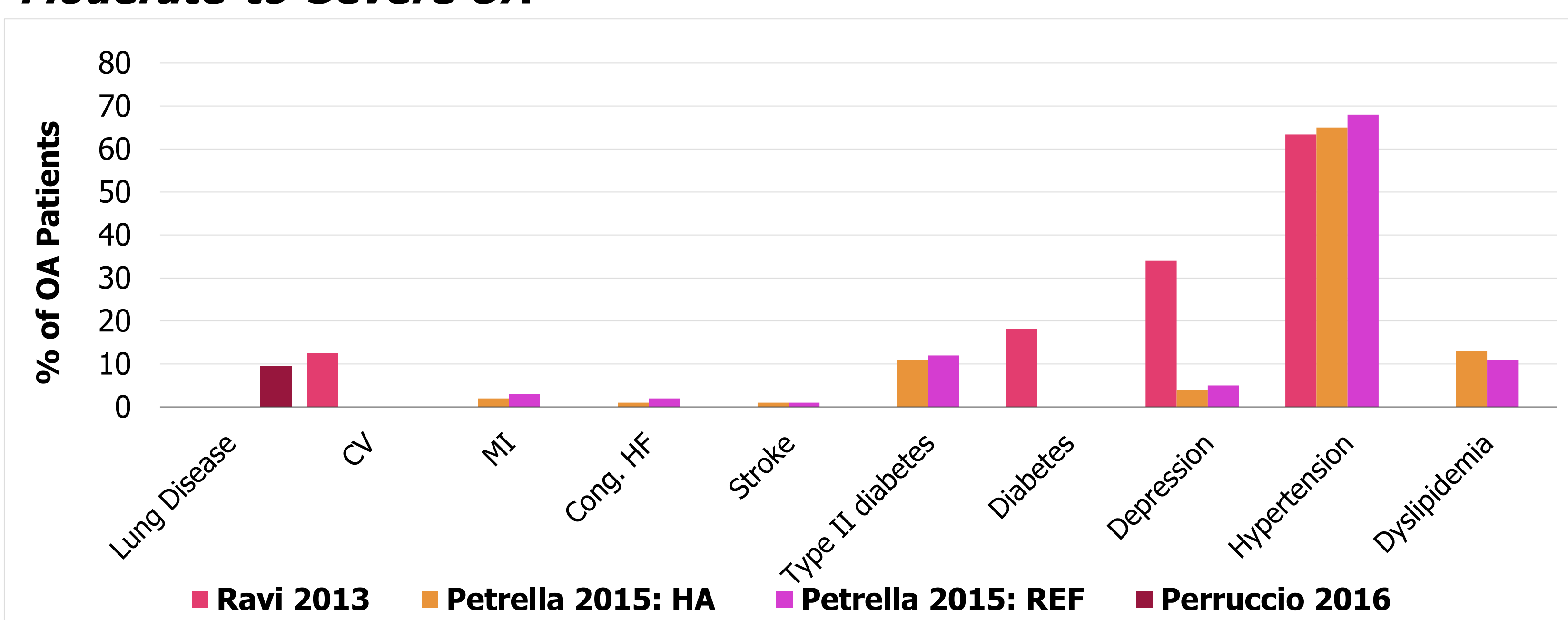
# of Symptomatic Joints	Perruccio 2014 ^{13, a}	Perruccio 2016 ⁸	Perruccio 2017 ^{25, a}
Mean	NR	4.4	3.0
Range	NR	1-20	0-17
Women scheduled for TJA	0-8	NR	NR
Men scheduled for TJA	0-5	NR	NR

*All patients in these three publications were scheduled for total knee or hip replacement for end-stage OA.

^aNot including surgical joint

Abbreviations: #: Number; NR: not reported; TJA: Total Joint Arthroplasty

Figure 3. Comorbid Conditions Reported Among Individuals with Moderate-to-Severe OA^{3, 7, 8}

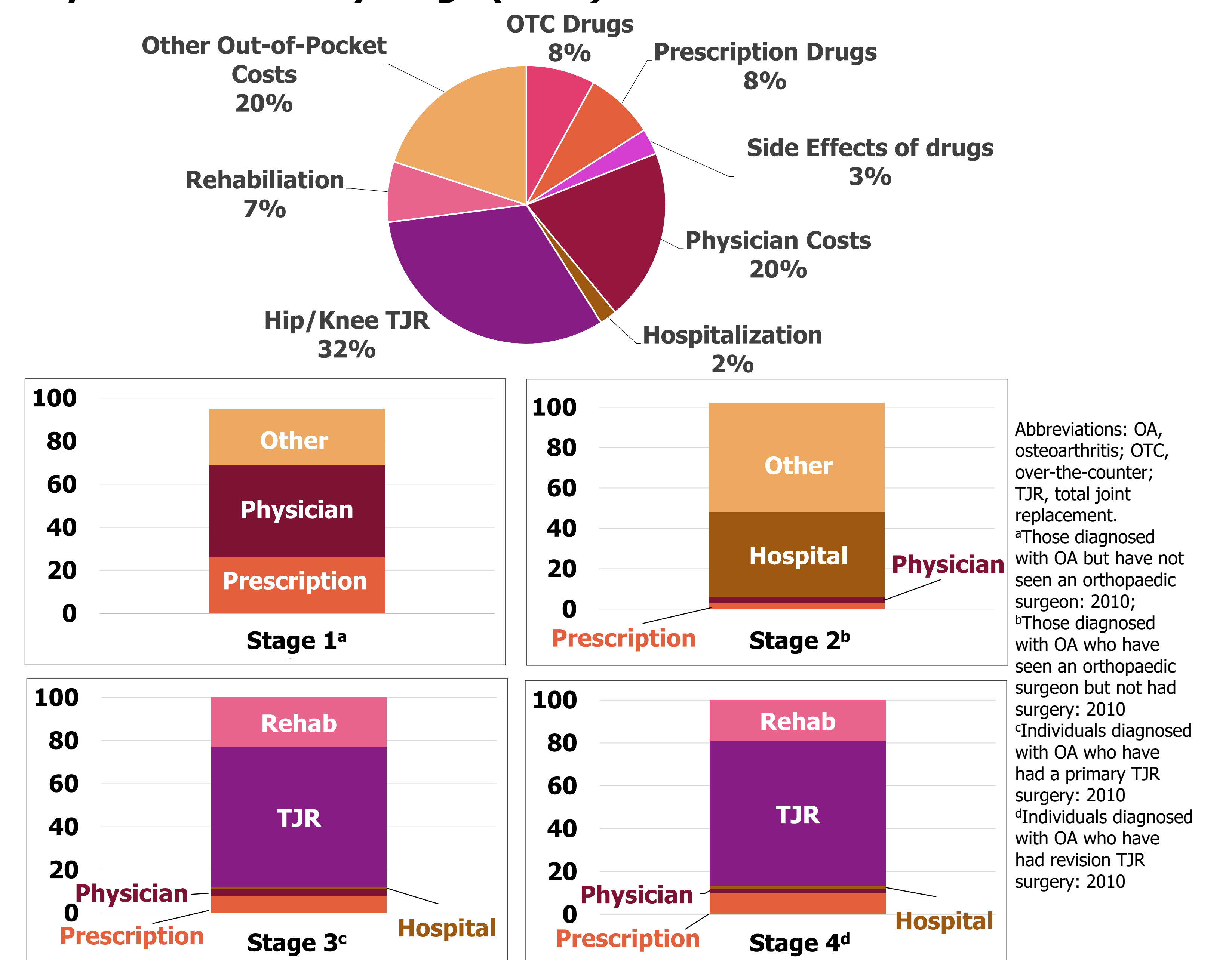


Abbreviations: OA: Osteoarthritis; Cong. HF: Congestive Heart Failure; MI: Myocardial Infarction; CV: Pre-existing Cardiovascular Disease; REF: Reference Group; HA: Hyalan G-F 20 Injection treatment group.

Economic Burden

- The estimated average annual cost of OA per person increased with disease severity (\$468 to \$3,185; 2017 \$CAD), with the highest costs for moderate-to-severe OA, with joint replacement being the largest cost driver (Figure 4).¹⁰

Figure 4. Average Annual Cost of OA per Person and Largest Proportion of Cost by Stage (2010)¹⁰



Abbreviations: OA, osteoarthritis; OTC, over-the-counter; TJR, total joint replacement. ^aThose diagnosed with OA but have not seen an orthopaedic surgeon; 2010; ^bThose diagnosed with OA who have seen an orthopaedic surgeon but not had surgery; 2010; ^cIndividuals diagnosed with OA who have had a primary TJR surgery; 2010; ^dIndividuals diagnosed with OA who have had revision TJR surgery; 2010

LIMITATIONS

- Due to lack of standardized definitions for disease severity, Canadian RWE studies were selected for inclusion as moderate-to-severe OA based on author definition.
- Canadian RWE studies ranged from retrospective, prospective, and cross-sectional designs, with analyses gathered from administrative databases, surveys/questionnaires, and interviews, which limited the synthesis of results.
- Most included citations were only published as conference abstracts, therefore, limited information was reported.
- The literature search involved selected Canadian conferences only, with the exception of ISPOR.

CONCLUSIONS

- The burden of moderate-to-severe OA in Canada seems significant.
- A lack of standardized severity definitions and sparse reporting of key outcomes such as depression, disability, opioid misuse, or pain, highlight an important gap in documenting prevention and treatment strategy effectiveness.
- Despite limited data, progressing disease and worsening disability leads to poor patient-outcomes and increased healthcare costs.

REFERENCES:

- Public Health Agency of Canada. Life Arthritis Canada: A personal and public health challenge; 2013.
- Birtwhistle et al. *CMAJ Open* 2015; **3**(3): E270-5.
- Ravi B et al. *BMJ* 2013; **347**: f6187.
- Sharif B et al. *Osteoarthritis Cartilage* 2017; **25**(2): 249-58.
- Hawker G et al. *Arthritis Rheumatol* 2015; **67**(7): 1806-15.
- Yakovov E et al. *Pain* 2014; **155**(10): 2040-6.
- Petrella RJ et al. *Drug Des Devel Ther* 2015; **9**: 5633-40.
- Perruccio AV et al. *Osteoarthritis and Cartilage* 2016; **24**: S222.
- Power JD et al. 2017 ACR/ARHP Annual Meeting; 2017; 2017.
- Shariff B et al. *Arthritis Care Res (Hoboken)* 2017; **69**(2): 243-51.
- Cagnin A et al. *Osteoarthritis and Cartilage* 2018; **26**: S365-56.
- Cagnin A et al. *Osteoarthritis and Cartilage* 2017; **25**: S338.
- Perruccio AV et al. *J Rheumatol* 2014; **41**(2): 334-7.
- Perruccio AV et al. *Osteoarthritis and Cartilage* 2017; **25**: S191-S2.
- De Polo L et al. *Osteoarthritis and Cartilage* 2018; **26**: S255-56.