Osteoarthritis is related to an increased risk of falls and fractures: a prospective multinational cohort study (the GLOW study)

Daniel Prieto-Alhambra, Xavier Nogués, M. Kassim Javaid, Nigel K. Arden, Cyrus Cooper, Allison Wyman, Adolfo Diez-Pérez, on behalf of the GLOW Investigators

Financial support for the GLOW study is provided by Warner Chilcott Company, LLC and sanofi-aventis to the Center for Outcomes Research, University of Massachusetts Medical School

Background

- Osteoarthritis (OA) and Osteoporosis (OP) are both very common in the elderly:
  - Lifetime risk for any fracture in women aged 60 years: 44%1
  - Lifetime risk of symptomatic knee and hip OA: at age 60: 45% and 25% respectively 2,3
  - Both related to increased health care costs.
  - High burden of morbidity and mortality 4,5,6

Disclosures

Daniel Prieto-Alhambra: no competing interests to declare.
Xavier Nogués: no competing interests to declare.
M. Kassim Javaid: Novartis, Amgen, Alliance Better Health, Lilly.
Nigel K. Arden: Merck, MSD, Roche, Novartis, Smith and Nephew, Q-MED, Nicox, Servier, GSK, Schering-Plough, Pfizer and Rottapharm
Cyrus Cooper: Amgen, sanofi-aventis and Warner Chilcott, Eli Lilly, Merck Sharp and Dohme, Servier, Novartis, and Roche-GSK.
Allison Wyman: sanofi-aventis and Warner Chilcott.

Aims

- To examine the association between self-reported OA and incident fractures.
- To study whether patients who report OA experience an increased number of falls.
- To explore whether the difference in falls rate accounts for an increase in fractures in patients reporting OA.

GLOW: a multinational study

7 countries around Europe
7 sites in the USA
1 site in Canada
1 site in Australia

References


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GLOW: Overview

- **Inclusion criteria:**
  - Non-institutionalized women ≥55 years
  - 2:1 over-sampling of women ≥65
  - Recruited through primary care networks

- **Annual mailed survey on:**
  - Demographics and risk factors for OP
  - Medication use
  - Prevalent and incident fractures
  - Other medical diagnoses

- **3-year follow-up data are available**

EXPOSURE

- **OA STATUS (baseline survey):**
  - “Has a doctor or other health provider ever said that you had osteoarthritis or degenerative joint disease?”
  - Concordance with GP records for self-reported OA is high (about 85-87% \(^{11,12}\)).
  - Baseline self-reported OA: N = 20,409 (40%). Comparable to other cohorts \(^{11,12}\).

OUTCOME/S

- **PRIMARY:**
  - Incident fractures: date and site

- **SECONDARY:**
  - Number of incident falls:
    - “In the last 12 months, how many times have you fallen?”
    - (None / Once / Two times or more)

Statistical methods

- Cox regression for incident fractures.
- Zero-inflated Poisson regression for number of falls.
- **Potential confounders:** age, BMI, OP medications, COPD, Parkinson’s disease, fracture history, parental hip fracture, oral corticosteroids, and secondary osteoporosis (as defined in FRAX)

RESULTS (1)

- **STUDY POPULATION:**
  - 51,386 GLOW participants with:
    - Baseline, year 1, year 2 and year 3 surveys
    - Current OA status at baseline
    - Known fracture status up to year 3 of follow-up

- Non-responders were:
  - Small differences in age: 68 vs 71 years
  - More likely ≥1 fall history: 38% vs 41%
  - More comorbidities: diabetes, Parkinson, COPD, stroke
  - Higher fracture prevalence: 23% vs 30%

Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Non-OA participants</th>
<th>OA participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>30,987 (60%)</td>
<td>20,409 (40%)</td>
</tr>
<tr>
<td>Age, years</td>
<td>67.5 (8.7)</td>
<td>69.1 (8.6) ***</td>
</tr>
<tr>
<td>BMI, kg/m(^2)</td>
<td>26.6 (5.7)</td>
<td>27.4 (6.2) ***</td>
</tr>
<tr>
<td>Current / past anti-OP drugs</td>
<td>7,427 (25%)</td>
<td>6,390 (32%) ***</td>
</tr>
<tr>
<td>Prior fracture</td>
<td>6,307 (20%)</td>
<td>5,596 (27%) ***</td>
</tr>
<tr>
<td>Parental fracture</td>
<td>4,677 (17%)</td>
<td>3,290 (18%) ***</td>
</tr>
<tr>
<td>Current smoker</td>
<td>2,795 (9.1%)</td>
<td>1,672 (8.2%) **</td>
</tr>
<tr>
<td>Alcohol &gt;20 drinks per week</td>
<td>154 (0.5%)</td>
<td>99 (0.5%)</td>
</tr>
<tr>
<td>Secondary osteoporosis (^\dagger)</td>
<td>5,784 (19%)</td>
<td>4,247 (21%) ***</td>
</tr>
</tbody>
</table>

\(^\dagger\) as defined in the FRAX™ tool
Kaplan-Meier estimates of cumulative fracture rate in OA (red) and non-OA (blue) participants

Crude estimates: fracture risk

<table>
<thead>
<tr>
<th>Fracture Site</th>
<th>Overall fracture incidence rate at 3 years (95% CI)</th>
<th>OA participants (n=20,409)</th>
<th>Non-OA (n=30,978)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANY</td>
<td>8.7 (8.3 to 9.0)</td>
<td>12.1 (11.6 to 12.6)</td>
<td>1.40 (1.32 to 1.48)</td>
</tr>
<tr>
<td>Hip</td>
<td>0.66 (0.57 to 0.77)</td>
<td>0.93 (0.80 to 1.1)</td>
<td>1.46 (1.17 to 1.81)</td>
</tr>
<tr>
<td>Clinical spine</td>
<td>0.84 (0.73 to 0.96)</td>
<td>1.5 (1.3 to 1.7)</td>
<td>1.80 (1.50 to 2.17)</td>
</tr>
<tr>
<td>Wrist/forearm</td>
<td>2.0 (1.8 to 2.2)</td>
<td>2.8 (2.6 to 3.1)</td>
<td>1.38 (1.22 to 1.57)</td>
</tr>
<tr>
<td>Upper arm</td>
<td>0.76 (0.66 to 0.88)</td>
<td>1.1 (0.96 to 1.3)</td>
<td>1.38 (1.13 to 1.69)</td>
</tr>
</tbody>
</table>

Incidence Rates are reported as/100 person-years at risk

Adjusted estimates for fracture risk

<table>
<thead>
<tr>
<th>Fracture Site</th>
<th>Unadjusted HR</th>
<th>Multivariable adjusted HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>OVERALL CLINICAL FRACTURE</td>
<td>1.40 (1.32 to 1.48)***</td>
<td>1.21 (1.13 to 1.39)***</td>
</tr>
<tr>
<td>Hip fracture</td>
<td>1.46 (1.17 to 1.81)***</td>
<td>1.22 (0.94 to 1.59)</td>
</tr>
<tr>
<td>Clinical spine fracture</td>
<td>1.80 (1.50 to 2.17)***</td>
<td>1.27 (1.02 to 1.58)*</td>
</tr>
<tr>
<td>Wrist/forearm fx</td>
<td>1.38 (1.22 to 1.57)***</td>
<td>1.24 (1.07 to 1.44)**</td>
</tr>
<tr>
<td>Upper arm fracture</td>
<td>1.38 (1.13 to 1.69)***</td>
<td>1.21 (0.96 to 1.54)</td>
</tr>
</tbody>
</table>

\(p<0.05; **p<0.01; ***p<0.001\)

Cox models adjusted for: age, body mass index, anti-osteoporosis medication use, chronic obstructive pulmonary disease or emphysema, Parkinson's disease, fracture history, parent's hip fracture history, baseline and corticosteroid use, and secondary osteoporosis (as defined by use of aromatase inhibitors, diagnosis of inflammatory bowel disease, type 2 diabetes, and menopause before age 45 years).

Number of falls

<table>
<thead>
<tr>
<th>Falls Rate</th>
<th>Unadjusted RR</th>
<th>Multivariable adjusted RR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.26</td>
<td>1.24</td>
</tr>
<tr>
<td></td>
<td>(1.24 to 1.28)***</td>
<td>(1.22 to 1.26)***</td>
</tr>
</tbody>
</table>

Poisson regression, adjusted for: age, body mass index, current or past hormone replacement therapy, anti-osteoporosis medication use, baseline and corticosteroid use, region of origin, NSAID/NSAI (AF or USA/Canada/Europe), asthmatic, chronic obstructive pulmonary disease or emphysema, stroke, Parkinson's disease, cancer, prior fracture, and smoking status.

Adjustment for falls

<table>
<thead>
<tr>
<th>Overall Clinical Fracture</th>
<th>Multivariable adjusted HR</th>
<th>Further adjusted for falls</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.21</td>
<td>(1.13 to 1.39)***</td>
<td>1.06 (0.98 to 1.15) **</td>
</tr>
<tr>
<td>p=0.13</td>
<td></td>
<td></td>
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Limitations

- Self-reported data on OA status
- Lack of data for:
  - OA joint site (s), severity and duration
  - Non-response bias: 10.2% withdrawn
Conclusions

- Postmenopausal women reporting OA are at:
  - 20% increased risk of fracture
  - 25% more falls than non-OA peers

- The increased risk of fracture is predominantly due to an increase of falls.

- Fall prevention strategies may form part of the whole person management of OA patients.

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- MRC Lifecourse Epidemiology Unit (Southampton, UK)

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