The Natural History of Osteoarthritis: Occurrence, presentation, and course of joint pain

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(4.7) Trend in knee replacement surgery, 2000-09, selected countries

What is OA?

Defining OA has important implications for prevention, diagnosis, and treatment of this condition. Based on evidence to date, there was consensus that OA is usually a progressive disease of synovial joints that results from stress that may be initiated by an abnormality in any of the synovial joint structures, including articular cartilage, subchondral bone, ligaments, menisci (when present), periarticular muscles, peripheral nerves, or synovial fluid. This ultimately results in the breakdown of cartilage and bone, leading to symptoms of pain, stiffness, and functional disability. Abnormal intrarticular stress and failure of repair may arise as a result of biomechanical 
biomechanical and/or genetic factors. This process may be localized to a single joint, a few joints, or generalized, and the factors that initiate OA likely vary depending on the joint site. The complexity and variability of OA etiology suggests the need for patient-specific, etiology-based treatment.
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Defining OA has important implications for prevention, diagnosis, and treatment of this condition. Based on evidence to date, there was consensus that OA is usually a progressive disease of synovial joints that opposes failure of joint damage that results from stresses that may be initiated by an abnormality in any of the synovial joints, including articular cartilage, subchondral bone, ligaments, menisci (when present), periarticular muscle, peripheral nerves, or synovium. This ultimately leads to symptoms of pain, stiffness, and functional disability. Abnormal intra-articular stress and failure of repair may occur as a result of biomechanical, biochemical, and/or genetic factors. This process may be localized to a single joint, a few joints, or generalized, and the factors that initiate OA likely vary depending on the joint site. The complexity and variability of OA etiology suggests the need for patient-specific, etiology-based treatments.

While late-stage OA is often characterized by both demonstrable structural damage and patient reports of joint pain, stiffness, and disability, there is only a weak correlation between symptoms and pathology, particularly in early stages of the disease. Further, FDA-approved treatments directed at reducing the symptoms of OA have not been shown, to date, to prevent ongoing joint structural damage. For this reason, the Working Group felt that future development of treatments for OA should consider the following:

- The effectiveness of the treatment on the structural changes at the joint level (the disease OA) separately from the effects on patient-reported symptoms (tissue OA). Future pharmacotherapy for OA may therefore be considered as "symptom-modifying" to prevent the development of joint failure, symptom modifying, or both.

Participants

- Registered with participating general practices at time of study recruitment
- Aged 50+ years
- Reported symptoms in past 12 months
- Consented to further contact
- Attended baseline research assessment clinic
**Data collection**

<table>
<thead>
<tr>
<th>Started</th>
<th>ACRONYM</th>
<th>Focus</th>
<th>N</th>
<th>Follow-up (months)</th>
<th>0</th>
<th>18</th>
<th>36</th>
<th>54</th>
<th>72</th>
</tr>
</thead>
<tbody>
<tr>
<td>2002/3</td>
<td>CAS-K</td>
<td>Knee</td>
<td>818</td>
<td></td>
<td></td>
<td>○○○</td>
<td>○○○</td>
<td>○○○</td>
<td>○○○</td>
</tr>
<tr>
<td>2004/5</td>
<td>CAS-MA</td>
<td>Hand</td>
<td>621</td>
<td></td>
<td></td>
<td>○○○</td>
<td>○○○</td>
<td>○○○</td>
<td>○○○</td>
</tr>
<tr>
<td>2010/1</td>
<td>CAS-F</td>
<td>Foot</td>
<td>560</td>
<td></td>
<td></td>
<td>○○○</td>
<td>○○○</td>
<td>○○○</td>
<td>○○○</td>
</tr>
</tbody>
</table>

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**Finding 1. Different pain trajectories**

<table>
<thead>
<tr>
<th>Pain Trajectory</th>
<th>N</th>
<th>Time (in years) since baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild, non-progressive</td>
<td>208</td>
<td>0, 2, 4, 6, 8, 10, 12</td>
</tr>
<tr>
<td>Moderate</td>
<td>137</td>
<td>0, 2, 4, 6, 8, 10, 12</td>
</tr>
<tr>
<td>Improving</td>
<td>65</td>
<td>0, 2, 4, 6, 8, 10, 12</td>
</tr>
<tr>
<td>Severe, non-improving</td>
<td>20</td>
<td>0, 2, 4, 6, 8, 10, 12</td>
</tr>
</tbody>
</table>

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**Finding 2. Intervening mid-trajectory**

**WOMAC Function (0-68): mean (95%CI)**

Intervention 12 weeks

Observation 6 years

Intervention 12 weeks

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“The median isn’t the message.”

Stephen Jay Gould

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• Trajectories may be (temporarily) modifiable by episodes of care
• Conversely, might trajectories be adversely modified by acute exacerbations?
• Cumulative effects??

Classic view of natural history

[Diagram showing the natural history of OA and the purported roles of biomarkers during the disease process.]

Finding 3. Prodromal symptoms

[Graphs showing Incidence radiographic OA over time.]
• Pre-radiographic phase is associated with increased symptoms up to 3 years prior to appearance of x-ray changes
• Nociceptive drivers of prodromal symptoms?
• Potential for early clinical recognition and intervention?

Finding 4. The symptom iceberg and the decision to consult

By 3 years, 50% have still had no knee-related consultation

Domenica Coxon
(PhD dissertation)

A. Apparent Structure of Medical Knowledge
B. Rear View


Not as simple as ‘degenerative’, ‘inevitably progressive’
• Attention is needed to pain and function in their own right
• Estimating the timing and sequence of events and state transitions in the natural history of osteoarthritis is extremely challenging

Determinant | % contribution
--- | ---
Level of disruption to everyday activities | 31
Perceived attitude of GP | 24
Anticipated thoroughness of assessment and investigations | 14
Competing comorbidity | 13
Available management options/treatments | 13
Pain characteristics | 5


Acknowledgements
Causal actions that initiate osteoarthritis are complex and cumulative

Mean lifetime body mass index (BMI) z-score and 95% CI (shaded area) in women among those with knee osteoarthritis (OA; solid line) at age 53 years.

Prevalence of chronic joint pain in the over-50s in North Staffordshire

Generic prognostic indicators of self-reported pain/functional outcome

Prognostic indicators at baseline:
- Current pain intensity
- Interference with activities
- Disability days
- Duration of present episode
- Pain at other sites
- Depression

Clinical interview, physical examination, and severity of ROA add little prognostic information

Brief, generic prognostic indicators at the point of care: better than clinical judgement (but not good enough)

Table 3. Prognostic Indicators for the Study Models Based on 80 Imputed Data Sets

<table>
<thead>
<tr>
<th>Prognostic Indicator</th>
<th>Model 1 (Physical Function)</th>
<th>Model 1 (Physical Function) Adjusted ES (95% CI)</th>
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Sources: Mallen et al. JAMA Intern Med 2013