How the TGA uses implant registry data
Experience with the Australian Orthopaedics Association’s National Joint Replacement Registry (AOANJRR)

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Outline

- The AOANJRR:
  - How it works, reporting, benefits, limitations

- How the TGA uses AOANJRR Data
  - Prostheses with a higher than anticipated rate of revision
  - Adverse Event and Complaint Investigations
  - Premarket Assessment of Submissions

- Conclusions
The AOANJRR: How it works

- A joint replacement procedure triggers data collection
  - Patient identifying details, consulting surgeon, reason for surgery, and the type of implant, including individual implant components
  - If the procedure is a revision: type of revision, reason for revision

- “Opt Out” System

- Outcome Measure: Revision
  - Reported as Cumulative Percent Revision from the time of the primary procedure

- Comparison between different “populations” is possible
  - e.g. primary diagnoses; gender; age; use of cement; type of implant; implant models; etc.
  - Hazard Ratios are used to compare rates of revision
The AOANJRR: Reporting

- **Annual Reports on Hip, Knee and Shoulder Replacement**
  - Published in October each year using data collected to the end of the previous year
  - Collection started in 1999 (2004 for shoulders)
  - Contains information about prostheses with a higher than anticipated rate of revision

- **Supplementary reports on joint replacement:**
  - E.g. demographics and mortality of Hip, Knee Arthroplasty; Cement in Hip and Knee Arthroplasty

- **Individual reports on prostheses with higher than anticipated rates of revision (since 2010)**

- **Ad-Hoc summary reports from an online web portal**
The AOANJRR: Benefits

• A wide variety of analyses is possible
  – Cumulative Percent Revision (Kaplan Meier Survivorship)
  – Breakdown of revision rates among particular patient populations, implant types, etc.

• Completeness of data arising from “opt out” method of enrolment

• Comprehensive outcome reports

• Online access to data
The AOANJRR: Limitations

• Privacy restrictions
  – The data can be used to track patients only in exceptional circumstances
    (NB: the TGA can get this information from other sources)

• Inaccurate coding
  – E.g. some evidence that loosening/lysis, pain, metal sensitivity are being used interchangeably
How the TGA uses AOANJRR data

- Prostheses with a Higher than Anticipated Rate of Revision
- Adverse Event and Complaint Investigations
- Pre-Market Assessment of Submissions
Prostheses with a higher than anticipated rate of revision

• Immediate regulatory action on identified prostheses is not appropriate
  – There are many reasons why the revision rate of a prosthesis is high, only some are related to the prosthesis
  – A prosthesis may also have redeeming features that make the higher revision rate “tolerable”

• Identification by the AOANJRR initiates an three stage investigation process that determines if the safety and performance of the implant is acceptable
Prostheses with a higher than anticipated rate of revision

1. The Sponsor/Manufacturer of the implant is invited to make a submission relating to the safety and performance of the implant.

2. A group of orthopaedic experts considers the information from the AOANJRR and the Manufacturer: Advises the TGA about safety, performance and benefits that may compensate for the high risk of revision.

3. The TGA considers the evidence AND the expert advice and makes a regulatory decision. Can be Recall, Hazard Alert, Safety Alert and/or Cancellation. Can also be do nothing.
Prostheses with a higher than anticipated rate of revision

In 2015 the AOANJRR identified 125 implant combinations (71 hips; 47 knees; 6 shoulders and 1 ankle) placing them into three categories:

<table>
<thead>
<tr>
<th>Category</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No Longer Used</strong> (74 Implants)</td>
<td>32 withdrawn from the market after TGA intervention</td>
</tr>
<tr>
<td></td>
<td>42 not supplied at the time they were identified</td>
</tr>
<tr>
<td><strong>Identified Prior to 2015, Still Used</strong></td>
<td>23 under observation after expert group advice.</td>
</tr>
<tr>
<td>(43 Implants)</td>
<td>12 subject of compliance action</td>
</tr>
<tr>
<td></td>
<td>8 still under investigation</td>
</tr>
<tr>
<td><strong>Newly Identified 2015</strong> (8 Implants)</td>
<td>5 under observation after expert group advice.</td>
</tr>
<tr>
<td></td>
<td>3 are being investigated</td>
</tr>
</tbody>
</table>
Adverse event and complaint investigations

- The TGA will routinely consider information available through the AOANJRR on-line portal during the investigation of implant adverse event reports.

**EVENT:** 2012 Device Incident Report; revision of an acetabular cup; triggers a routine query of the information held about the implant by the AOANJRR

**FINDINGS:** The Cumulative Percent Revision rises sharply 3 years after implantation. This was not yet manifested in a rise in the revisions per 100 observed years used by the AOANJRR to “identify” outliers

**OUTCOME:** Hazard Alert and contra-indication of the use of the device in total conventional hip replacements
Premarket assessment of submissions

• In the absence of direct clinical evidence, the TGA has used AOANJRR reports on clinically equivalent implants….
  … and predicates can work both ways

• Is the clinical study large enough? Is the minimum follow up long enough?
  – AOANJRR data on clinically equivalent implants can provide guidance
Conclusions

• Implant registries that can provide comparative analyses on outcomes are an invaluable tool for post-market vigilance and monitoring. Registry information is used for pre-market decisions as well.

  However: The outcome measures must be subjected to thorough clinical/technical assessment to ensure that appropriate regulatory measures are taken.

• Patient tracking is not particularly useful to Regulatory Agencies
  – The information can be obtained from other sources
  – In case of a problem, it is best for the patient to be contacted by a medical practitioner

  However: Outcomes registries will still need to track patients to ensure the integrity of the data analysis.