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Registry Data – Valuable Lessons but Beware the Confounders

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Abstract

A mature national joint registry with widespread adoption and audit can successfully demonstrate trends and influence future orthopaedic practice. Correlations can be identified; however, this should not be misinterpreted as causality. It is essential to consider confounding when analysing observational data sets.

This commentary serves to discuss what we have learnt from a mature national joint registry, its influence on orthopaedic practice, but also the limitations of observational data sets.

Outcomes have been measured as early as the earliest total hip arthroplasty (THA). Reporting on the Wiles THA in 1938 [1], which utilized screw fixation and a metal on metal head, "there was a measure of success in that those who were previously bed-ridden were thereby enabled just to walk." It was documented that "she had 20^{o} of active flexion." "The radiographs of their hips were destroyed during the war, not by enemy action but deliberately by those responsible for the care of hospital records." Not only does this highlight the low expectations at the time but the need for outcome data to be recorded independent of the surgeon or hospital.

Approximately 160,000 THA and total knee arthroplasty (TKA) procedures are performed in England and Wales each year. In the United States (US), more than one million THA and TKA are performed annually [2, 3], with over 7.2 million currently in-situ in the general population [4]. Arthroplasty datasets are widely used at surgeon, hospital, hospital owner [5], national [6] and international [7] level. National arthroplasty registries are utilised by many countries such as Denmark, Norway, Sweden, Catalonia, Portugal, Australia, New Zealand, and Canada.

The National Joint Registry (NJR) of England, Wales, Northern Ireland and the Isle of Man was created in 2003 to identify implants with high failure rates, and is currently the largest registry, with more than 2.1 million entries [I]. More than 800,000 primary hip arthroplasties and 90,000 revision hip arthroplasties are recorded in the NJR. It is broadly adopted with over 95% of primary THAs entered into the registry. Since 2006, using revision data, the percentage of cases that can be linked to the primary arthroplasty has increased [8]. A number of external studies have investigated the validity of data within the NJR [8, 9].

In comparison, the American Joint Replacement Registry (AJRR) is in its infancy. Since its inception in 2010, it has documented approximately ~550,000 joint arthroplasties, only representing 7-8% of those implanted [6].

The NJR [10] has been able to show the trends in fixation, bearing surfaces, demographics and complications.

Fixation

The changing use of implant fixation has been documented and observed. Figure 1. There was a steady fall in cemented fixation between 2003 and 2009 where levels have plateaued at 30%. Uncemented fixation remains the most popular at 39% but there has been a steady increase in hybrid fixation from 2010 to 26%.

Bearing Surfaces

Trends in selection of bearing surfaces for uncemented primary hip arthroplasties have shown marked fluctuations. Figure 2. Metal-on-metal (MoM) bearings increased in popularity from 2003, peaking in 2007 at 30% usage. There was a sharp decline from 2008 to 2011 where it has remained at 1%. This decline coincided with more favourable use of ceramic-on-ceramic (CoC) and ceramic-on-polyethylene (CoP) bearings. Metal-on-polyethylene (MoP) has consistently remained a widely used bearing surface, currently the most popular at 40% usage.

The trends in bearing surface utilisation on the NJR reflects known changes in practice such as the decline of MoM hips in 2007 following widespread concern in the orthopaedic community and the re-adoption of polyethylene bearings with use of highly cross linked polyethylene. The increased use of ceramic femoral heads maybe due to concerns regarding taperosis and higher patient demands in both the UK and USA.

Revision Rates

The emergence of highly cross linked polyethylene has seen a dramatic reduction in revision rate for loosening. In contrast to MoM, the revision data up to 15 years confirms that this innovation has worked. [11] Figure 3. MoM bearing surfaces have overall poorer outcomes, with 12-year revision rates of 20% compared to <5% for all other bearing surfaces. Overall cumulative revision rate follows a linear progression, after an initial spike within 3 months consistent with early complications such as dislocation, infection and fracture. When compared to primary arthroplasty surgery, revision arthroplasty have a higher failure rate nearing 15% at 10 years.

The risk of re-revision was examined in patients who required revision surgery of their primary arthroplasty. Two groups were compared; those with primary arthroplasty listed on the NJR and those without. This comparison demonstrated that those listed on the NJR had a significantly higher 10-year re-revision rate. Those listed on the NJR are likely to have had their primary surgery after 2003, and therefore earlier failure. Observation of these trends demonstrates that early failure significantly increases the risk of re-revision. A review of multiple joint registries reported that 30-50% of arthroplasty failures occurred in the first one to two years[12] suggesting catastrophic failure due to sepsis, gross malpositioning, dislocation or fracture. This stresses the importance of getting it right the first time [13].

Demographic Outcomes

The UK National Institute of Clinical Excellence Guidelines [14] suggest that 95% of hip replacements should last at least 10 years. Review of the NJR [10]indicates that only males over 75 and females over 65 achieve this threshold. Figure 4. Generally younger patients have a higher revision rate and women in particular do poorly, with a 10-year revision rate in the under 55s of over 12.5%. The higher revision rates for females undergoing MoM identified using NJR data has been used to change practice [10] and policy [15] to the extent that in 2013 almost 99% of hip resurfacings were performed in men only. If MoM hips are excluded, the revision risk is slightly greater in males than females at around 5% at 10 years in those <55 years old. Figure 5.

The underlying aetiology of hip disease requiring THA in younger patients may explain the higher revision rate. Corrected or uncorrected dysplasia, adaptive gait patterns, abnormal version and offset may result in an unfavourable biomechanical environment compared to osteoarthritis in the elderly. Higher activity levels and expectations further compound arthroplasty in the younger patient.

Linking Databases

Linking good quality databases enables investigators to answer complex questions. Case reports and basic science data commented that the release of metal ions from metal on metal hip replacement and from taperosis is carcinogenic and that patients with these devices may increase a patient's cancer risk. [16]

Smith et al [17] using (Hospital Episode Statistics) (HES) data concluded that compared to an age and sex matched population, patients who have a total hip replacement, have a lower incidence of cancer (1.25% vs 1.65%). Resurfacing MoM procedures were less likely to get a diagnosis of any cancer and a lower risk of death than any other bearing surface.

The risk ratio of heart failure, cancer and mortality were 0.389, 0.624 and 0.389 respectively in patients who underwent MoM hip arthroplasty compared with controls. [17]

Confounding

There is a danger of using large observational data series to make erroneous conclusions. Correlations can be identified but causation cannot be concluded. For example, 'people with grey hair have a higher risk of cancer' therefore 'grey hair causes cancer'. Clearly these statements hold no scientific merit but misinterpreting observational data is commonplace, particularly to make headlines in the lay press.

It is a valid observation that patients taking anti-epileptics have a 50 times greater risk of having a seizure than a matched population. Figure 6. They are confounded by their indication [18]There is a four times risk of dying in the three months following stopping a statin. The risks and benefits of statins extend beyond the scope of an orthopaedic readership but why would a physician stop a low risk preventative medication? Figure 7. This observation is confounded by patients being placed on a palliative care pathway for terminal illness. Similarly the risk of rheumatoid arthritis is five times greater in NSAID takers and the risk of being hospitalised with pneumonia is nine times higher in patients prescribed amoxicillin. On a lighter note, if you have seen a doctor, the risk of dying within the next two weeks is 30 times higher! Table 1.

There is always some confounding and when analysing observational data it is important to consider this especially if the authors are biased towards an exciting headline.

Orthopaedic data comparison is often age matched but within our scope of practise we see 70 year olds running marathons and 50 year olds walking 10 yards with a Zimmer frame. Patient expectation is multifactorial and can not be easily statistically controlled for. Revision rate particularly of an implant perceived to be easily revised may be increased, not because it is mechanically inferior or defective but because its indication is in high functioning, high demand patients. However this rationale was used by metal on metal hip manufacturers to defend a product which we subsequently know has design concerns.

Conclusion

In summary, registry data and large datasets can be an asset to arthroplasty surgeons, manufacturers and policy makers to identify trends and outcomes. The NJR is successful due to widespread adoption and auditing to ensure high quality, representative data is reported.

Analysis of the NJR has highlighted that total hip arthroplasty in young patients lags behind surgeons and policy maker's expectations. The choice of bearing surface, fixation technique and role of centralisation of this complex subgroup continues to be debated. This may be an opportunity to use technology to improve outcome to meet an unmet need. The rate of re-revision is greater if the revision occurred closer to the primary arthroplasty suggesting revision for indications other than aseptic loosening are less likely to be successful.

Big data can be very powerful. [19] Linking databases can answer complex questions across a range of conditions than a single database. However, small data-sets, data mining and over interpretation can result in incorrect conclusions. Observational data may demonstrate a correlation but does not prove causality. It is important to critically analyse the population characteristics, complexity and risk factors for outcomes. It is beholden on us all who interpret large observational datasets to make sure they have considered confounding.

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Figures

Figure 1. Fixation method used in primary hip replacements. [10]

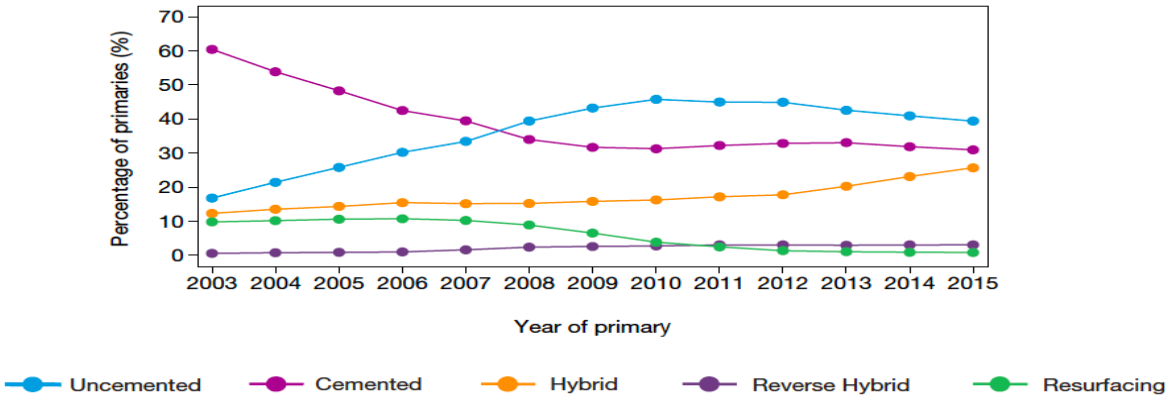


Figure 2. Bearing Surface used in uncemented primary hip replacements. [10]

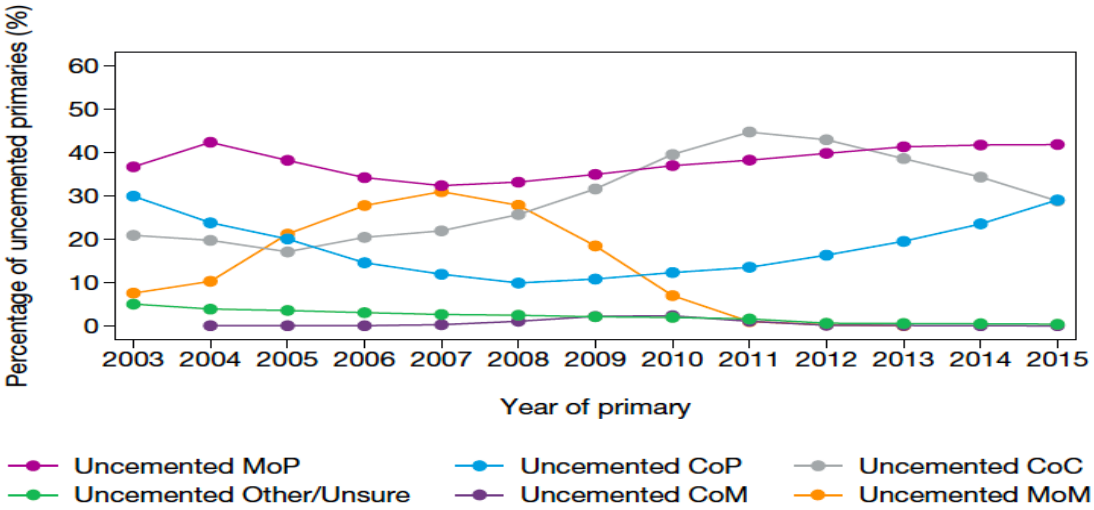


Figure 3. Comparison of revision data comparing cross-linked versus non cross-linked polyethylene. [11]

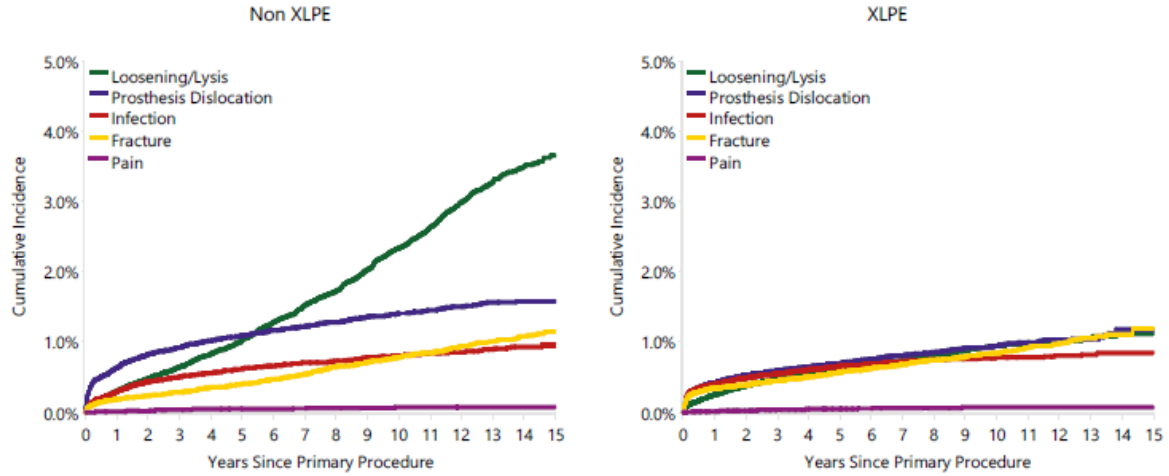


Figure 4. Revision Rate by age group comparing males and females. [10]

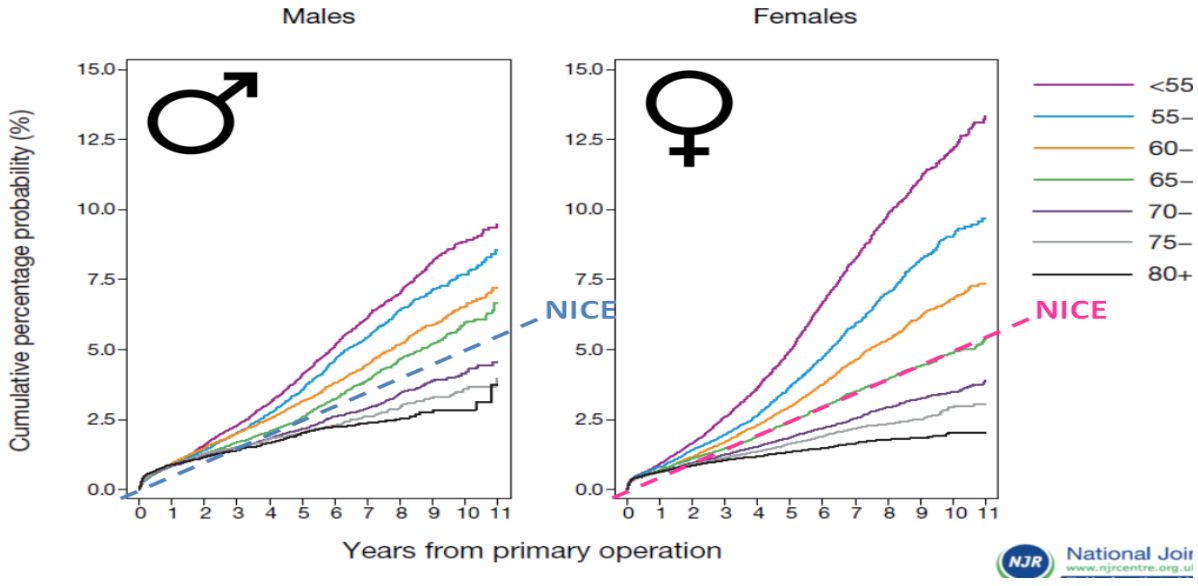


Figure 5. Revision Rate, excluding metal on metal, by age group comparing males and females. [10]

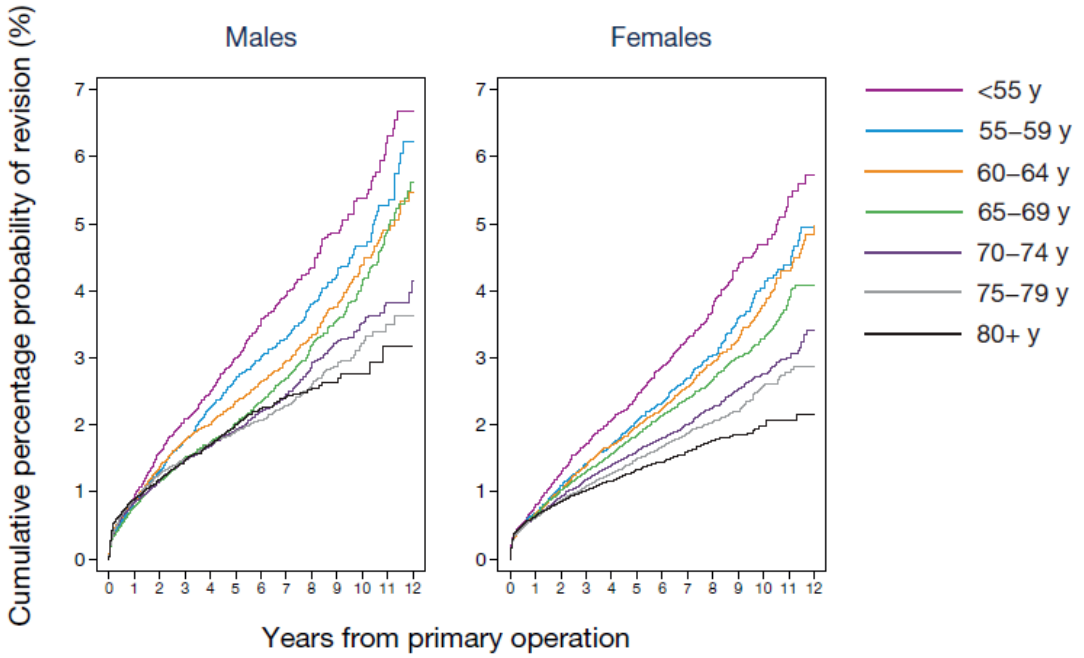


Figure 6. Health outcomes are confounded by indication for intervention.

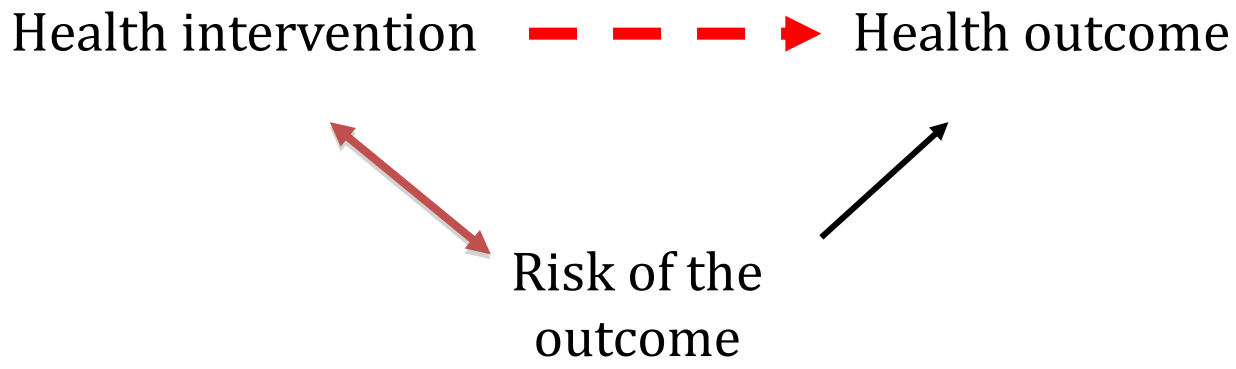
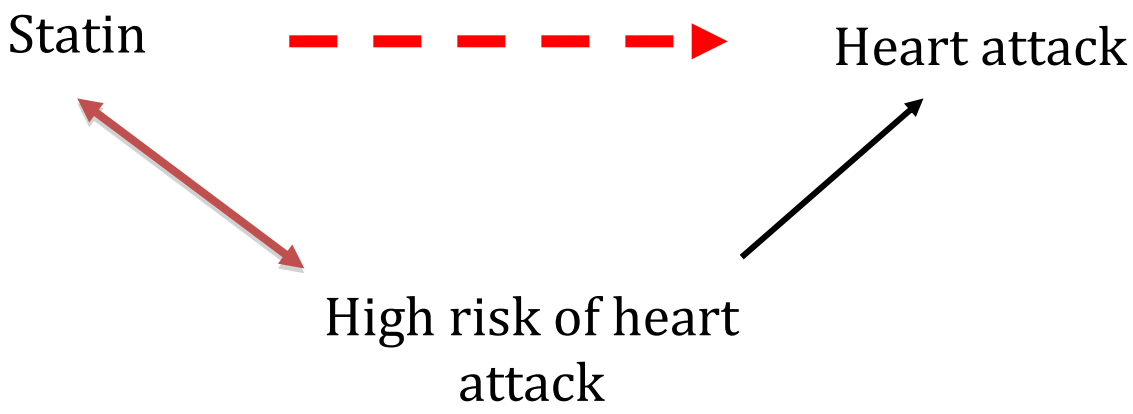


Figure 7.



306 Table 1. Risk of outcome confounded by indication.

Intervention	**Outcome**	**Risk**
Anti-epileptics	Seizure	50x
NSAIDS	Rheumatoid Arthritis	5x
Amoxicillin	Hospitalization Pneumonia	9x
Stopping statins	Death within 3 months	4x
Seeing a doctor	Death within 2 weeks	30x

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