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Corresponding Author: Mr. John Stammers, MBBS, BSc (hons), FRCS (Orth)

Corresponding Author's Institution: The Royal National Orthopaedic Hospital

First Author: John Stammers, MBBS, BSc (hons), FRCS (Orth)

Order of Authors: John Stammers, MBBS, BSc (hons), FRCS (Orth); Alex Kuo; Alister Hart, MA, MD, FRCSG(Orth); Liam Smeeth, MBChB FRCGP FFPH FRCP MSc PhD FMedSci; John A Skinner, MBBS, FRCS (Eng), FRCS (Orth)

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Registry Data – Valuable Lessons but Beware the Confounders

John Stammers¹ MBBS, BSc (Hons), FRCS (Orth)

Alex Kuo²

Alister Hart¹ MA, MD, FRCSG(Orth)

Liam Smeeth³ MBChB FRCGP FFPH FRCP MSc PhD FMedSci

John Skinner¹ MBBS, FRCS (Eng), FRCS (Orth)

1. UCL Institute of Orthopaedics and Musculoskeletal Science and the Royal National Orthopaedic Hospital. Brockley Hill, Stanmore, Middlesex, HA7 4LP, United Kingdom.
2. Medical Student. University of Western Sydney. Parramatta NSW 2150, Australia.
3. London School of Hygiene and Tropical Medicine. Keppel St, London WC1E 7HT, United Kingdom.

Corresponding Author

John Stammers
The Royal National Orthopaedic Hospital,
Brockley Hill
Stanmore,
Middlesex,
HA7 4LP
United Kingdom

Tel 02089095621
Fax 02089095100

John.stammers@nhs.net

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Registry Data – Valuable Lessons but Beware the Confounders

31 **Abstract**

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

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

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

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

76 The National Joint Registry (NJR) of England, Wales, Northern Ireland and the Isle of Man was
77 created in 2003 to identify implants with high failure rates, and is currently the largest registry, with
78 more than 2.1 million entries [1]. More than 800,000 primary hip arthroplasties and 90,000 revision
79 hip arthroplasties are recorded in the NJR. It is broadly adopted with over 95% of primary THAs
80 entered into the registry. Since 2006, using revision data, the percentage of cases that can be linked
81 to the primary arthroplasty has increased [8]. A number of external studies have investigated the
82 validity of data within the NJR [8, 9].

83 In comparison, the American Joint Replacement Registry (AJRR) is in its infancy. Since its inception in
84 2010, it has documented approximately ~550,000 joint arthroplasties, only representing 7-8% of
85 those implanted [6].

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

88 **Fixation**

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

93 **Bearing Surfaces**

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

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

105 **Revision Rates**

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

113 The risk of re-revision was examined in patients who required revision surgery of their primary
114 arthroplasty. Two groups were compared; those with primary arthroplasty listed on the NJR and
115 those without. This comparison demonstrated that those listed on the NJR had a significantly higher
116 10-year re-revision rate. Those listed on the NJR are likely to have had their primary surgery after
117 2003, and therefore earlier failure. Observation of these trends demonstrates that early failure
118 significantly increases the risk of re-revision. A review of multiple joint registries reported that 30-
119 50% of arthroplasty failures occurred in the first one to two years[12] suggesting catastrophic failure
120 due to sepsis, gross malpositioning, dislocation or fracture. This stresses the importance of getting it
121 right the first time [13].

122 **Demographic Outcomes**

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

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

136 **Linking Databases**

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

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

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

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148 **Confounding**

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

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

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

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

172 **Conclusion**

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

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

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

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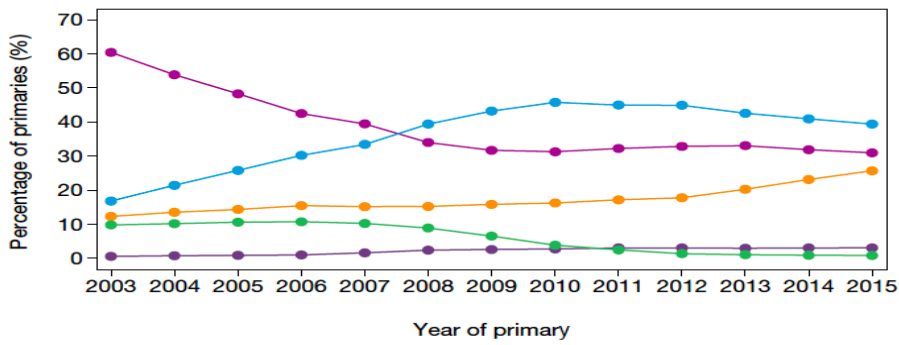
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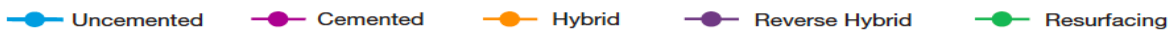
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Figures

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

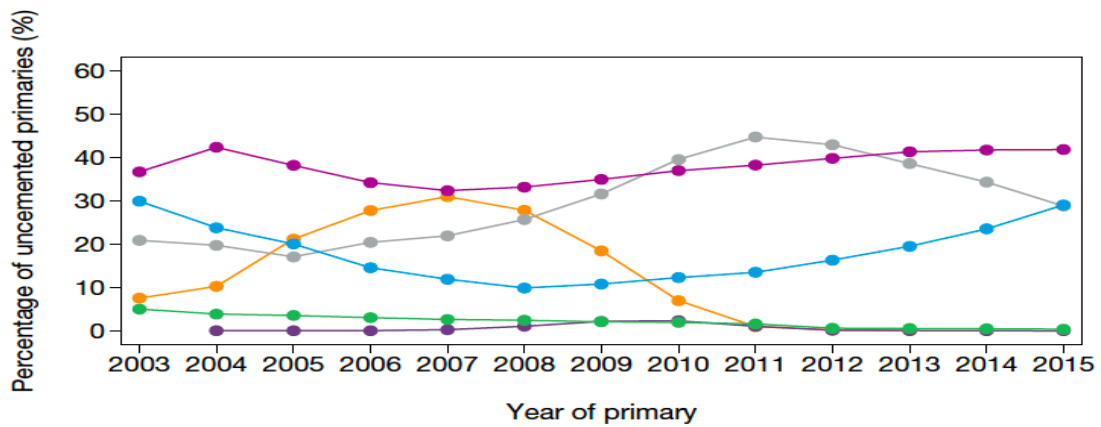


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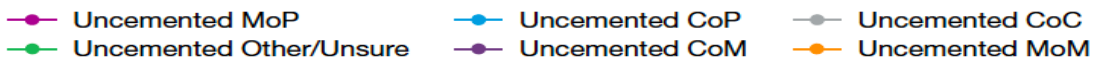


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278 Figure 2. Bearing Surface used in uncemented primary hip replacements. [10]

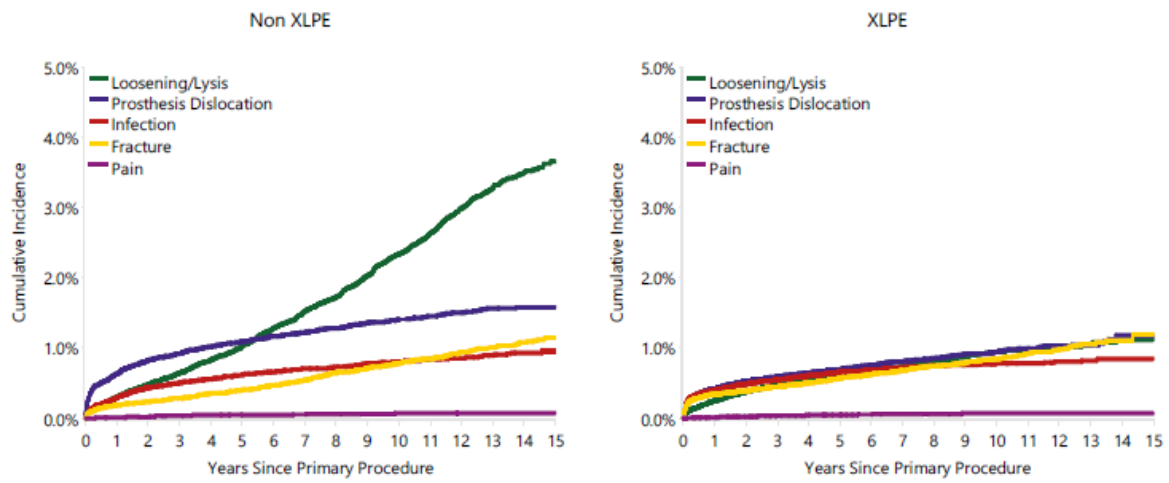


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281 Figure 3. Comparison of revision data comparing cross-linked versus non cross-linked polyethylene.
 282 [11]

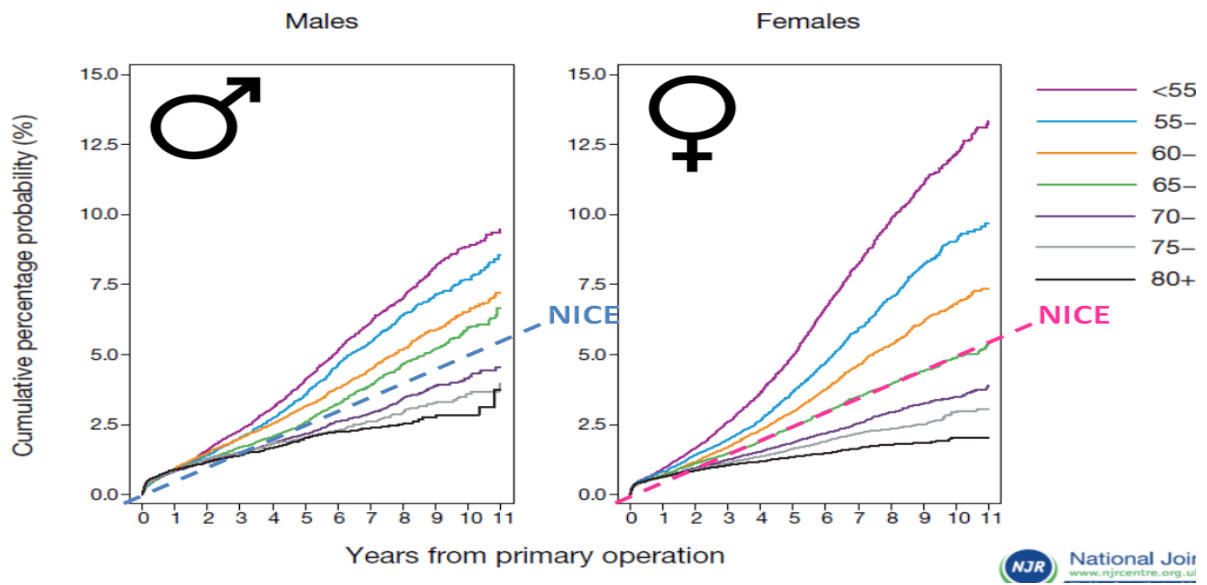


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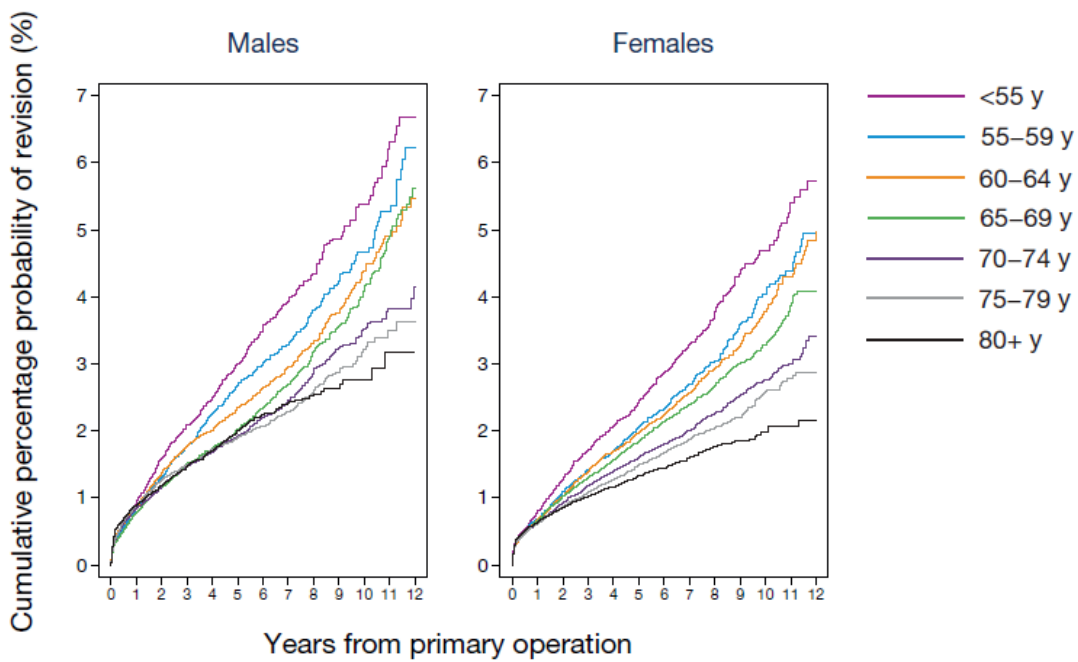
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286 Figure 4. Revision Rate by age group comparing males and females. [10]



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



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290

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

292

293 Health intervention  Health outcome

294

295

296  Risk of the
297 outcome

298

299 Figure 7.

300 Statin  Heart attack

301

302

303

304  High risk of heart
305 attack

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

307