MINIMUM REQUIREMENTS, CLINICAL PRACTICE AND LESSONS LEARNT FROM THE PAST

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Consultant Arthroplasty Surgeon
Chairman Bone and Joint Publishing
ODEP and Beyond Compliance Member
Past President of BOA
DECLARATION OF INTERESTS

- I think we should all recognise that we are biased!
- Past BOA President
- Past President of BASK
- Previous member NJR Steering Committee
- Previous member NJR MAC
- Previous member MHRA Medical Devices Committee
- Member of ODEP and Beyond Compliance
- Previous paid Consultant to Smith and Nephew Designer Surgeon Journey Knee
- On speaker Panel for S&Nephew, Zimmer Biomet, Stryker
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IS THERE A PROBLEM WITH OUR MONITORING OF IMPLANT PERFORMANCE?

- Over the years systems have failed to detect problems EARLY with numerous implants:
  - Teflon “Charnley” Sockets 1960’s
  - Alteration of Exeter to Matt Stem 1970’s
  - Irradiated POLY in the knee leading to delamination wear 1980’s
  - Heat pressed POLY leading to delamination wear 1990’s
  - 3M Capital Hip 1990’s
  - M-O-M Hips 2000’s
  - FOOLISH TO ASSUME NO LONGER A PROBLEM!!
WHY SO AFTER ALL THIS TIME?

• It’s Complicated!

• Different failure modes occur at different times

• Implants are introduced at different rates

• Patient and surgeon factors contribute much to failure rates

• Changes in practice during the use of an implant can change the failure mode/rate
SURGEONS GENERALLY ASSUME

- An Implant available on open market has been tested adequately

- They are free and SAFE to use an implant that is so offered

- They can rely on the information put out by Industry about their implants because
  - 1) Regulatory Bodies have already assessed the device
  - 2) Advertising Standards demand and ensure such information is truthful and accurate
SOME OF THESE ASSUMPTIONS ARE NOT VALID!
SURGEONS NEED TO KNOW

• That new implants have been adequately assessed for clinical efficacy and durability

• That new implants are being monitored to ensure that unexpected failure modes are picked up in timely fashion

• That lessons have been learnt from past failures of monitoring

• That a new implant is at least as safe as the predecessors
WE NEED REASSURANCE

• That new implants have been clinically proven **BEFORE** they are available on the open market

• That **PROBLEMS** and **DEFECTS** will be identified as **EARLY** as possible

• That these **PROBLEMS will be OPENLY admitted and shared with surgeons as **SOON** as Company or Regulator is aware
MINOR DESIGN CHANGES?

- Exeter Cemented Polished tapered stem introduced 1970 with excellent results

- Identical ‘matt’ finish stem from 1978-85 for commercial reasons of cosmetic appearance

- Disastrous increase in aseptic loosening!!

- Would “MATT” stem now be allowed an automatic CE MARK based on similarity to the predicate?
PAST PROBLEMS

• ASR resurfacing – Significant changes in the “minutiae” of the design compared to BHR
ASR ‘DESIGN MODIFICATIONS’ COMPARED TO BHR

- Different Metal
- Thinner shell
- Bevelled edge
- Less area of femoral head covered
- Smaller clearance
COULD WE HAVE SEEN IT COMING?

- Prototype BHR was unashamedly ‘Novel’ although contained elements of the M-O-M designs of the 1960’s

- Prototypes also drew on elements of double cup arthroplasty

- TWO early ‘Prototypes’ were discarded by the designer of the BHR: at least one because it had relatively high failure rates

- Some lessons from that re-design were NOT incorporated into the competitor’s designs and this was not challenged by the CE marking process NOR by the FDA
EARLY AND CAREFUL MONITORING

- It is not always clear even in retrospect why these minor changes cause problems

- No Surgeon Team of Designers is deliberately trying to design a less good implant

- No Implant Company is deliberately spending millions designing something to fail
MONITORING WILL THEREFORE REMAIN THE MAINSTAY OF DETECTING PROBLEMS AND MINIMISING IMPACT ON PATIENTS

• We can either monitor every implant closely

• OR FOCUS on Newer devices/changes
SOME FAILING IMPLANTS ARE OBVIOUS

- 3M THR failed by femoral loosening

- Often the surgeons had used the Charnley before and therefore were used to the follow-up appearance

- Some surgeons themselves observed within a few years that these stems loosened much more frequently

- THE SYSTEM DIDN’T

- Not ALL implant failures will be so simple to identify!!
INTRODUCTORY TKR IN UK

### Cumulative Procedures

- Yearly procedures from 2002 to 2019, showing a steady increase.

### Cumulative Surgeons and Centres

- Surgeons and centres over the same period, with a sharp rise from 2013 onwards.

### Year of Implantation Table

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
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<tr>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>7</td>
<td>9</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>24</td>
<td>1.5%</td>
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<td>192</td>
<td>252</td>
<td>410</td>
<td>701</td>
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<td>1611</td>
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<td>0</td>
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<td>202</td>
<td>257</td>
<td>421</td>
<td>704</td>
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</table>
SURVIVORSHIP – INTRODUCTORY IMPLANT

Endpoint: All reasons for revision

Cumulative Revision Rate

Implantation time / years

0.0% 1.0% 2.0% 3.0% 4.0% 5.0% 6.0% 7.0% 8.0% 9.0% 10.0%

0 2 4 6 8 10 12
## REASONS FOR REVISION

<table>
<thead>
<tr>
<th>Reason for Revision</th>
<th>Revised †</th>
<th>Expected Revisions *</th>
<th>p value</th>
</tr>
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<tbody>
<tr>
<td>Infection</td>
<td>5</td>
<td>4.28</td>
<td>0.625</td>
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<tr>
<td>Progressive Arthritis Remaining</td>
<td>9</td>
<td>0.71</td>
<td>&lt;0.001</td>
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<tr>
<td>Aseptic Loosening Femur</td>
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<td>0.83</td>
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<td>Aseptic Loosening Tibia</td>
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<td>1.98</td>
<td>0.456</td>
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<tr>
<td>Aseptic Loosening Patella</td>
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<td>0.46</td>
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<td>Pain</td>
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<td>1</td>
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<td>Stiffness</td>
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<td>1.60</td>
<td>0.217</td>
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<tr>
<td>Malalignment</td>
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<td>1.30</td>
<td>0.646</td>
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<tr>
<td>Instability</td>
<td>1</td>
<td>2.43</td>
<td>0.74</td>
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<tr>
<td>Dislocation / Subluxation</td>
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<td>0.49</td>
<td>1</td>
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<tr>
<td>Periprosthetic Fracture</td>
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<tr>
<td>Wear of Polyethylene Component</td>
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<tr>
<td>Lysis - Tibia</td>
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<tr>
<td>Lysis - Femur</td>
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<tr>
<td>Component Dissociation</td>
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<tr>
<td>Implant Fracture</td>
<td>0</td>
<td>0.06</td>
<td>1</td>
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<tr>
<td>Other / Not recorded</td>
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<td>1.16</td>
<td>0.323</td>
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<td><strong>Total Revised</strong></td>
<td><strong>24</strong></td>
<td><strong>14.80</strong></td>
<td><strong>0.026</strong></td>
</tr>
</tbody>
</table>

† multiple reasons may be listed for one revision procedure
* Adjusted for agegroup, gender and indications

Significantly better, p < 0.001
Significantly better, p < 0.05
Significantly worse p < 0.05
Significantly worse p < 0.001
FUNNEL PLOT SHOWING ALL TKR IN NJR
UNITS IMPLANTING IMPLANT UNDER SCRUTINY

![Graph showing revisions per 100 component years vs implant-years.](image-url)
PTIR FOR THIS IMPLANT

NJR DATA EXCLUDING single ‘outlier’ unit

WHERE THEY OFTEN DO NOT RESURFACE PATELLA

Revisions Per 100 Component Years

- 99.8% Upper limit
- 95% Upper Limit
- 95% Lower Limit

Journey II BCS Oxinium
PTIR - LEAD SURGEONS

ALL NJR

EXCLUDING LEAD SURGEONS THAT UNIT

Revisions
  Per
  100
  Component
  Years

Implant-Years

99.8%
Upper
limit

95%
Upper
Limit

99.8%
Lower
Limit

95%
Lower
Limit
PTIR FOR THIS IMPLANT

ALL SITES

EXCLUDING ‘outlier Unit’
ABILITY TO CHECK DETAILS

- Regulators MUST be able to access AND assess details to stratify results

- ‘Failures’ due to a subset of patients, MUST be identified as such and the information made available to surgeons immediately

- ‘Satisfactory’ Implants may “hide” Unsatisfactory subsets of patients

- ‘Unsatisfactory’ Implants may “hide” Satisfactory subsets of patients
KNEE IMPLANT WITH FAIRLY LARGE NUMBERS
SOME CONCERNS EXPRESSED ABOUT IMPLANT

Revision and Survivorship

Patient - Time Incidence Rate

All TKRs in NJR, by Brand

Need Large Numbers

Yellow diamonds show increasing revision rate of New Implant over first 10000 patient/years
DATA SHARING CAN INCREASE CERTAINTY

• Data sharing is difficult

• Patient identifiable data are unlikely to be shared freely between Nations and Registries

• Subsets of patients may exist in some countries and not in others

• Such subsets may be too small to give meaningful results in one registry

• MUST be able to follow-up suspicions arising in one place by interrogation of other countries’ registry data

• NETWORKS ALLOWING THIS TRANSFER OF ANONYMISED OUTCOME DATA IS VITAL
UNFORESEEN AREAS OF CONCERN

• Bearing Surfaces were not initially thought to be the issue when ODEP Ratings were started

• Trunnion problems have only recently come to light

• No Doubt there are further hidden issues in our future!

• ONLY ACTUALLY MEASURING OUTCOMES AS WE GO ALONG IS LIKELY TO FIND THESE PROBLEMS EARLY
HOW AND WHEN TO MEASURE?

- Revision Rates – Necessary but not Sufficient
- PROMS
- Functional Outcomes
- XRAYS? RSA?
FUNNEL PLOTS REVISION RATES
HOW AND WHEN TO MEASURE?

- “Real Time” Monitoring
- Delay in RCTs can be years or decades
- Registries report Annually - ie some results 2 years late!
- Active monitoring online should be the norm
PATIENT - TIME INCIDENCE RATE : CONFIDENCE INTERVALS

![Graphs showing patient-time incidence rate over time with confidence intervals.](image)
HOW AND WHEN TO MEASURE?

• Variable threshold depending upon risk assessment?

• Some implants OBVIOUSLY a significant risk

• Some APPEAR innocent

• Is it reasonable to follow some much more carefully than others?
HOW AND WHEN TO MEASURE: DURATION OF MONITORING

Using “Probability of becoming an outlier” charts?
WHEN TO MEASURE WHAT?

• Early failures are often Infection-related or technical errors

• Medium term failures may be implant related and often seem to dominate later...around 6-8 years post-op

• Implants are usually put in in much higher numbers between 5-10 years than in first 5 years, so many patients are at risk if we don’t notice problems by then!
CONFLICTS OF INTEREST

• The more time and money you spend inventing and developing something the more difficult it is to be scientifically objective.

• An entirely independent monitor of Implant Performance is therefore essential.

• There will always be debate as to whether the failures are process-related or implant-related.

• These are difficult for the design team to sort out fairly.
POLYETHYLENE WEAR RATES

• Wear performance improves with radiation dosage

• Improvements lost under microabrasive conditions
CROSSLINKED UHMWPE PROCESSING – KNEES
DATA FROM SMITH AND NEPHEW

<table>
<thead>
<tr>
<th>Tradename</th>
<th>Resin</th>
<th>Total Dose (Mrad)</th>
<th>Source</th>
<th>Heat Treatment</th>
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<tbody>
<tr>
<td>Biomet</td>
<td>E-Poly</td>
<td>?</td>
<td>10</td>
<td>?</td>
</tr>
<tr>
<td>DePuy</td>
<td>XLK</td>
<td>1020</td>
<td>5</td>
<td>Gamma</td>
</tr>
<tr>
<td>Stryker</td>
<td>X3</td>
<td>1020</td>
<td>3×3=9</td>
<td>Gamma</td>
</tr>
<tr>
<td>Zimmer</td>
<td>Prolong</td>
<td>1020</td>
<td>6.5</td>
<td>E-beam</td>
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</tbody>
</table>

*Note: Not on market*
WEAR IMPROVEMENT BY CROSS-LINKING

Radiation cross-linking reduces wear

*But the irradiation process introduces free radicals*

- **Decreases** resistance against mechanical-chemical aging
- **Decreases** important mechanical properties
- **Reduces** resistance to oxidation
- **Increases** brittleness

Non-crosslinked PE

85% reduction at 5 Mrads

95% reduction at 10 Mrads

Heisel et al. *JBJS: 85-A: 2003*
X3: WEAR RESISTANCE

Note for 6M cycles/yr debris load:
- Std PE is 208mm³/yr
- X3 is 44mm³/yr

NEW SEQUENTIALLY CROSSLINKED POLYETHYLENE X³™

- First generation irradiated and remelted polyethylene addressed the issue of wear at the expense of compromised mechanical properties
- X³™ - sequentially irradiated and annealed polyethylene is only highly cross-linked polyethylene that addresses issues of oxidation, wear and mechanical properties without compromise
  - Reduces wear debris generated by more than 79%
  - Eliminates delamination wear as a failure mode
  - More forgiving to malalignment
  - Has superior strength
## TKA CROSSLINKED PE MARKET (S&N)

<table>
<thead>
<tr>
<th>Material</th>
<th>GUR Resin</th>
<th>Dose (Mrad)</th>
<th>Thermal Treatment</th>
<th>Free Radicals</th>
<th>Oxidation</th>
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<tbody>
<tr>
<td>Smith &amp; Nephew XLPE</td>
<td>1020</td>
<td>7.5</td>
<td>Re-melt</td>
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<td>No</td>
</tr>
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<td>DePuy XLK</td>
<td>1020</td>
<td>5</td>
<td>Re-melt</td>
<td>No</td>
<td>No</td>
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<td>Zimmer Prolong</td>
<td>1020</td>
<td>6.5</td>
<td>Re-melt</td>
<td>No</td>
<td>No</td>
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<tr>
<td>Stryker X3</td>
<td>1020</td>
<td>9 = 3×3</td>
<td>Sub-melt</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>
KNEE WEAR RATES: SMITH AND NEPHEW

![Bar chart showing wear rates for different conditions: Virgin, 5 Mrad, 6.5 Mrad, 9 Mrad SQXL, and VERILAST. The chart compares wear rates between pristine and roughened conditions for each condition.](image-url)
WE RELY SOLELY ON INFORMATION FROM THE MANUFACTURER AT OUR PATIENTS’ PERIL

• BUT – surgeons all over the world are being told we cannot afford to follow-up our patients

• We can no longer rely on surgeons “noticing” that something is failing more frequently than it should be!!
IMPLANT COMPANIES

• Are keenly aware that there are significant differences between the results obtained by some surgeons and by others

• Have made huge investments and may understandably feel that the failures are surgeon-related

• Usually have ‘Evidence’ to support this view in the form of papers produced by their surgeon champions

• We have seen from the UK Registry Data how dramatic this effect can be!
IS IT SURGEON OR IMPLANT?

• We cannot accept that it is the surgeon on the Companies Say-so….or Vice Versa!

• We MUST have individualised data allowing separation of surgeon and implant outcomes

• If Revision is the problem, outcome needs testing against other parameters

• If some outcomes are good while others are bad : More study is required!
SMALL CHANGES ARE IMPORTANT!

• Many implants have been modified WITHOUT any mention

• Many have never been “re-trialled”

• Many have not had close scrutiny of the changes outside the company….not even by the Notified Body

• We have the opportunity to put this right within Europe

• The New Device Regulations will not achieve this on their own
PARALLEL REGULATORY FAILINGS

• A massive tower block burnt down last year in London killing 76 people

• The cosmetic plastic cladding has been blamed for spreading the inferno

• Today it was announced that the cladding, “Reynobond” had an ‘Official’ rating of “B” where “A” is good and “F” is bad

• Another testing agency had awarded it an “E” and a third agency a “C”

• “Official” agency say they were never told of changes to the material used in the cladding by the manufacturer who knew of all these ratings and changes
REFLECTION OF P.I.P BREAST IMPLANTS?