MINIMUM REQUIREMENTS, CLINICAL PRACTICE AND LESSONS LEARNT FROM THE PAST

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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

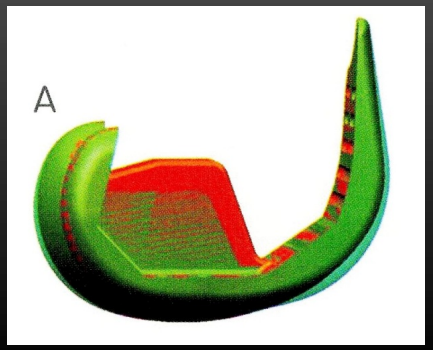
- FOOLISH TO ASSUME NO LONGER A PROBLEM!!

WHY SO AFTER ALL THIS TIME?

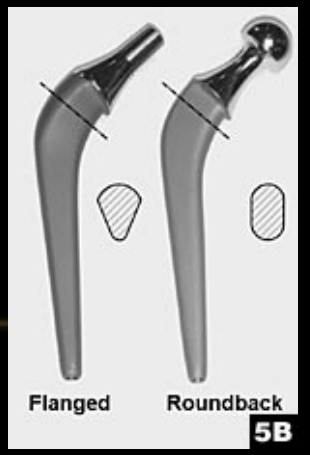
- It's Complicated!
- Different failure modes occur at different times
- Implants are introduced at different rates
- Patient and surgeon factors contribute much to failure rates
- Changes in practice during the use of an implant can change the failure mode/rate

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

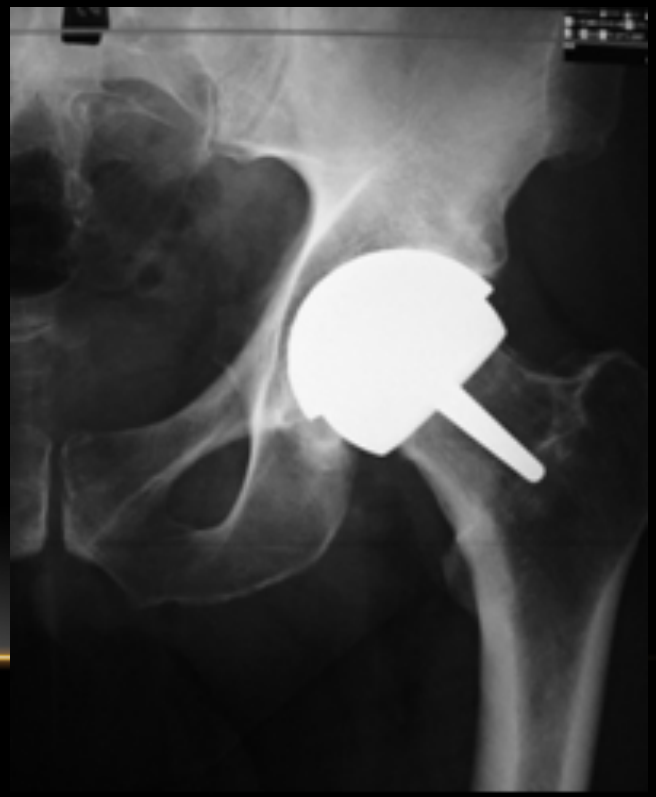
- That new implants have been clinically proven BEFORE they are available on the open market
- That PROBLEMS and DEFECTS will be identified as EARLY as possible
- That these PROBLEMS will be OPENLY admitted and shared with surgeons as SOON as Company or Regulator is aware

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

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

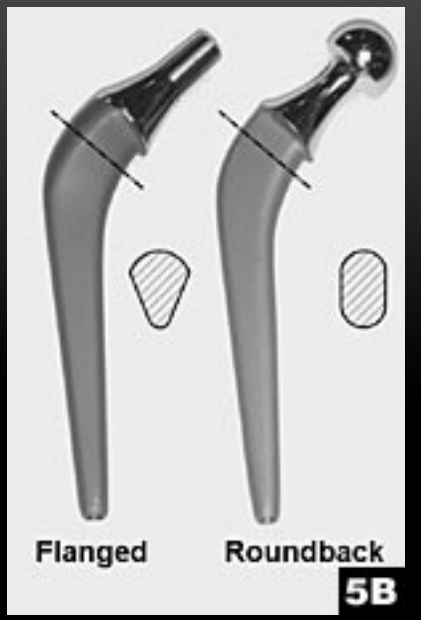
EARLY AND CAREFUL MONITORING

- 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

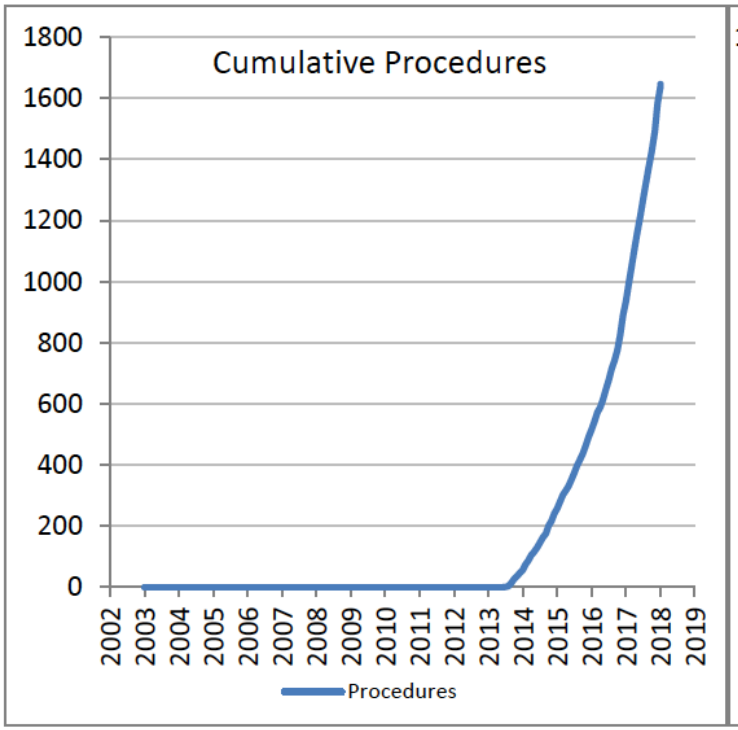
- We can either monitor every implant closely
- OR FOCUS on Newer devices/changes

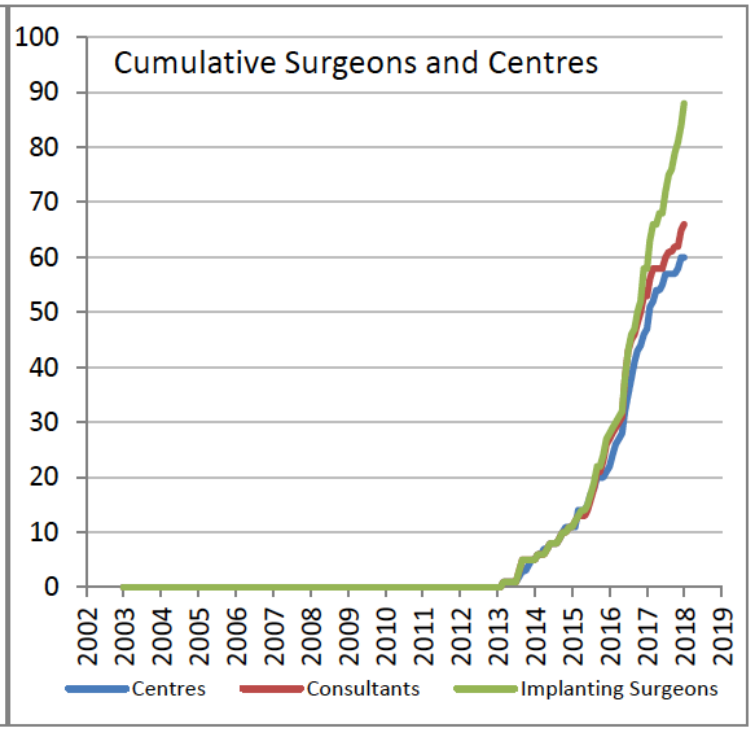
SOME FAILING IMPLANTS ARE OBVIOUS



- 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!!

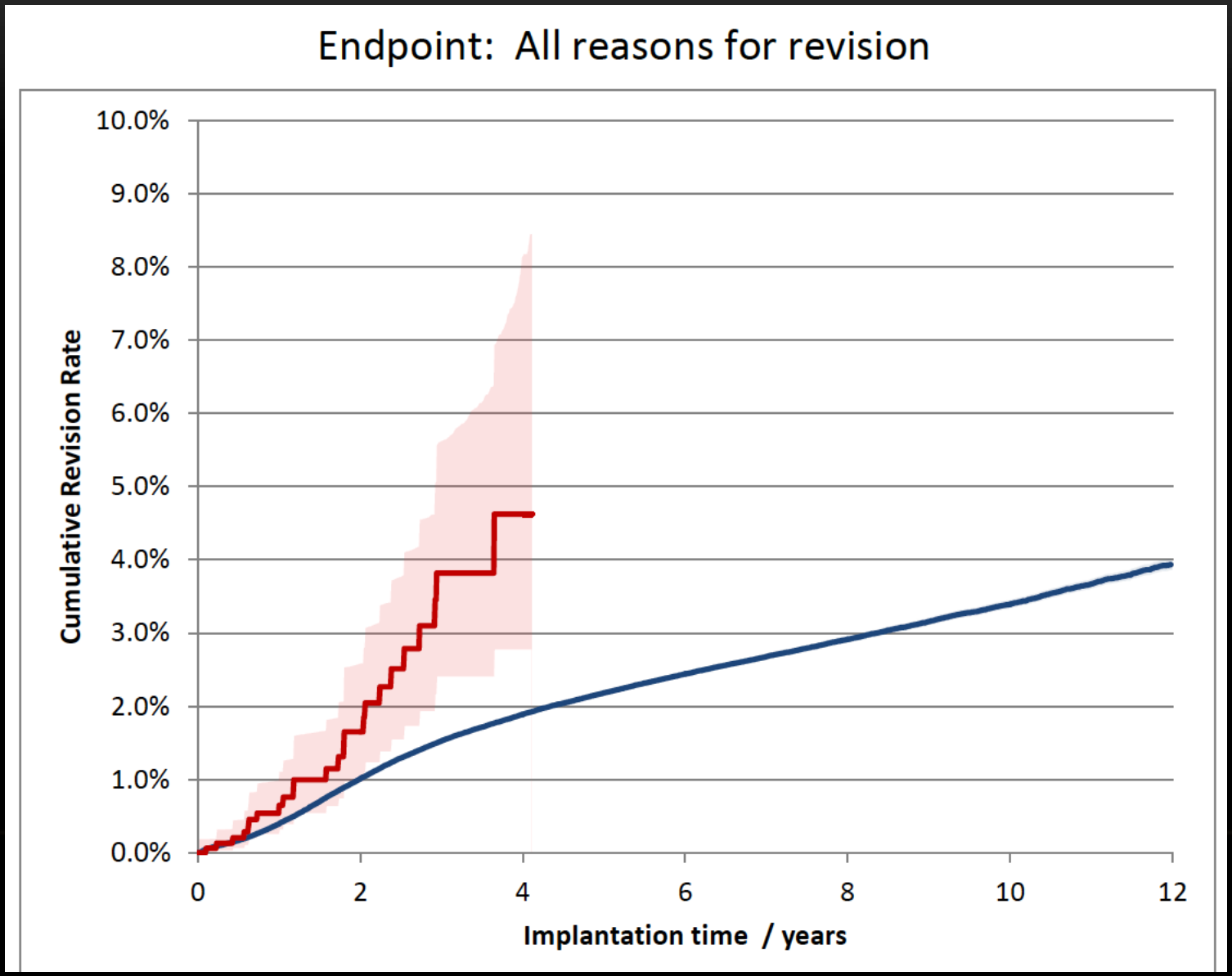
INTRODUCTORY TKR IN UK





	Year of implantation														
Current Outcome	Pre-2007	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	Total	%
Death	0	0	0	0	0	0	0	0	1	5	4	2	0	12	0.7%
Revised	0	0	0	0	0	0	0	7	9	0	7	1	0	24	1.5%
Unrevised	0	0	0	0	0	0	0	49	192	252	410	701	7	1611	97.8%
Total	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**56**	**202**	**257**	**421**	**704**	**7**	**1647**	**100%**

SURVIVORSHIP – INTRODUCTORY IMPLANT



REASONS FOR REVISION

Reason for Revision	Revised †	Expected Revisions*	p value
Infection	5	4.28	0.625
Progressive Arthritis Remaining	9	0.71	<0.001
Aseptic Loosening Femur	0	0.83	1
Aseptic Loosening Tibia	3	1.98	0.456
Aseptic Loosening Patella	0	0.46	1
Pain	2	2.49	1
Stiffness	3	1.60	0.217
Malalignment	0	1.30	0.646
Instability	1	2.43	0.74
Dislocation / Subluxation	0	0.49	1
Periprosthetic Fracture	0	0.34	1
Wear of Polyethylene Component	0	0.26	1
Lysis - Tibia	0	0.39	1
Lysis - Femur	0	0.23	1
Component Dissociation	0	0.12	1
Implant Fracture	0	0.06	1
Other / Not recorded	2	1.16	0.323
Total Revised	**24**	**14.80**	**0.026**

† multiple reasons may be listed for one revision procedure

* Adjusted for agegroup, gender and indications

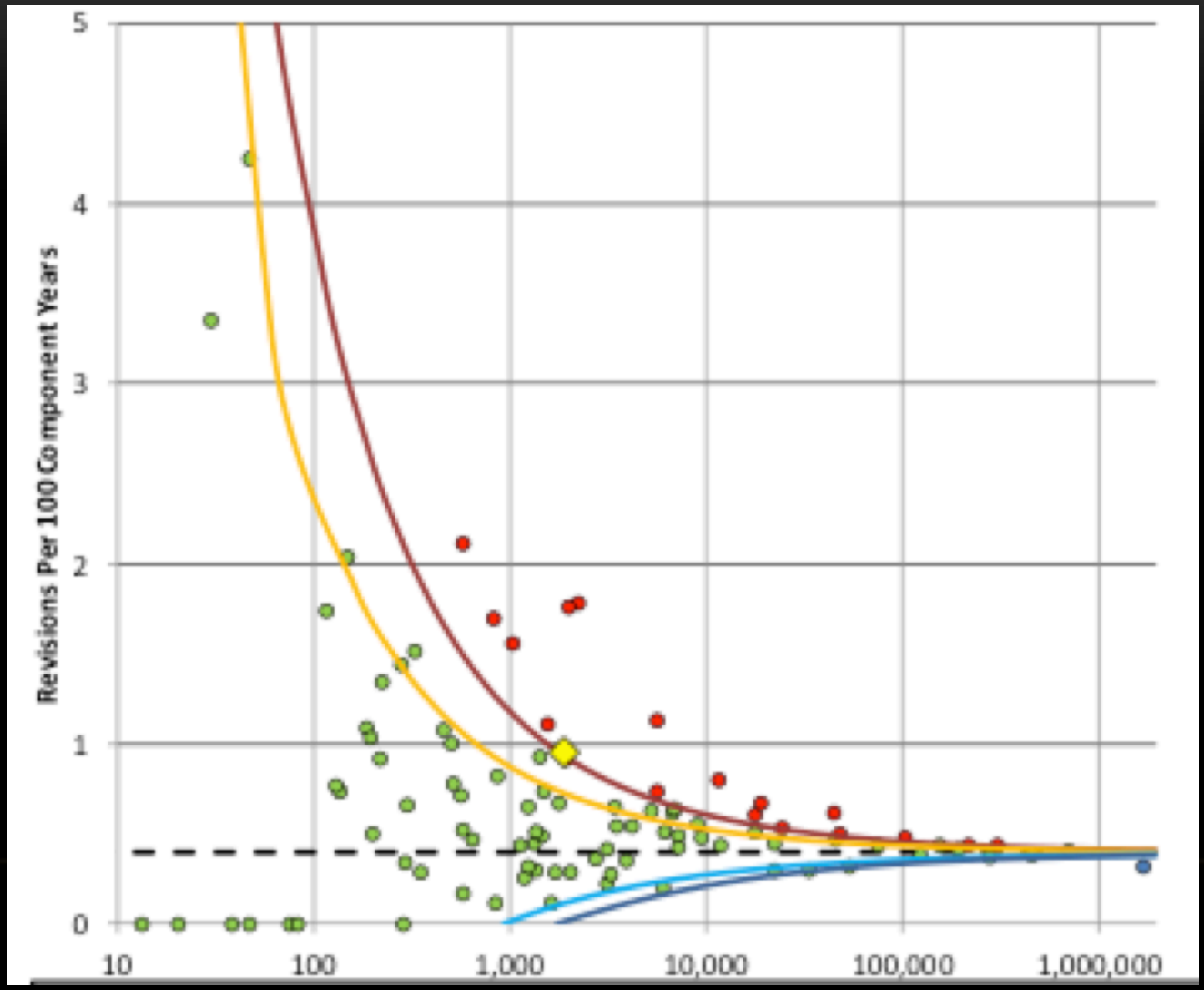
Significantly better, $p < 0.001$

Significantly better, $p < 0.05$

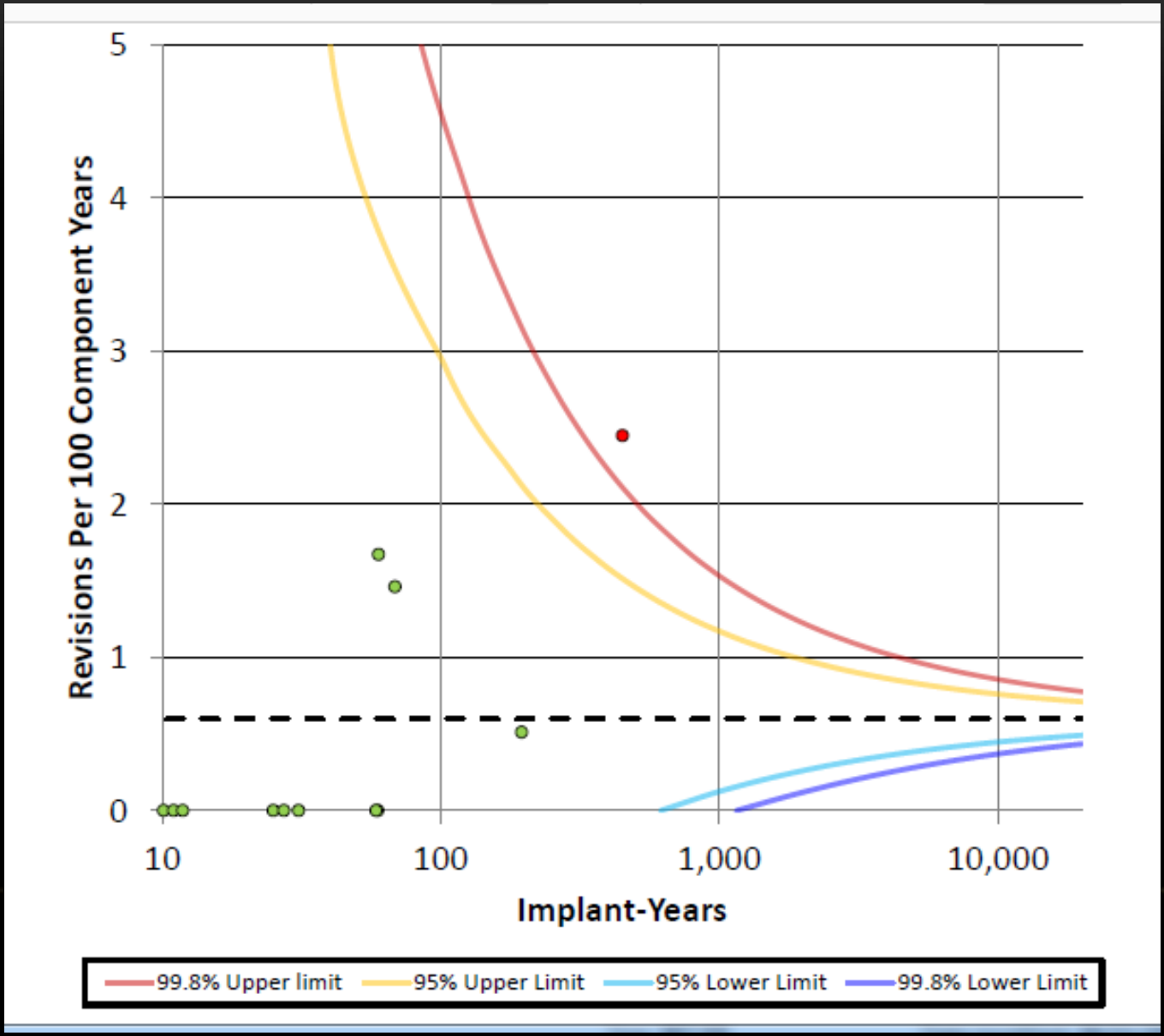
Significantly worse $p < 0.05$

Significantly worse $p < 0.001$

FUNNEL PLOT SHOWING ALL TKR IN NJR

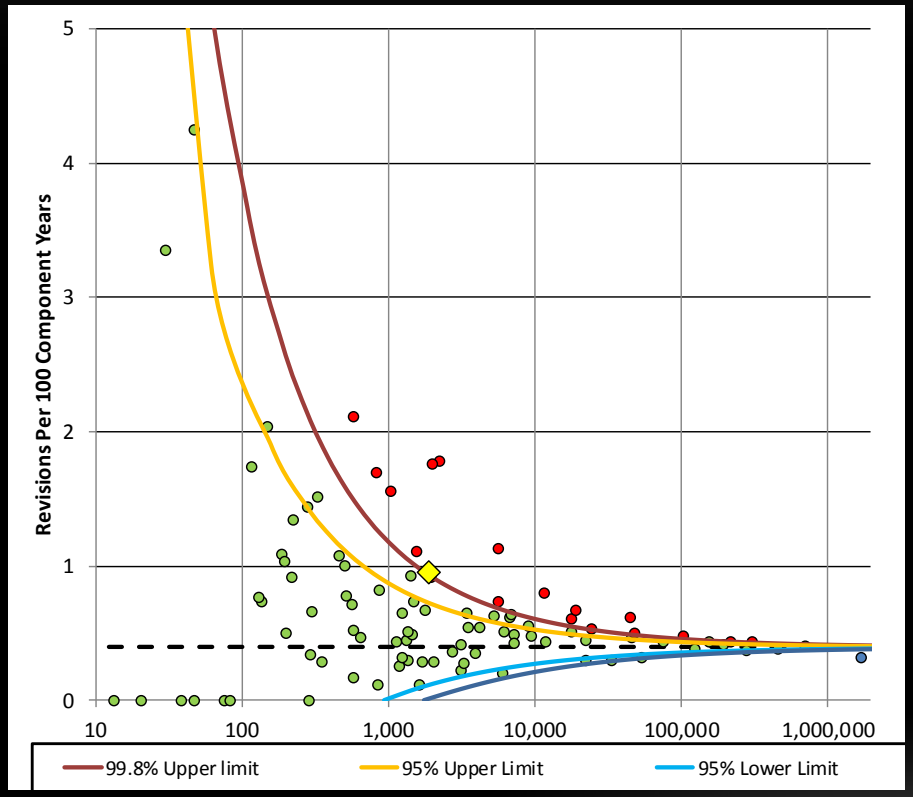


UNITS IMPLANTING IMPLANT UNDER SCRUTINY



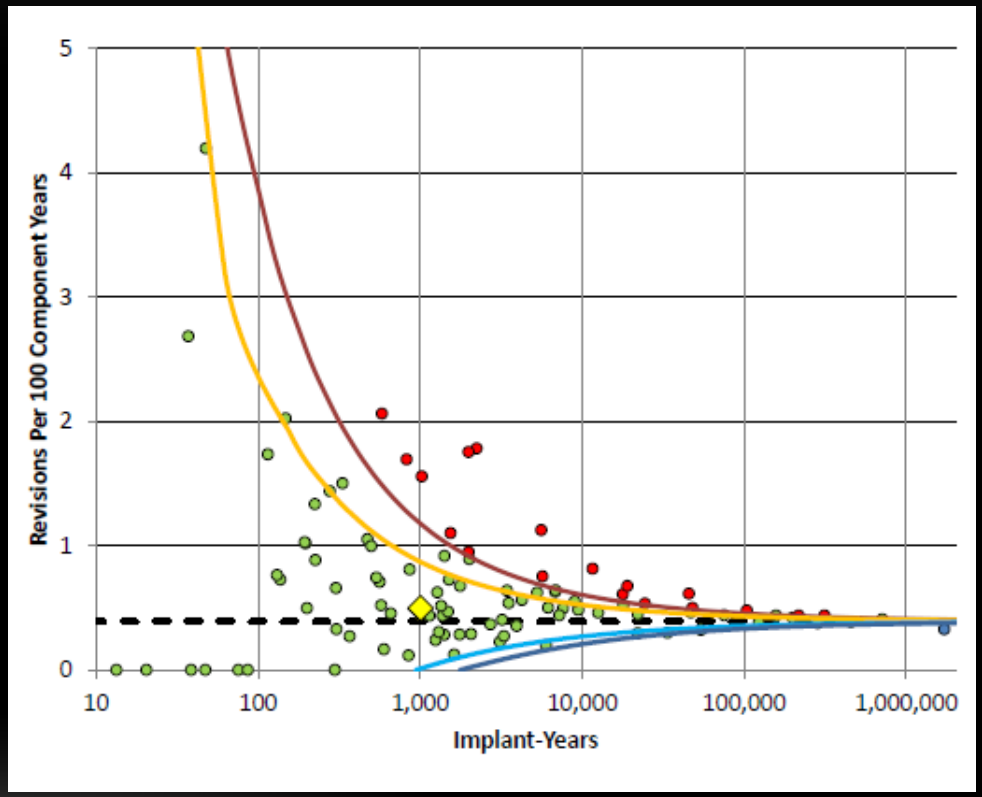
PTIR FOR THIS IMPLANT

ALL NJR DATA



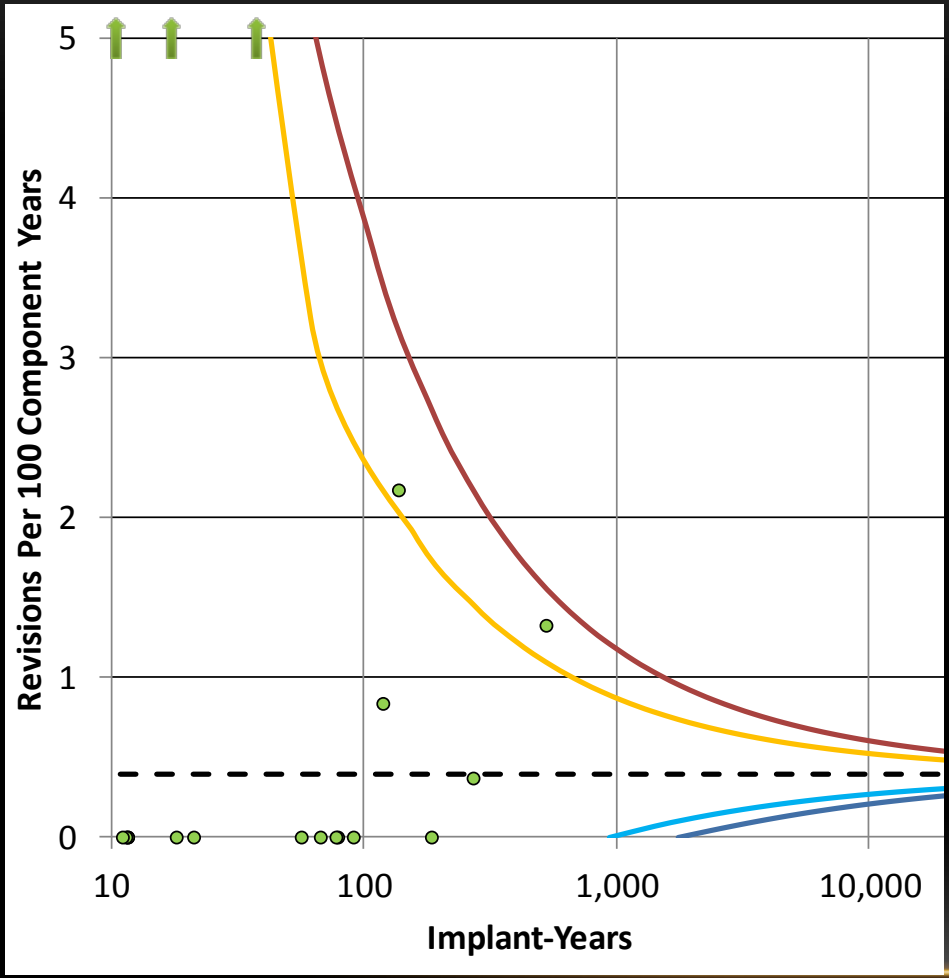
NJR DATA EXCLUDING single 'outlier' unit

WHERE THEY OFTEN DO NOT RESURFACE PATELLA

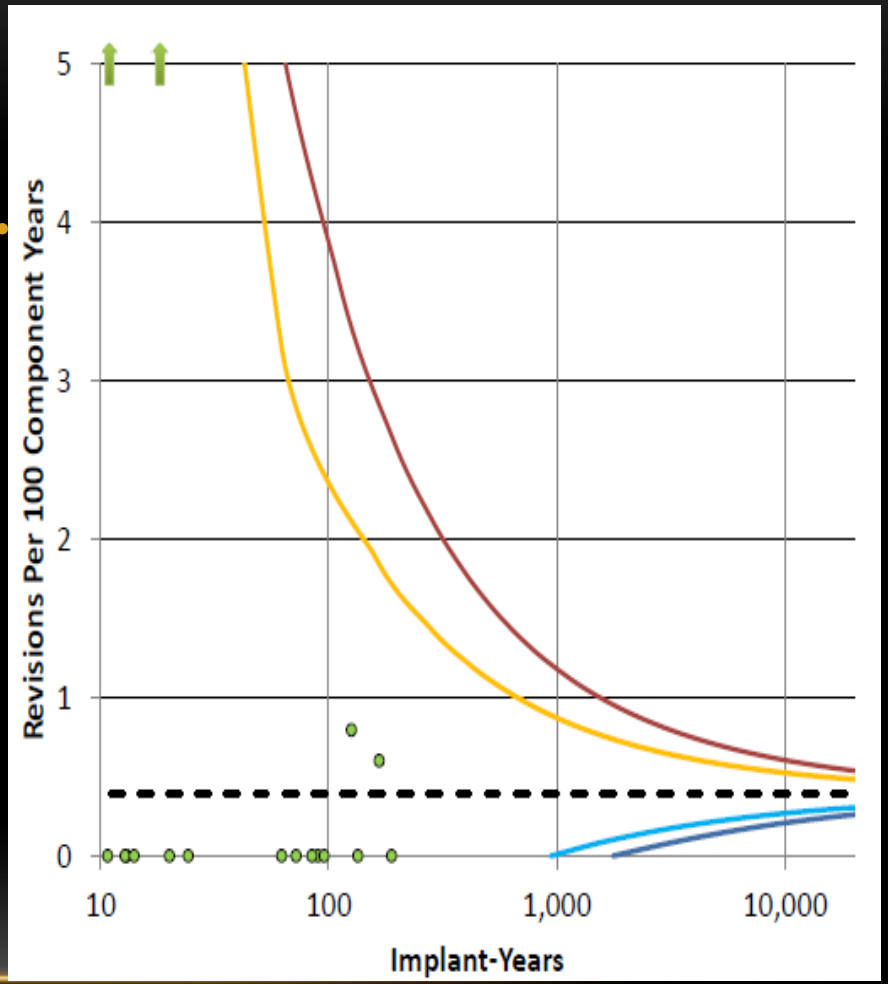


PTIR - LEAD SURGEONS

ALL NJR

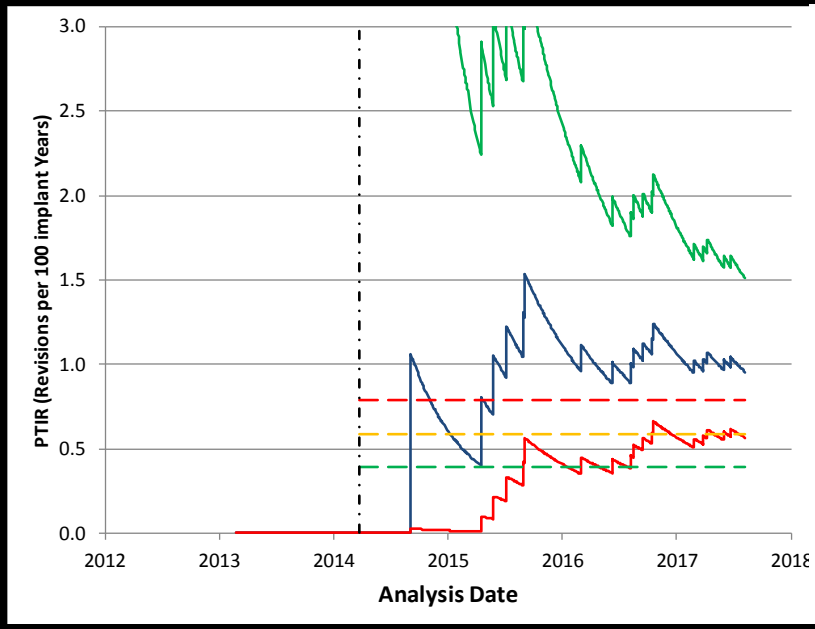


EXCLUDING LEAD SURGEONS THAT UNIT



PTIR FOR THIS IMPLANT

ALL SITES

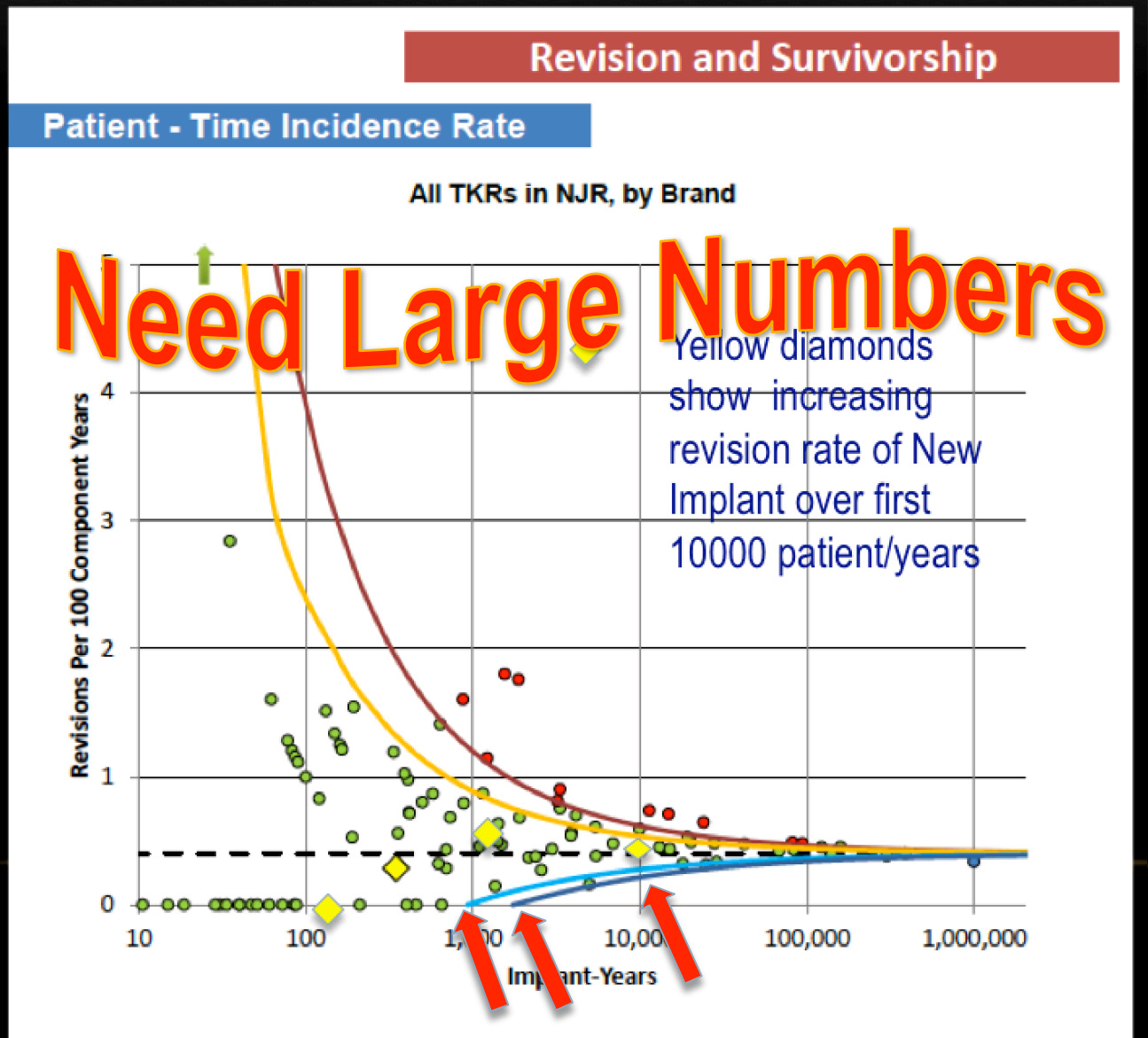


EXCLUDING 'outlier Unit'

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



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

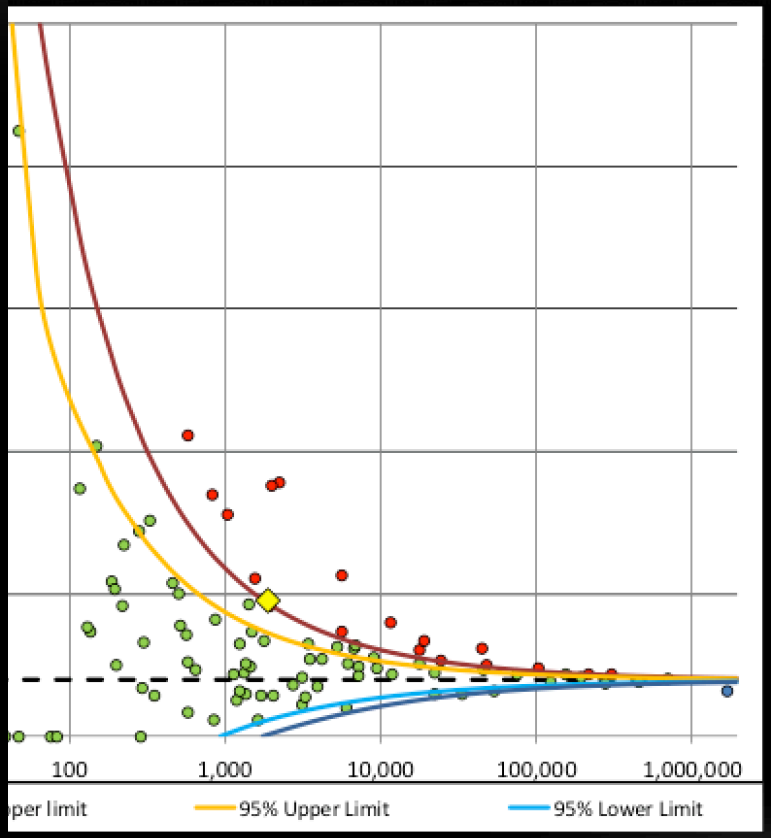
UNFORESEEN AREAS OF CONCERN

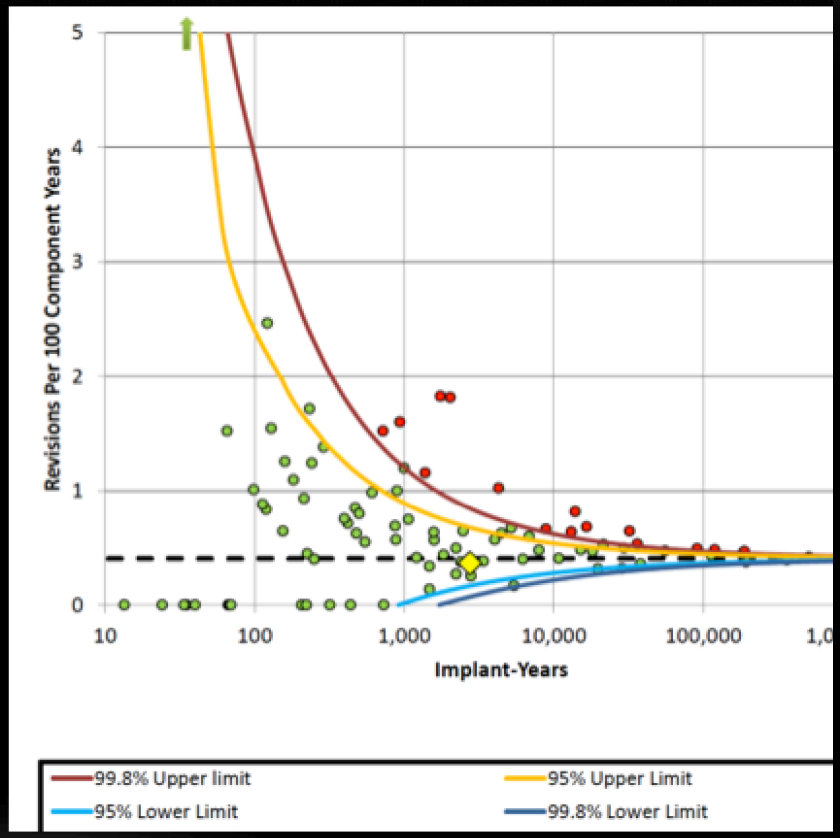
- Bearing Surfaces were not initially thought to be the issue when ODEP Ratings were started
- Trunnion problems have only recently come to light
- No Doubt there are further hidden issues in our future!
- ONLY ACTUALLY MEASURING OUTCOMES AS WE GO ALONG IS LIKELY TO FIND THESE PROBLEMS EARLY

HOW AND WHEN TO MEASURE ?

- Revision Rates – Necessary but not Sufficient
- PROMS
- Functional Outcomes
- XRAYS? RSA?

FUNNEL PLOTS REVISION RATES

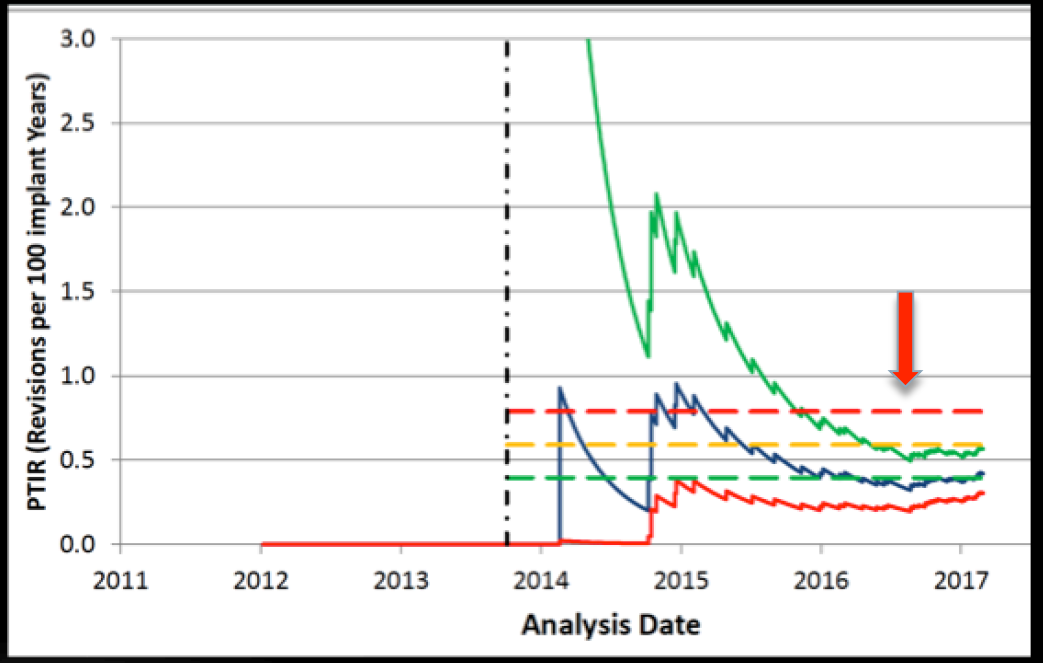




HOW AND WHEN TO MEASURE ?

- "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

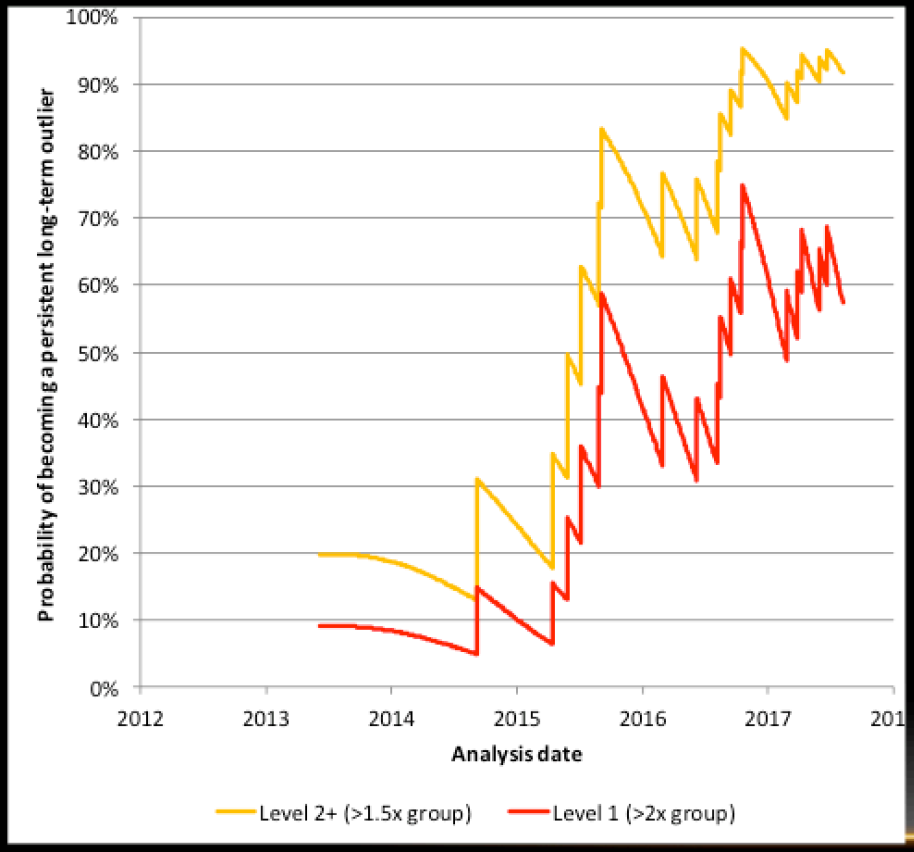


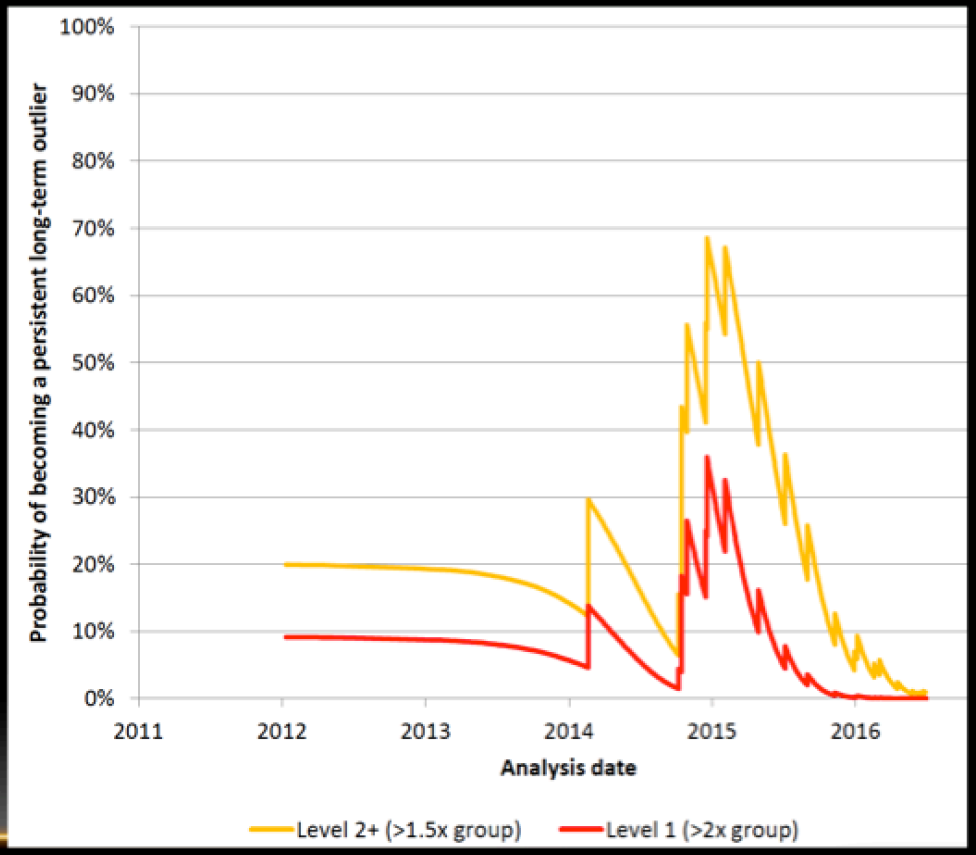
HOW AND WHEN TO MEASURE ?

- 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?

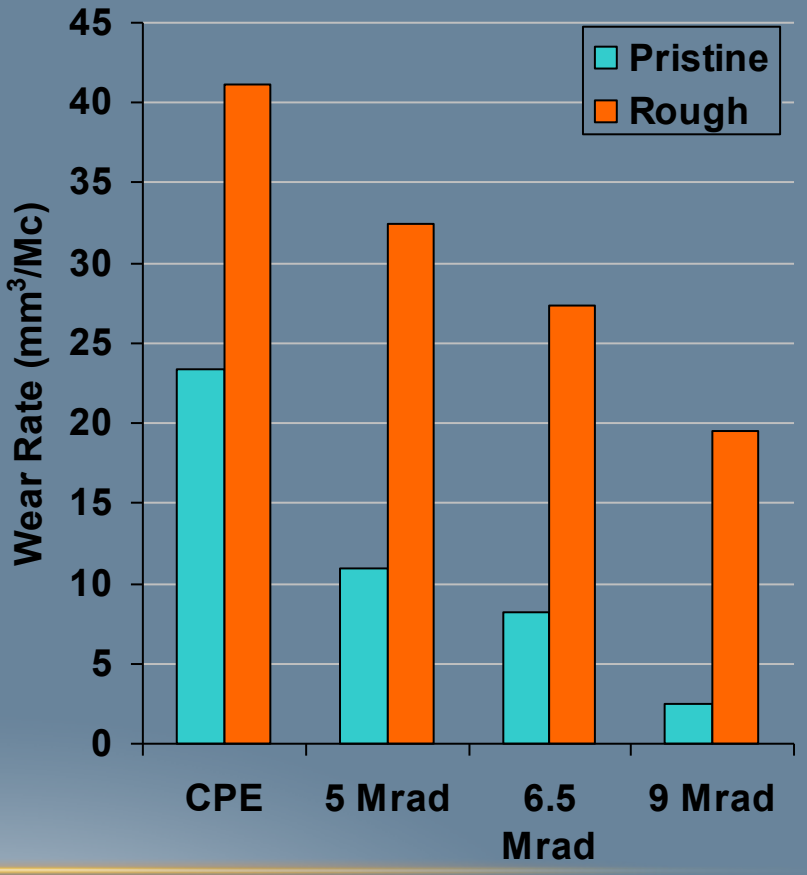
- Early failures are often Infection-related or technical errors
- Medium term failures may be implant related and often seem to dominate later…around 6-8 years post-op
- Implants are usually put in in much higher numbers between 5-10 years than in first 5 years, so many patients are at risk if we don't notice problems by then!

CONFLICTS OF INTEREST

- The more time and money you spend inventing and developing something the more difficult it is 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

	Tradename	Resin	Total Dose (Mrad)	Source	Heat Treatment
Biomet	E-Poly	?	10	?	None / Vitamin E
DePuy	XLK	1020	5	Gamma	Re-melt
Stryker	X3	1020	3×3=9	Gamma	Anneal
Zimmer	Prolong	1020	6.5	E-beam	Re-melt

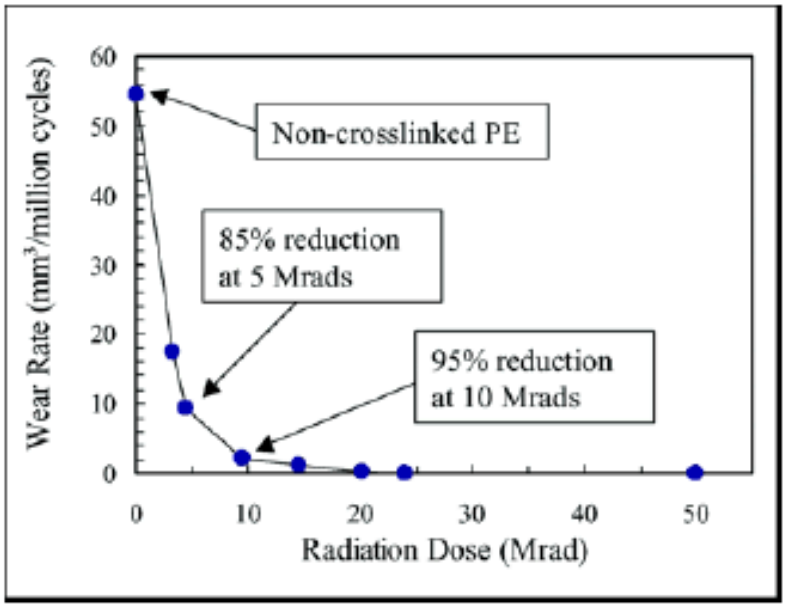
SLIDE FROM PROF TONY MILES

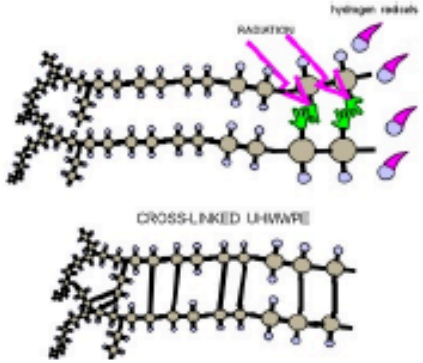
WEAR IMPROVEMENT BY CROSS-LINKING

centre for orthopaedic biomechanics

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

Heisel *et al* **JBJS**:85-A:2003

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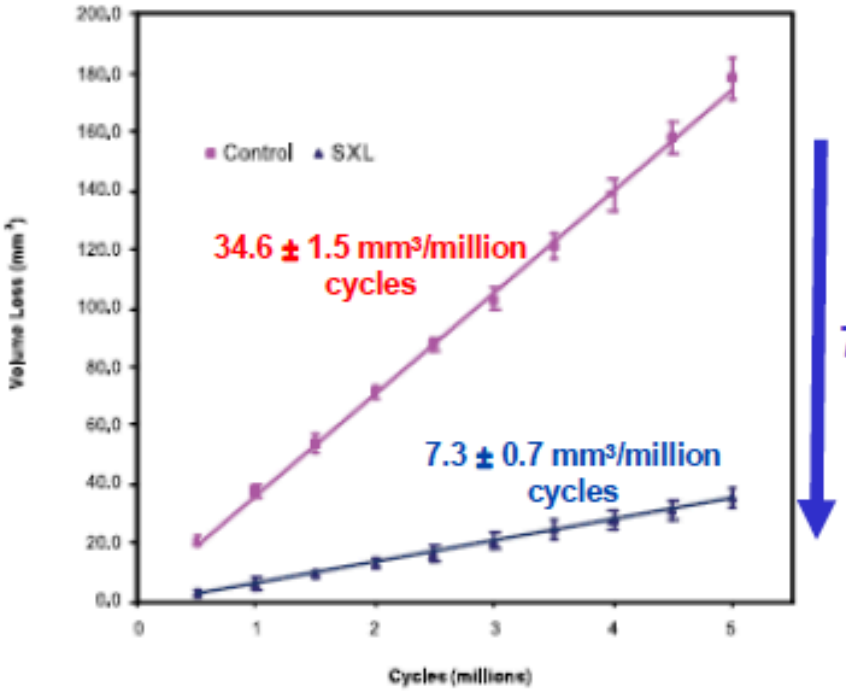
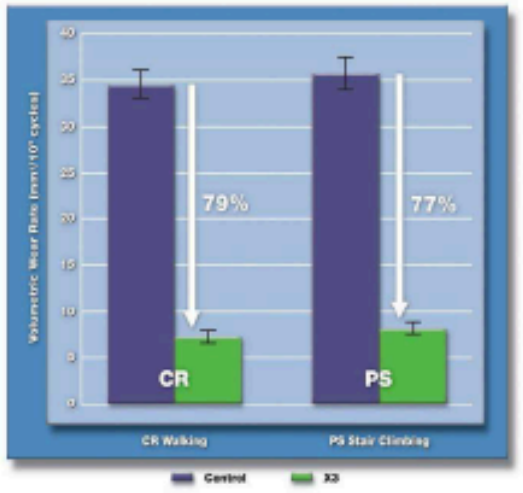
X3: WEAR RESISTANCE

centre for orthopaedic biomechanics



Note for 6M cycles/yr debris load:

- **Std PE is 208mm³/yr**
- **X3 is 44mm³/yr**



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Scorpio CR Knee, Essner *et al* **ORS** (2004)

SLIDE FROM PROF TONY MILES

NEW SEQUENTIALLY CROSSLINKED POLYETHYLENE X3™

centre for orthopaedic biomechanics

- 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*

X3™ The Power of Technology

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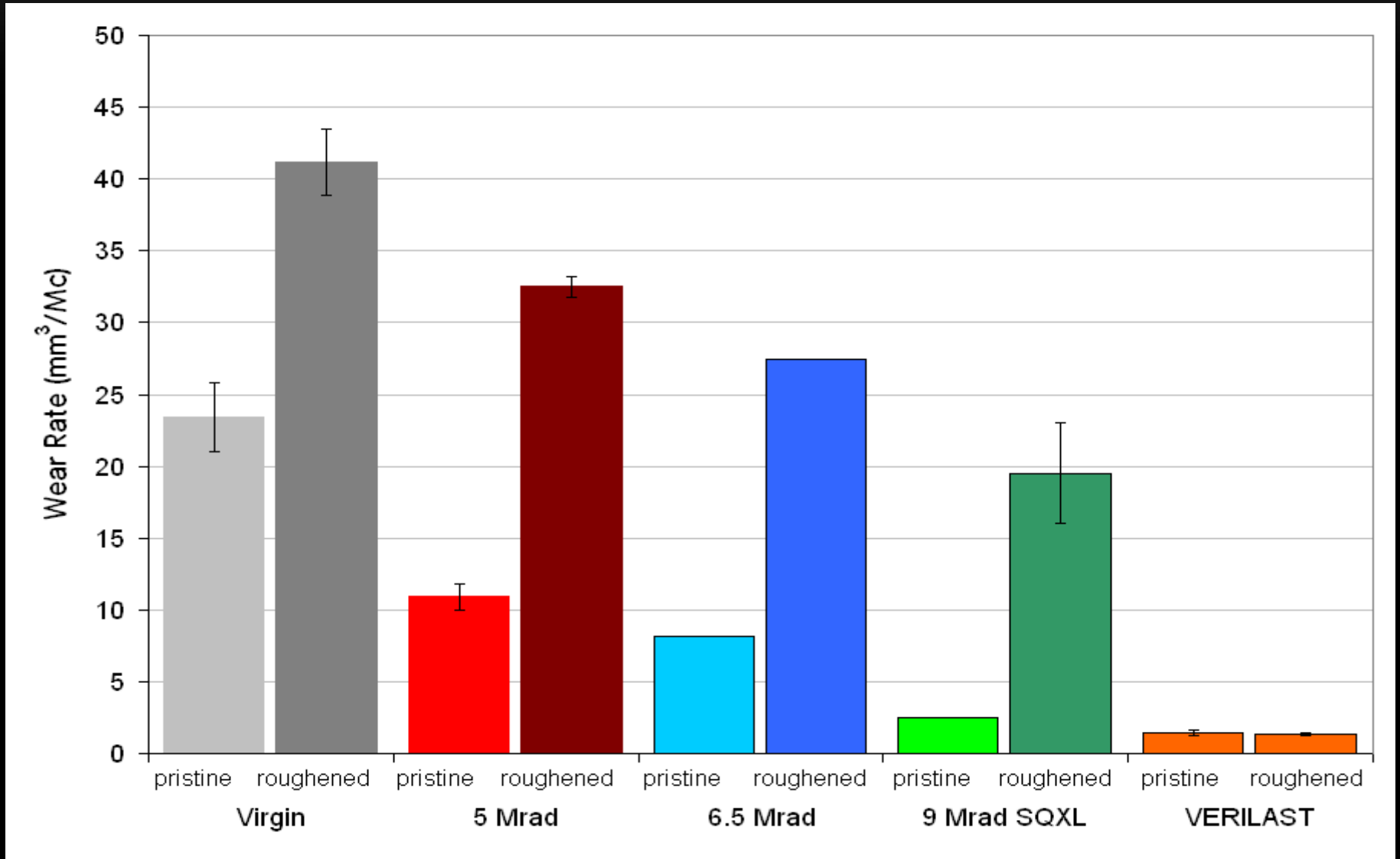
Hedley **TribOS** 2008

TKA CROSSLINKED PE MARKET (S&N)

Material	GUR Resin	Dose (Mrad)	Thermal Treatment	Free Radicals	Oxidation
Smith & Nephew XLPE	1020	7.5	Re-melt	No	No
DePuy XLK	1020	5	Re-melt	No	No
Zimmer Prolong	1020	6.5	Re-melt	No	No
Stryker X3	1020	9 = 3×3	Sub-melt	Yes	Yes

KNEE WEAR RATES : SMITH AND NEPHEW



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?