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Coordinating Research and Evidence for Medical Devices

Clinical evidence for high-risk orthopaedic implants - Insights from the CORE-MD project

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Clinical evidence for high-risk orthopaedic implants – Insights from the CORE-MD project

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Introduction:

- Focus on devices used in elective total hip arthroplasty (THA) and total/partial knee arthroplasty (TKA)
- Among most frequently performed surgical interventions (1.7 million hips and 1.5 million knees in OECD countries in 2015)
- **Large benefit** (pain relief, functional improvement, quality of life) over **short- and long-term**

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Objectives:

1. To give an overview of clinical investigations regarding THA & TKA - in particular **methodologies** and **clinically relevant outcomes** – reported in **peer-reviewed literature**

   Availability of clinical investigations assessed prior and subsequent to regulatory approval (CE-marking)

2. To identify and aggregate **all-cause revision rates** of THA & TKA implants in 1. **registry reports** and 2. **peer-reviewed literature**

Methods – Literature methodology and outcomes

- Random selection of 30 (in total) hip and knee devices from ODEP* and registry reports from European countries for inclusion in systematic review

- For each device
  - Identification of year of CE-mark
  - Systematic search to identify peer-reviewed literature available 10 yrs. before and 20 yrs. after CE-marking

- Protocol registered on open science framework (https://osf.io/6gmyx)

*ODEP=Orthopaedic data evaluation panel

Search strategy - Literature methodology and outcomes

Search strategy and articles screened

Total N articles: 2901

Search terms

Device name AND hip/knee AND date range AND Humans[MeSH Terms]

Date range = 10 years before to 20 years after CE marking

Implant type	Embase	PubMed	Web of science	N after deduplication*	N other sources*	N studies included
Hip stem	408	238	293	751	9	63
Hip cup	199	50	137	302	1	34
Knee	825	399	352	1078	1	54
Total	**1432**	**687**	**782**	**2131**	**11**	**151**

Results – Literature: Implants

- Prior to CE-mark: 0 publication
- Post-market:
  - 0-19 publications
  - 8 implants (26.7%) with no publication

	Device name	N pre-market publications	CE-mark year found	N post-market publications
Hip Stem	Accolade II	0	Yes	12
	Alloclassic Zweymuller SL	0	Yes	19
	Avenir	0	Yes	4
	BiContact Cementless	0	Yes	8
	COLLO-MIS	0	Yes	2
	C-Stem AMT Total Hip System	0	Yes	2
	Filler 3ND	0	Yes	1
	MiniHip	0	Yes	8
	QUADRA	0	Yes	7
	Stelia stem	0	Yes	0
Hip Cup	ANA.NOVA cup	0	Yes	2
	aneXys	0	Yes	0
	Cenator	0	Yes	0
	EcoFit Cementless	0	Yes	0
	Exceed ABT Cup	0	Yes	4
	IP X-LINKed acetabular cup	0	Yes	0
	Plasmacup SC	0	Yes	9
	POLARCUP™ Cemented	0	Yes	3
	RM pressfit Vitamys	0	Yes	8
	Versafit CC Trio	0	Yes	8
Knee system	ACS Unc, Unicondylar	0	No	0
	balanSys CR	0	Yes	4
	Innex Gender	0	Yes	0
	LCS Complete	0	Yes	10
	Logic PS	0	Yes	4
	NexGen CR	0	Yes	18
	Optetrak CR	0	Yes	0
	Sigma High Performance Partial Knee	0	Yes	3
	TREKKING CR	0	No	2
	Vanguard CR	0	Yes	13

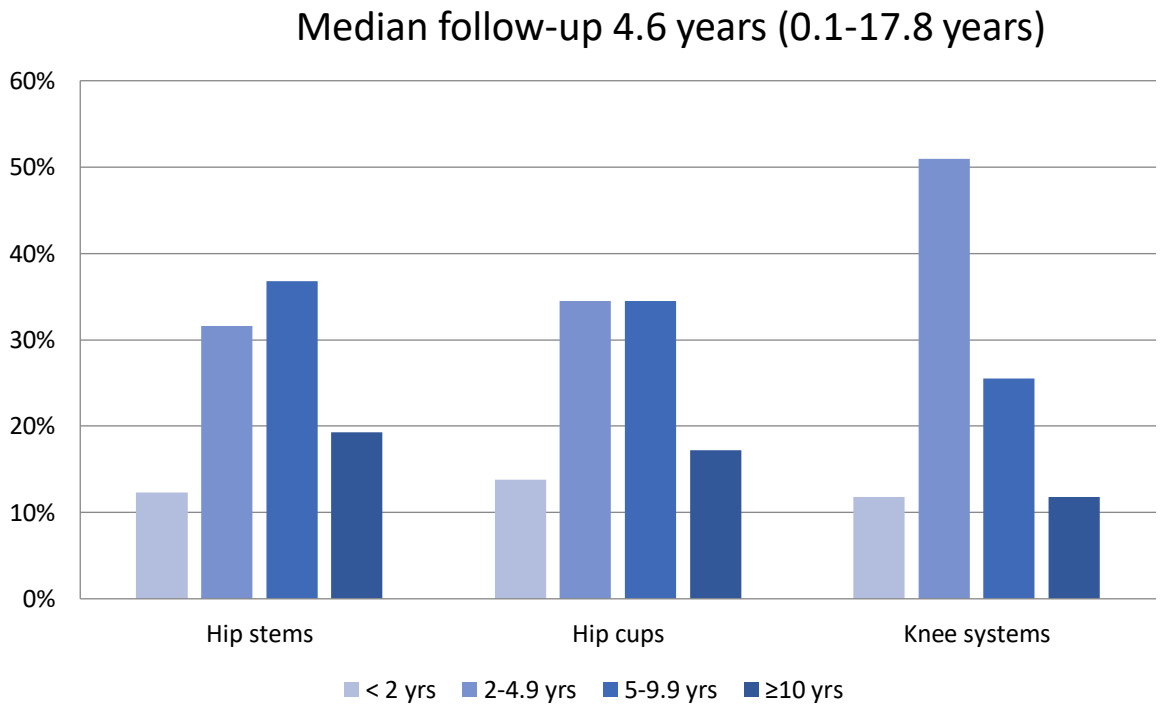
Results – Literature: General study characteristics and methodology

	Hip stems (N =63)	Hip cups (N =34)	Knees (N =54)	All (N =151)
Publication period	1995-2021	2007-2021	2002-2021	1995-2021
Location EU/America/Asia/Other	66.7/23.8/1.6/7.9%	70.6/0/23.5/11.8%	61.1/29.6/9.3/1.9%	**63.6**/19.9/9.3/5.3%
Study type				
Case report	3.2%	11.8%	1.9%	4.6%
Case-control	-	-	5.6%	2%
Cohort registry-bas.	7.9%	11.8%	18.5%	**12.6%**
Other cohorts	84.1%	67.6%	59.3%	**71.5%**
Retrospective*	83.0%	56.5%	62.5%	72.2%
RCT	4.8%	8.8%	14.8%	**9.3%**
Comparator group yes	41.3%	23.5%	59.3%	**43.7%**

Results – Literature: General study characteristics and methodology

	Hip stems (N =63)	Hip cups (N =34)	Knees (N =54)	All (N =151)
N prostheses included, mean – median (range)	615 - 139 (1-14'147)	613 - 95 (1-14'147)	1460 - 180 (1-27'193)	917 - **139** (1-27'193)
Inclusion period, median years	3	2	3	3
First inclusion date to publication in years, median, range	10 (4-22)	9 (2-21)	11 (3-20)	10 (2-22)
CE-mark date to first publication in years, median, range	9 (3-13)	10 (7-12)	7 (5-10)	9 (3-13)
FDA approval to first publication in years, median, range	5 ((-8)-10)	2 (1-3)	5 ((-3)-8)	5 ((-8)-10)

Results – Literature: Follow-up time



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Results – Literature: Outcomes

	Hip stems (N =63)	Hip cups (N =34)	Knees (N =54)	All (N =151)
Type of outcome reported				
All-cause revision	81%	67.6%	70.4%	**74.2%**
N revisions reported, median, range	4.5 (0-440)	1.5 (0-440)	3 (0-437)	4 (0-440)
Time-to-event analysis (95%CI)	25.4%	29.4%	33.3%	29.1%
PROs	23.8%	44.1%	46.3%	**36.4%**
Imaging	77.8%	85.3%	55.6%	**71.5%**
RSA study	8.3%	5.9%	9.3%	7.3%
Functional measures	1.6%	2.9%	59.3%	22.5%
Complications	79.4%	73.5%	66.7%	73.5%

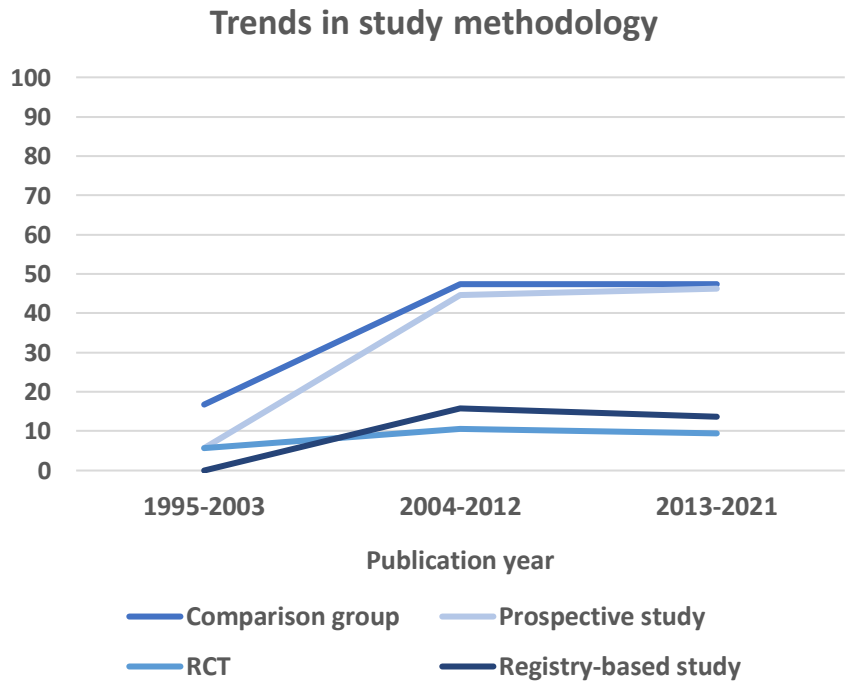
Results – Literature: Comparative outcomes reporting by implant

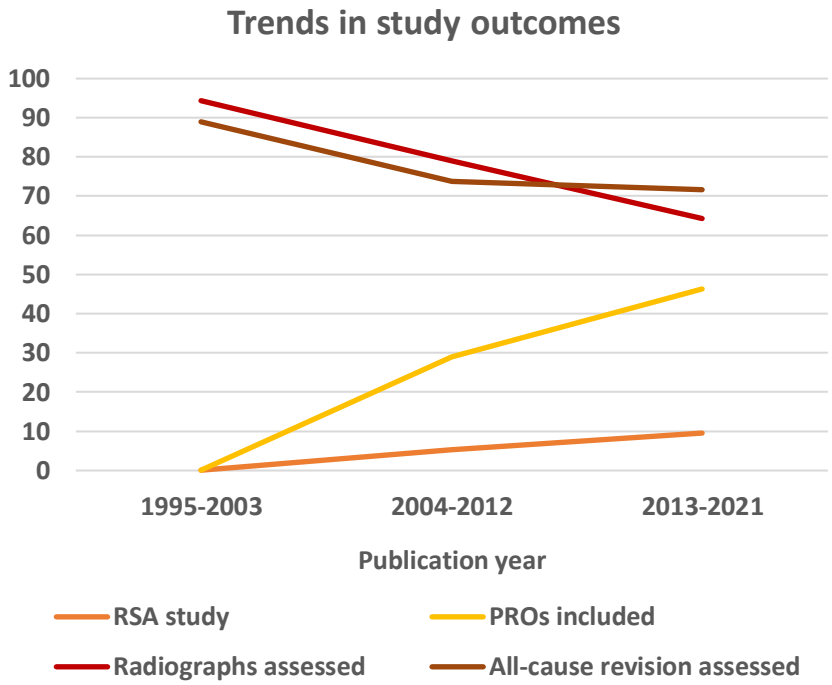
- At least 1 comparative revision study found for 11 implants (36.7%)
- At least 1 comparative PROs study found for 12 implants (40%)

Results – Literature: Outcomes

	Hip stems (N = 63)	Hip cups (N = 34)	Knees (N = 54)	All (N = 151)
"Concern" reported in study				
No concern expressed	87.3%	82.4%	90.7%	87.4%
Potential	4.8%	11.7%	7.4%	7.3%
Yes	7.9%	5.9%	1.9%	5.3%
"Concern" yes/potential based on (%)				
Imaging/Revision/PROs/Other	37.5/25/0/37.5	77.8/11.1/0/11.1	0/60/40/0	45.5/27.3/9.1/18.2

Results – Literature: Trends





Results – Literature: Registry based cohorts vs. not

Comparison cohort study based in registry vs. not (Median follow-up, 5 years)

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Introduction – Registries in Orthopedics

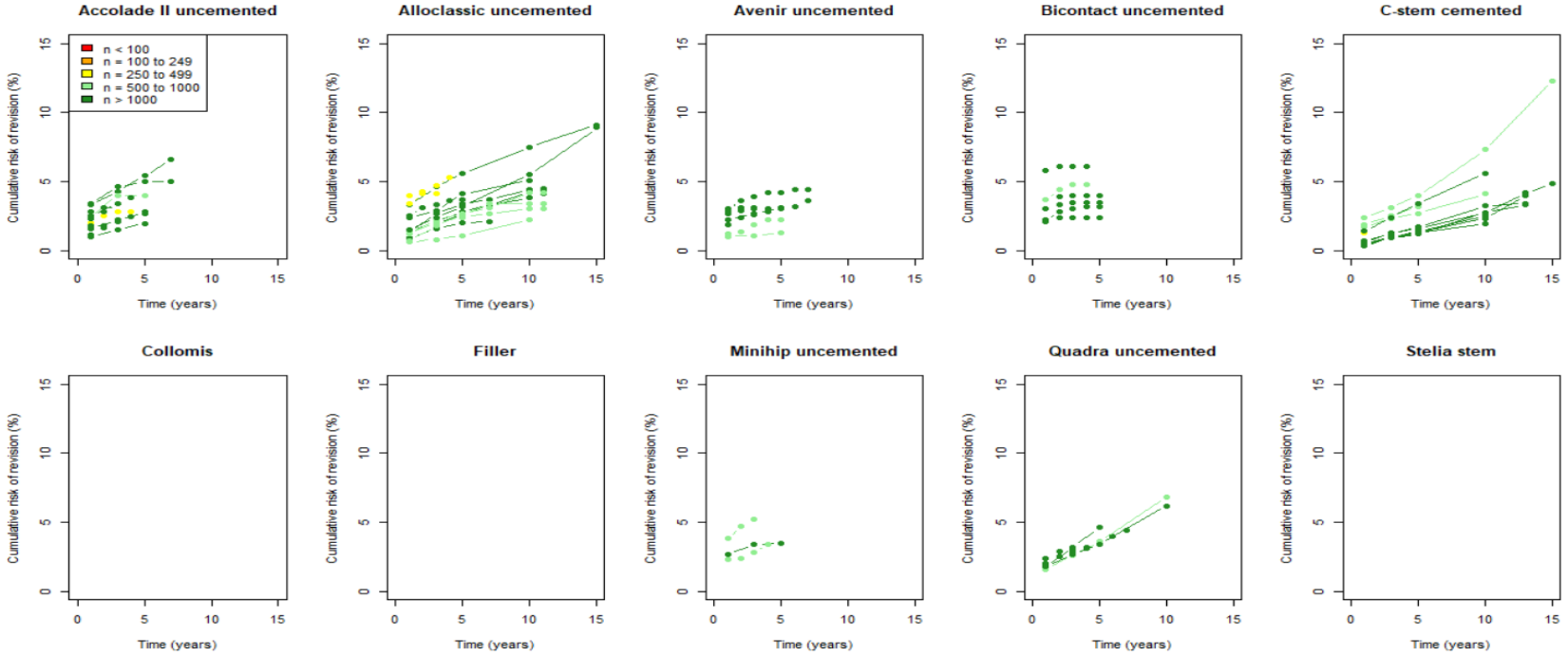
Registries:

- Major source of information
- Monitor long-term, real-world performance and safety of multiple hip and knee implants simultaneously for country/region
- Longstanding (first national 1975 in Sweden)
- Most publicly funded, independent, transparent reporting, high coverage and completeness (90-100%)

Malchau et al. Arthroplasty Implant Registries Over the Past Five Decades: Development, Current, and Future Impact. J Orthop Res 2018

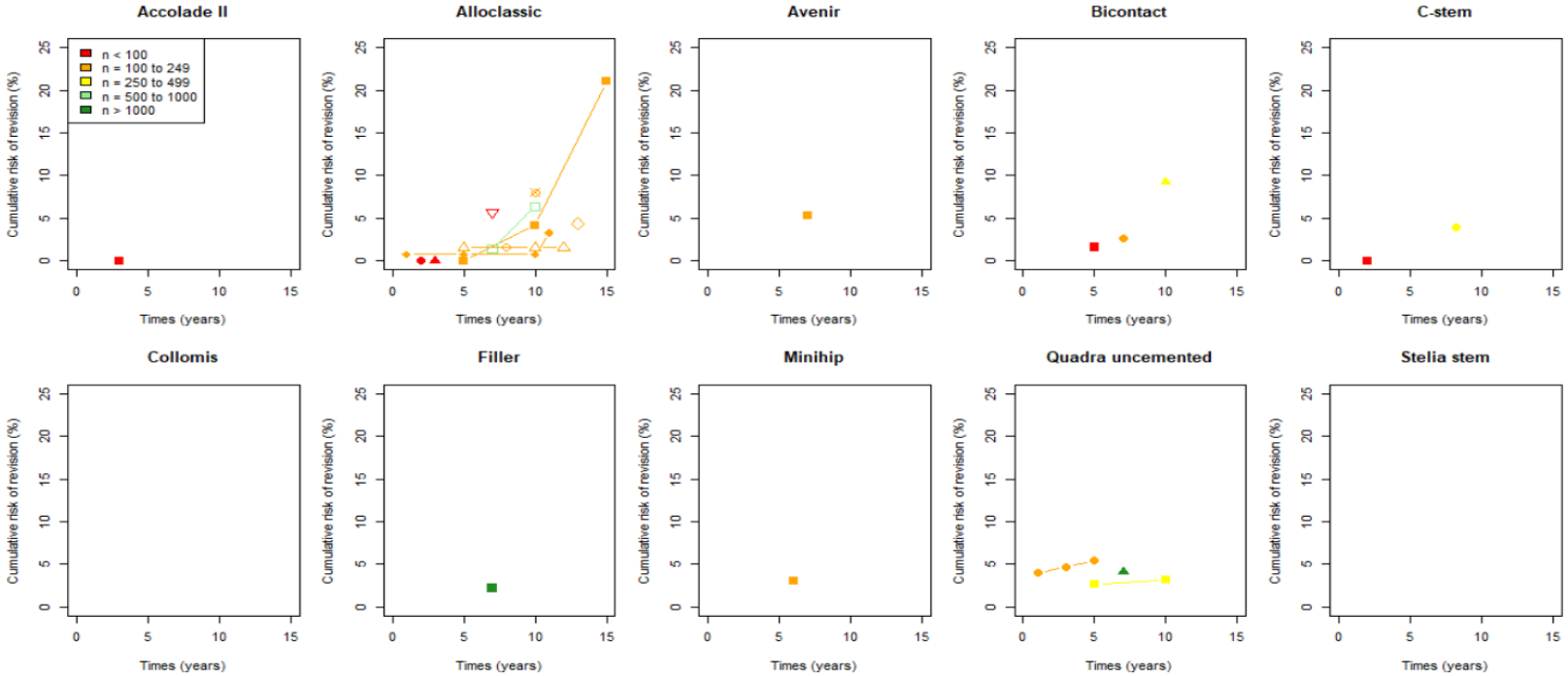
Results – Hip revision reported by registries

Cumulative risk of revision for each **hip stem** as reported in publicly available registry reports (N=203994)



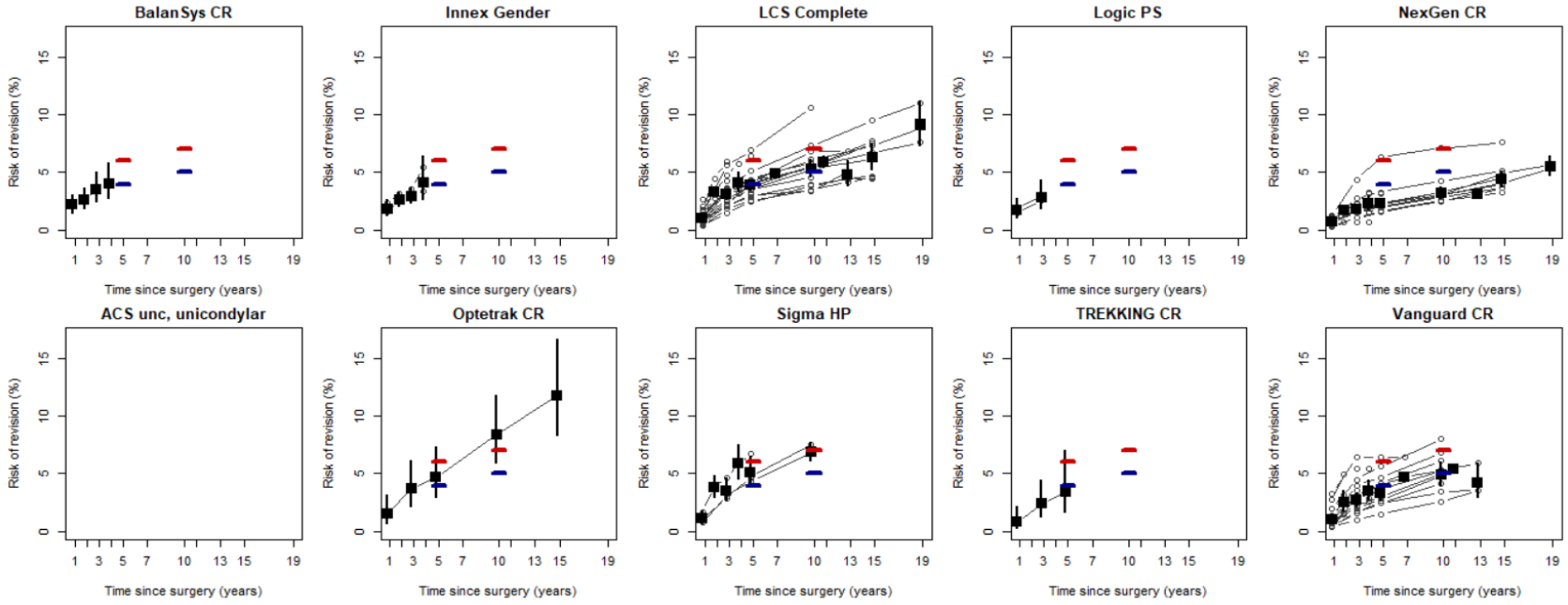
Results – Hip revision reported in literature

Cumulative risk of revision for each **hip stem** as reported in peer-reviewed literature



Results – Knee revision reported by registries

Cumulative risk of revision for each **knee system** as reported in publicly available registry reports



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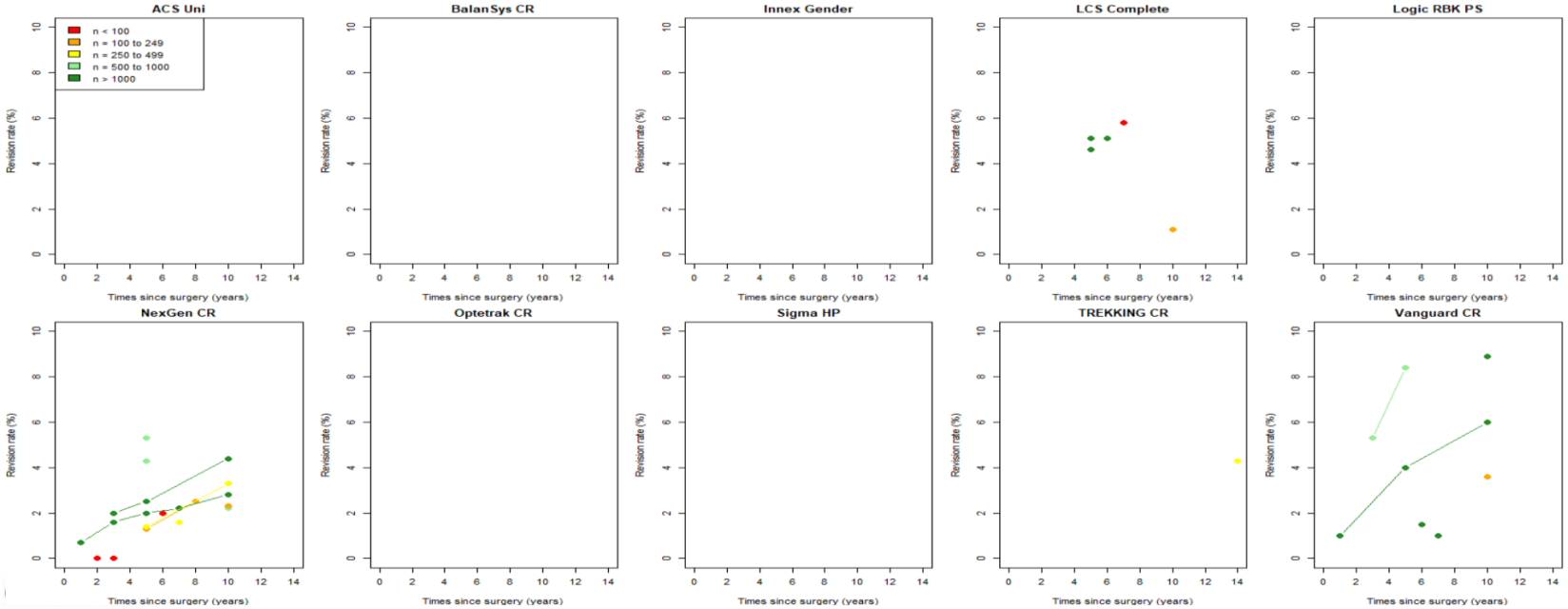
Results – Knee revision reported in literature

Cumulative risk of revision for each **knee system** as reported in peer-reviewed literature



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Summary

Under new EU MDR, post-market surveillance: proactive, continuous and involves comparison to clinically meaningful comparator group and use of clinically relevant endpoints (risks & benefits)

- No pre-CE-mark peer-reviewed publication for the 30 implants
- For 27% of implants no post-market publication either, similar to previous literature
- 9% RCTs, similar to previous literature
- Literature: Focus on imaging results (recognized surrogate for failure), increasingly PROs
- Registries (publications and annual reports): large sample size – prospective – comparative – long-term – revision – PROs reporting increasing
- Aggregating results from registries is feasible

Kynaston-Pearson et al. Primary hip replacement prostheses and their evidence base. BMJ 2013
Cunningham et al. Have Levels of Evidence Improved the Quality of Orthopaedic Research? CORR 2013
Bohm ER et al. Collection and Reporting of Patient-reported Outcome Measures in Arthroplasty Registries. CORR 2021

CORE-MD, Coordinating Research and Evidence for Medical Devices, aims to translate expert scientific and clinical evidence on study designs for evaluating high-risk medical devices into advice for EU regulators.

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For more information, visit: www.core-md.eu

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Paediatric Section of U.E.M.S
EPF European Patients Forum
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Thank you for your attention!