CORE-MD

Coordinating Research and Evidence for Medical Devices

Improving the quality of post-market surveillance

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On behalf of the CORE-MD team

Current regulation on performance and safety of medical devices

- Medical device regulation (MDR 2021) requires continuous monitoring of performance and safety of medical devices after CE marking

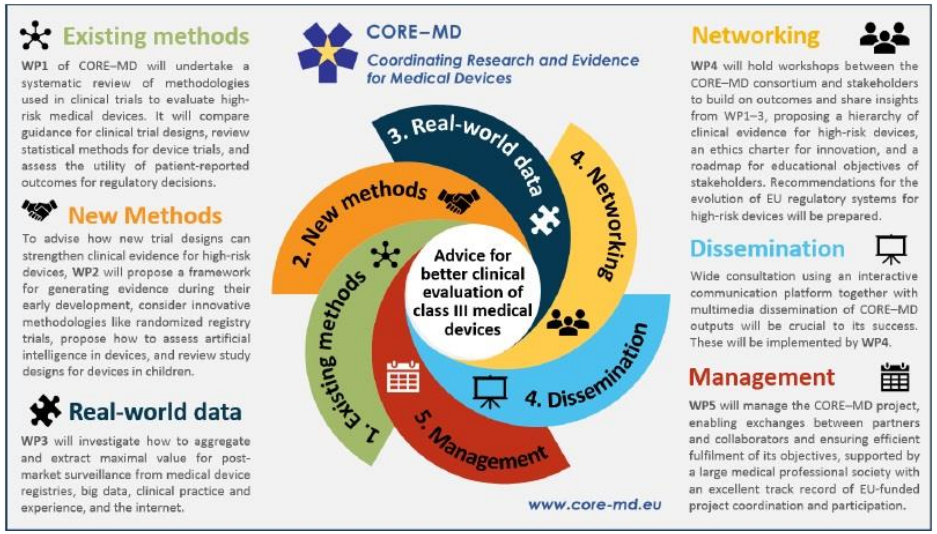
- Real-world data may provide insights on performance in daily clinical practice:
  - ✓ Unselected population-based data
  - ✓ Longer follow-up
  - ✓ Non-frequent adverse events

→ How can real-world data supplement evidence from RCTs?

Challenges for regulators to use real-world data

Real-world data in CORE-MD project:

- Assessing quality of evidence from real-world data
- Combining data across real-world data sources
- Different definitions, reporting criteria and nomenclatures complicate access to safety incidents and reports
- Unclear how (often) conditions are applied to certificates of conformity



Different types of real-world data

ELECTRONIC HEALTH RECORDS

ADMINISTRATIVE DATA

REGISTRIES

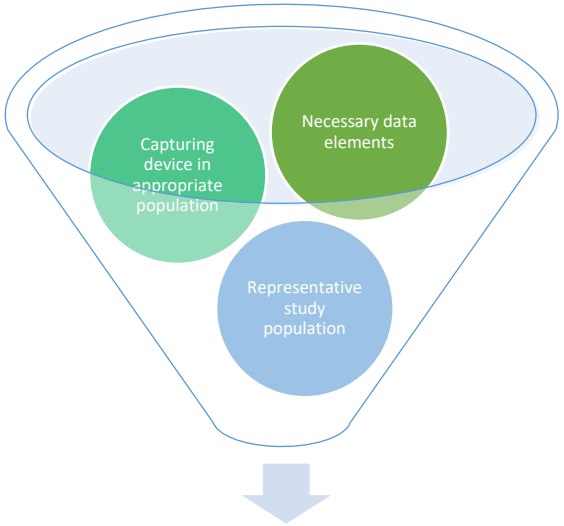
SAFETY NOTICES

PATIENT GENERATED DATA

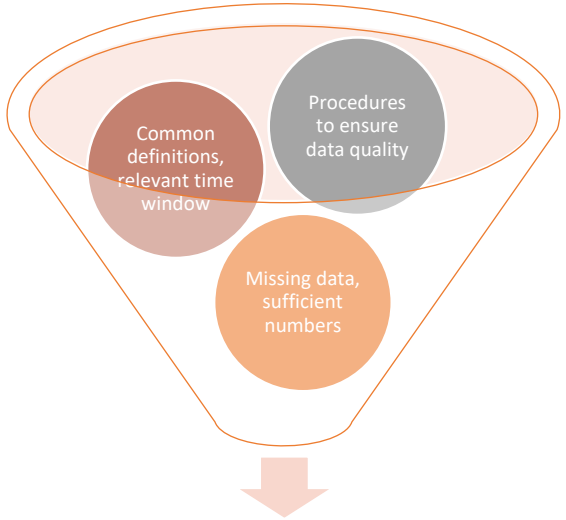
Need good quality evidence that can be generalized

Regulatory considerations for real-world evidence

- Key considerations: data quality, validity and transparency (e.g. EMA, FDA)
- Factors to assess real world data:



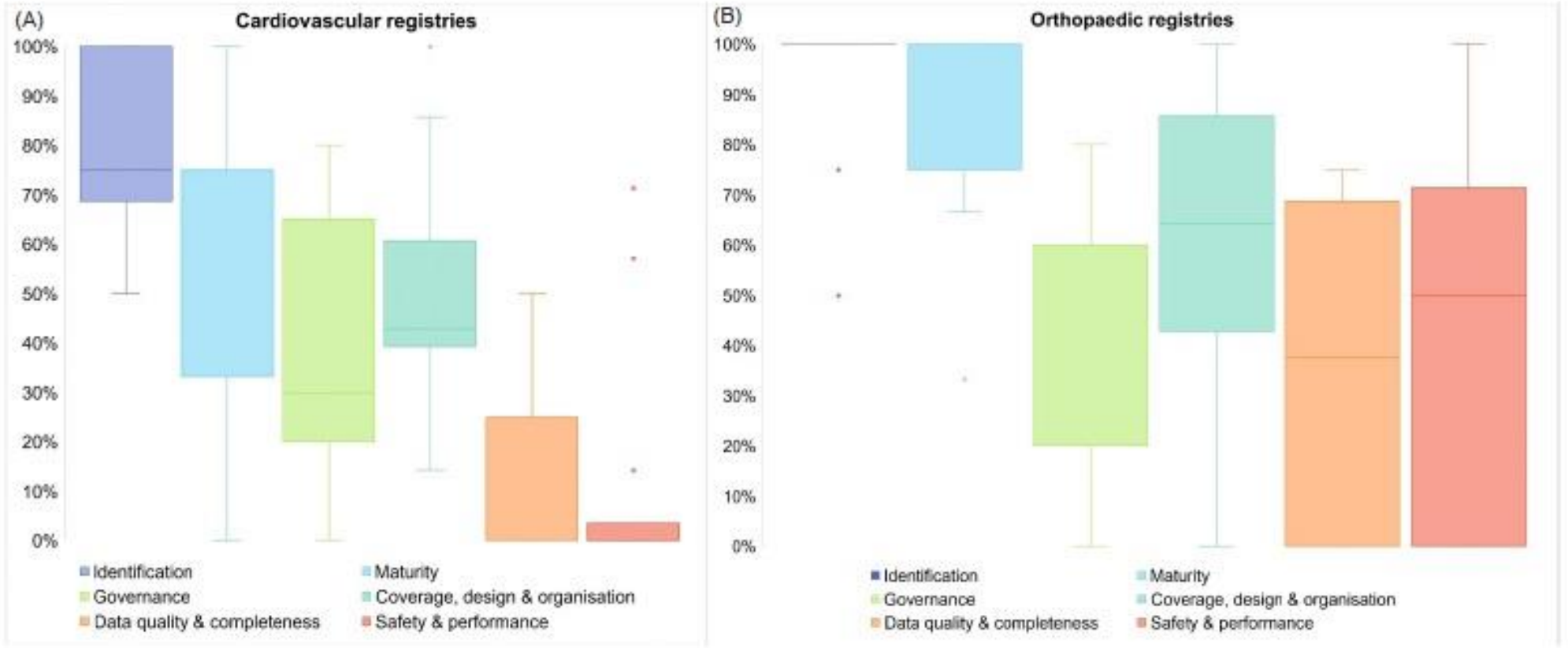
Relevance



Reliability

Reporting on 33 items influencing quality of registry data

L.A. Hoogervorst et al. Int J Health Policy Manag 2023;12:7648



20 cardiovascular registries 26 orthopaedic registries

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Examples of specific results

Cardiovascular registries

- Mostly publications of selected patient groups, 20% report total number of implant recipients
- Patient-level completeness: not reported
- Hospital-level coverage: 30% of registries, median 26 hospitals
- Funding: 45% (mostly public)
- Procedures to check data quality: 55%
- Missing data: 5%

Orthopaedic registries

- Mostly annual reports, total and annual volume of implants
- Patient-level completeness: in 16 (62%) registries, varying from 19-99%
- Hospital-level coverage: 35% of registries, median 71 hospitals
- Funding: 38% (mixed)
- Procedures to check data quality: 50%
- Missing data: 4%

→ **Agreement needed on items that all registries report**

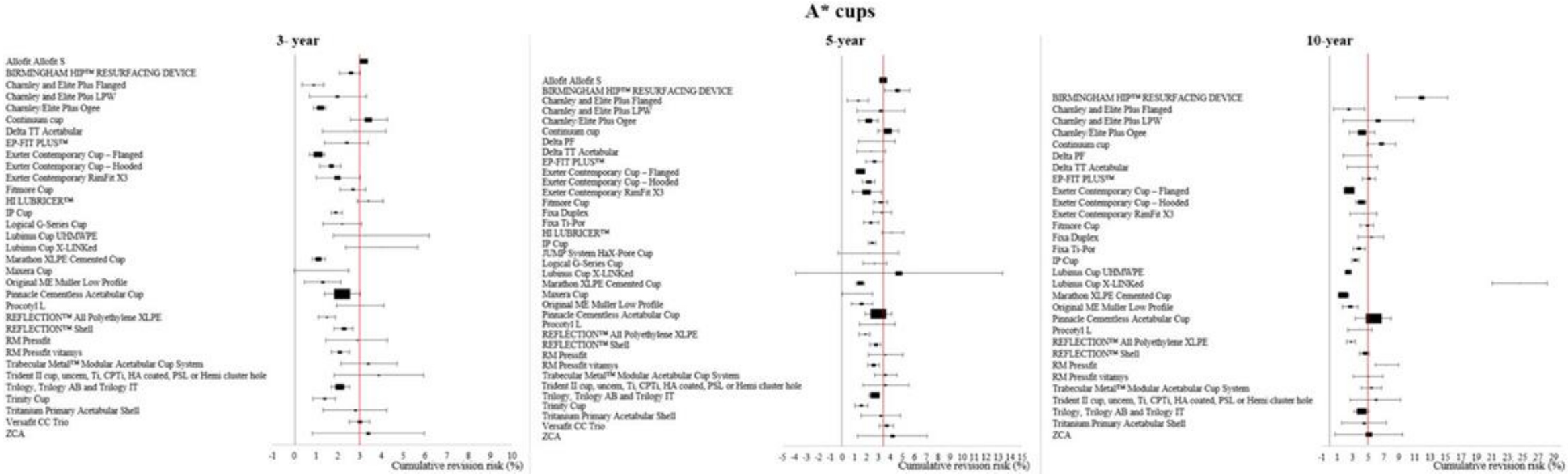
Heterogeneity in reported outcomes, definitions & follow-up

Cardiovascular registries	Orthopaedic registries
Mortality: 18 (90%) registries - 70 different time points, up to 21 years - 30-day mortality: 80%	Revisions for any cause: 20 (77%) registries - 30 different time points, up to 25 years - 1-year revision: 38% - Large variation of reasons for revision
MACE: 8 (40%) registries - 17 different combinations of included complications - 7 different time points, 3-year MACE (33%)	PROMs: 5 (19%) registries - 8 different scores for knee surgery patients - 11 different scores for hip surgery patients - different time points up to 10 years

→ **Agreement needed on a common dataset**

Need to evaluate performance across registries

L.A. Hoogervorst et al. Validating Orthopaedic Data Evaluation Panel (ODEP) ratings across nine orthopaedic registries. JBJS (in press)



ODEP A*-rating: based on maximum revision risk

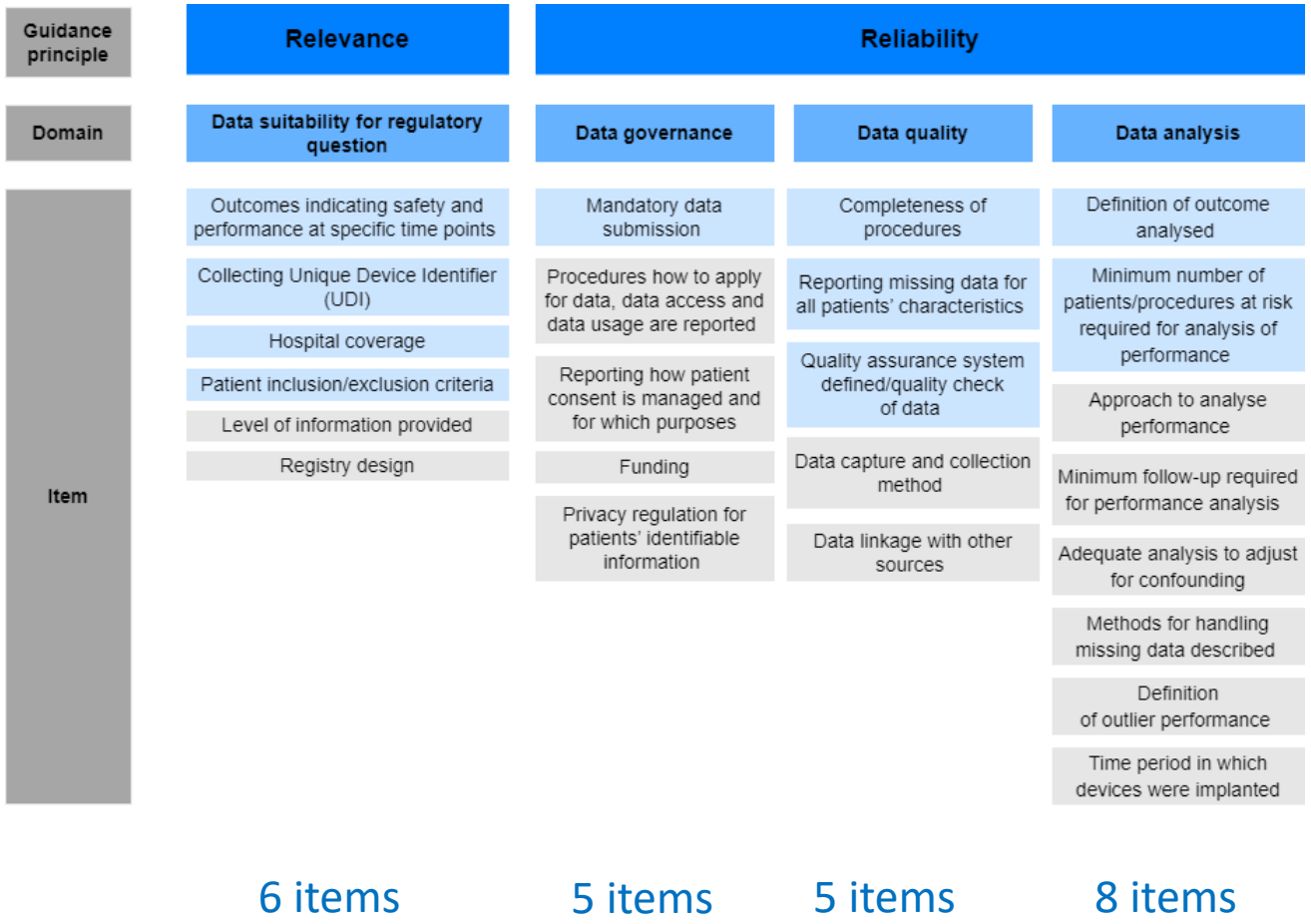
About 30-40% of A* rated cups & stems receives A* rating based on evidence across 9 registries

→ **Variable performance, rating may not apply across registries**

Decision framework to assess medical device performance

- Delphi study
  - ✓Consensus on minimum dataset to judge quality and analysis of registry data
  - ✓ Ranking importance of items

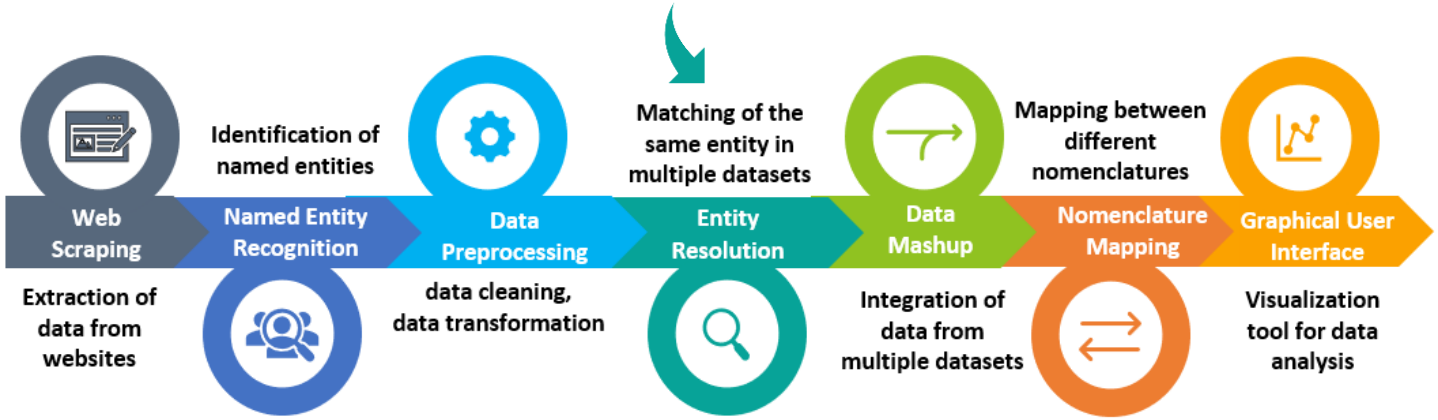
- Participants: regulators, notified bodies, healthcare professionals, registries, methodological experts



L.A. Hoogervorst et al. Consensus recommendations for a minimum dataset to assess the quality and analysis of registry data for regulatory post-market surveillance of high-risk medical devices

CORE-MD PMS tool: framework of operations

If a reference list of devices was not available for that specific country, then we considered the list of devices for **Italy** and **Portugal** (**including EMDN codes**).



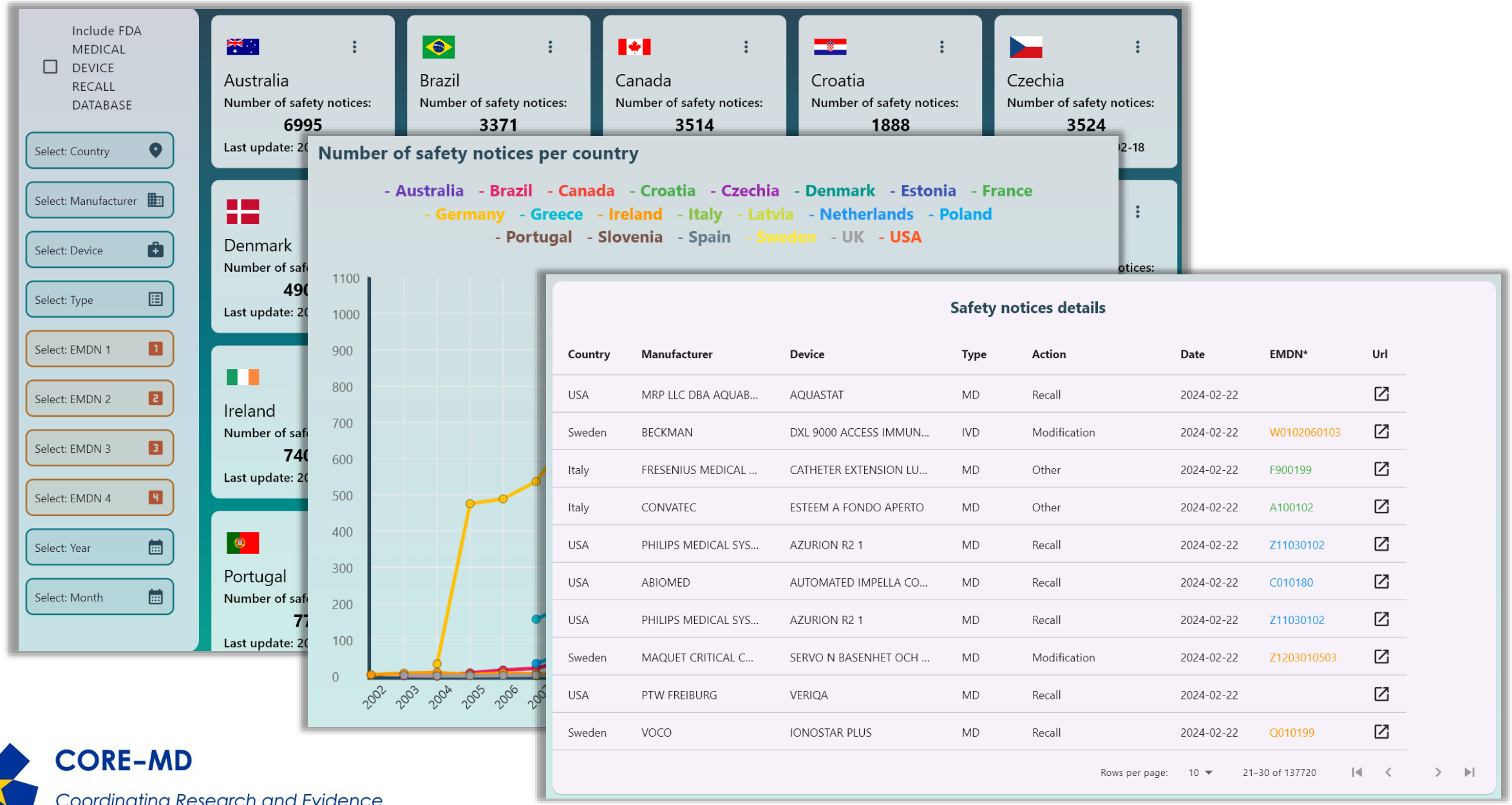
If **manufacturer and device name** were not clearly retrievable:

- Regular Expressions
- Transformer models

If the adopted **nomenclature** differs from EMDN:

- nomenclature mapping algorithm (GMDN→EMDN)
- manual mapping

Y. Ren et al. Validation of CORE-MD PMS Support Tool: A Novel Strategy for Aggregating Information from Notices of Failures to Support Medical Devices' Post-Market Surveillance



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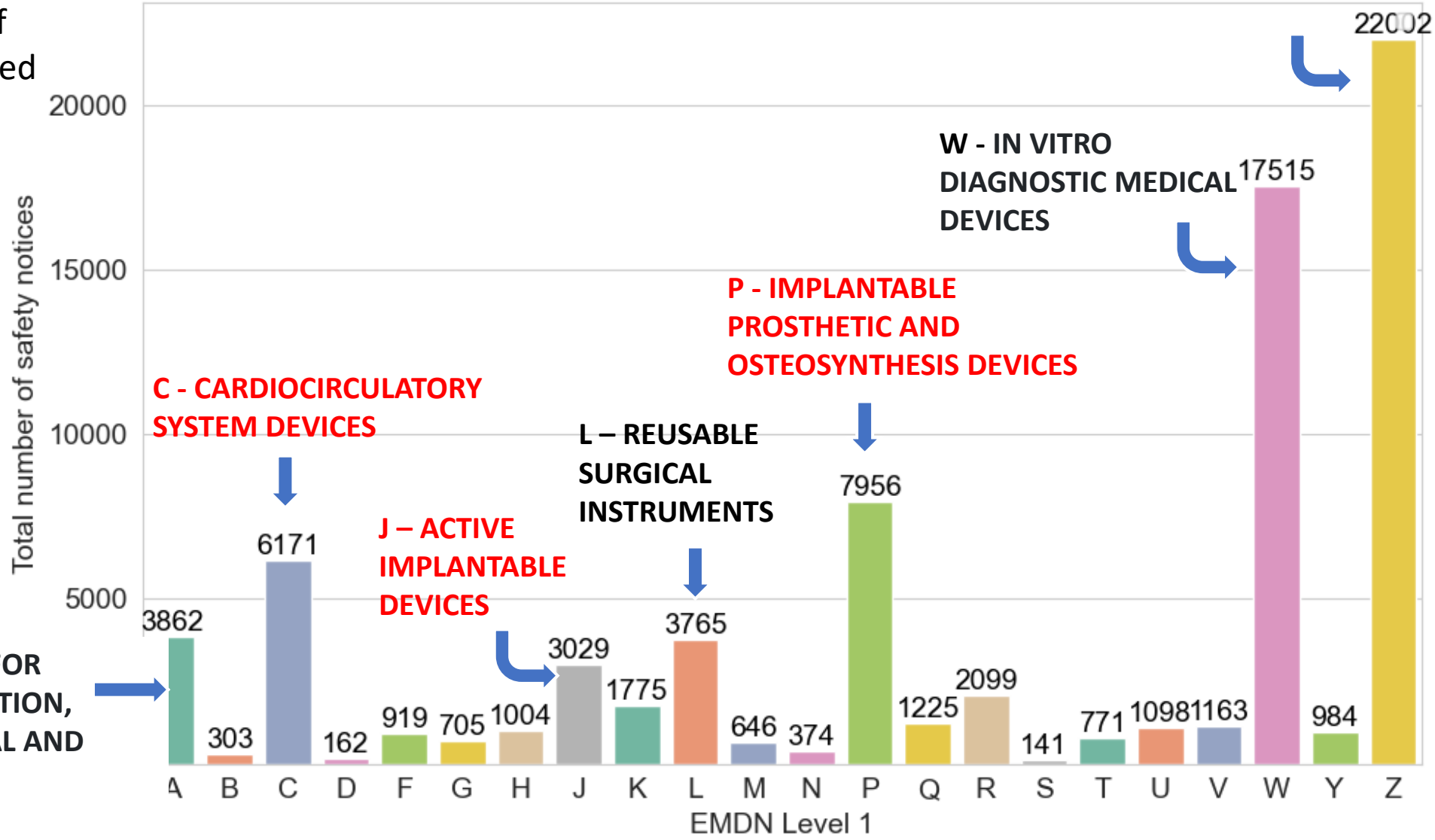
CORE-MD PMS tool: selection of device categories

Total number of SNs with assigned EMDN code: **77669**



A - DEVICES FOR ADMINISTRATION, WITHDRAWAL AND COLLECTION

C - CARDIOCIRCULATORY SYSTEM DEVICES

J – ACTIVE IMPLANTABLE DEVICES

L – REUSABLE SURGICAL INSTRUMENTS

P - IMPLANTABLE PROSTHETIC AND OSTEOSYNTHESIS DEVICES

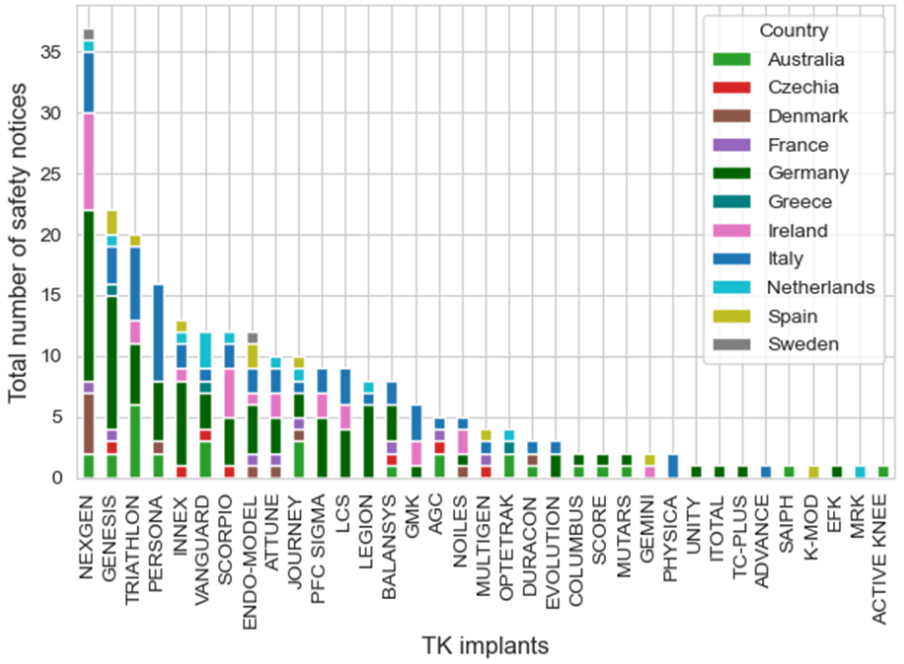
W - IN VITRO DIAGNOSTIC MEDICAL DEVICES

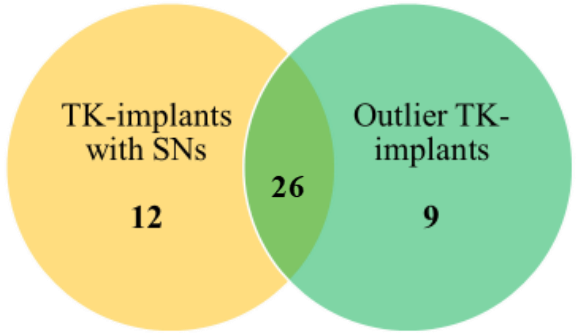
Z - MEDICAL EQUIPMENT AND RELATED ACCESSORIES, SOFTWARE AND CONSUMABLES

Validation of CORE-MD post-market surveillance tool

Example Total Knee implants:

- CORE-MD tool identified 787 safety notices for 38 total knee implants
- Registries identified 35 implants with significantly higher revision risk
- Safety notices signal the same but also different implants





L.A. Hoogervorst, Y. Ren et al. Safety notices and registry outlier data measure different aspects of safety of total knee implants

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Applying conditions to certificates of conformity: literature

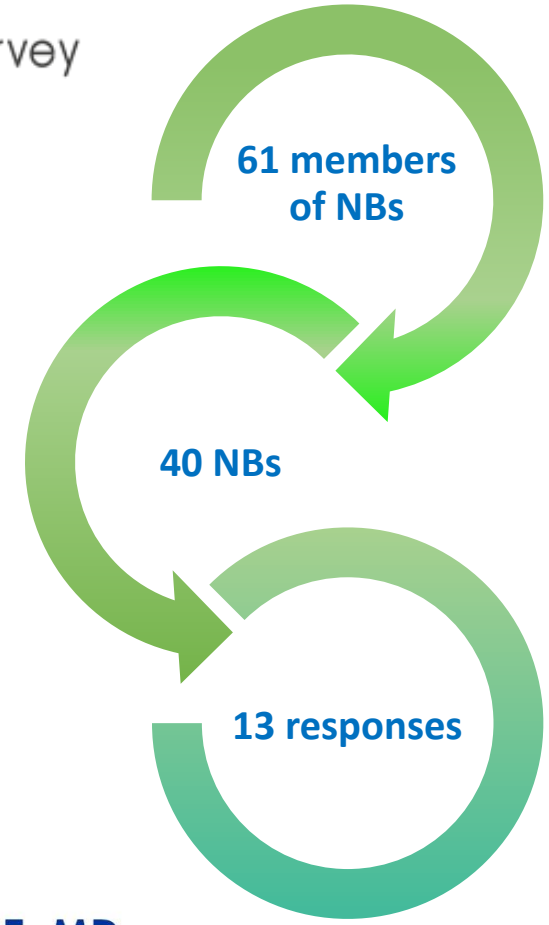
Agnieszka Dobrzynska, Jesús Aranda López, María Piedad Rosario Lozano, Juan Carlos Rejón-Parrilla, David Mark Epstein, Juan Antonio Blasco Amaro

Systematic review

- 7 studies: 5 systematic reviews, 2 HTA reports
- None discussed conditions or restrictions on certificates
- 2 papers discussed coverage with evidence development restrictions
- Key elements of post-marketing surveillance and vigilance activities: adverse event / vigilance reporting

→ Very limited evidence on applying conditions to certificates of conformity of medical devices in Europe

Applying restrictions to certificates of conformity: experiences



How many certificates of class III and implantable medical devices were issued **in total**	• 0- ≈1000/NB
How many applications for certificates of class III and implantable medical devices were **refused**	• 0-20%
How many certificates of class III and implantable medical devices were issued with **restrictions and limitations**	•3 NBs issued 3-25 certificates with restrictions or limitations
Describe the device providing its **intended purpose, indications and area of medicine**, please also describe the type of **restriction or limitation** that was placed on the certificate	• Restriction of **intended purpose** • **Novel technologies** • Concerns about **safety and performance**

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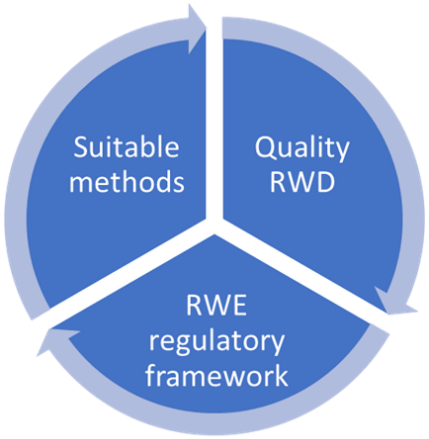
Improving the quality of post-market surveillance

- Regulators can use the decision framework to ensure good quality real-world evidence
- Real-world data may help to streamline trials
- Combining data across countries
  - Earlier detection
  - Possible variable performance



- CORE-MD tool facilitates access to safety notices, may signal different implants and types of problems than registries
- More evidence is needed on applying conditions, particularly to facilitate access for devices that respond to unmet medical need

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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