Advancing the Real-World Evidence for Medical Devices through Coordinated Registry Networks

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ABSTRACT

Objectives Generating and using real-world evidence (RWE) is a pragmatic solution for evaluating health technologies. RWE is recognized by regulators, health technology assessors, clinicians, and manufacturers as a valid source of information to support their decision-making. Well-designed registries can provide RWE and become more powerful when linked with electronic health records and administrative databases in coordinated registry networks (CRNs). Our objective was to create a framework of maturity of CRNs and registries, so guiding their development and the prioritization of funding.

Design, setting, and participants We invited 52 stakeholders from diverse backgrounds including patient advocacy groups, academic, clinical, industry and regulatory experts to participate on a Delphi survey. Of those invited, 42 participated in the survey to provide feedback on the maturity framework for CRNs and registries. An expert panel reviewed the responses to refine the framework until the target consensus of 80% was reached. Two rounds of the Delphi were distributed via Qualtrics online platform from July to August 2020 and from October to November 2020.

Main outcome measures Consensus on the maturity framework for CRNs and registries consisted of seven domains (unique device identification, efficient data collection, data quality, product life cycle approach, governance and sustainability, quality improvement, and patient-reported outcomes), each presented with five levels of maturity.

Results Of 52 invited experts, 41 (79.9%) responded to round 1; all 41 responded to round 2; and consensus was reached for most domains. The expert panel resolved the disagreements and final consensus estimates ranged from 80.5% to 92.7% for seven domains.

Conclusions We have developed a robust framework to assess the maturity of any CRN (or registry) to provide reliable RWE. This framework will promote harmonization of approaches to RWE generation across different disciplines and health systems. The domains and their levels may evolve over time as new solutions become available.

Key messages

What is already known about this subject?

⇒ Several initiatives have been launched on national and international levels by the US Food and Drug Administration and the International Medical Device Regulators Forum to develop a real-world evidence (RWE) framework to provide supportive evidence for regulatory purposes.

⇒ Registries are a key source of RWE, building from which coordinated registry networks (CRNs) have been introduced to describe systems that aim to produce all the necessary evidence for regulators and key stakeholders, by obtaining data from multiple sources.

What are the new findings?

⇒ We developed an innovative and robust framework to assess the maturity of registries and CRNs for device research and surveillance, to address increasing evidentiary needs of stakeholders.

⇒ We defined the maturity of CRNs by how close they come to providing all the required information in an accessible, thorough, relevant, and reliable form using seven domains - unique device identification, efficient data collection, data quality, product lifecycle approach, governance and sustainability, quality improvement, and patient-reported outcomes.

How might these results affect future research or surgical practice?

⇒ This maturity framework for CRNs and registries will promote harmonization of approaches to RWE generation across different disciplines and health systems.

⇒ This framework will also help to prioritize investment in systems and processes that are sustainable and that will supply the evidence needed for regulatory and other evaluations requested by stakeholders.

INTRODUCTION

Modern healthcare is being transformed by the introduction of unprecedented numbers of new technologies, including many that require invasive procedures to implant medical devices. This creates a major challenge for evidence development needed for evaluation of these technologies. It is not only the number of new devices but also their complexity and speed of development that compound the challenge. Comprehensive evidence about short-term and long-term safety and effectiveness of devices is needed to support decision-making by regulators, health technology assessors, clinicians, patients, and other stakeholders if these devices are to be adopted in healthcare systems worldwide. The need for thorough and timely data on implanted devices has been highlighted by problems that have emerged related to certain hip implants,[1] [2] urogynecological surgical meshes,[3] [4] breast implants,[5] and cardiovascular devices.[6] If better information systems have been available during early dissemination of these technologies, it is possible that these problems may have been recognized and addressed sooner.

Using real-world evidence (RWE) is a pragmatic solution for the evaluation of many therapeutics and technologies.[7] [8] RWE can be produced by a variety of study designs using data from routinely collected sources such as electronic heath records, registries, and patient-generated data, including patient-reported outcomes (PROs). Registries, as a major source of RWE, have received global attention, especially since the launch of specific initiatives by the International Medical Device Regulators Forum (IMDRF), exploring the possibilities of prospective national data collection in multiple countries, with the potential for subsequent data linkage to provide information from very large numbers of patients longitudinally.[9] In the USA, the Food and Drug Administration (FDA) has spearheaded an initiative to develop an RWE framework to provide supportive evidence for regulatory purposes.[10] [11]

Building on registries, the concept of coordinated registry networks (CRNs) has been introduced to describe systems that aim to produce all the necessary evidence for regulators and other stakeholders by obtaining data from multiple sources.[12] In theory, it is possible for a single registry to do this, but in practice, that is usually not feasible. The solution is linkage of registries and a diverse range of other datasets to provide the whole spectrum of information needed for device evaluation. In the USA, the development of CRNs has been led by the FDA and the Medical Device Epidemiology Network (MDEpiNet), with the aim of creating national and international partnerships and methodologies for leveraging RWE to evaluate medical devices throughout the total product life cycle (TPLC).[13] CRNs not only provide the prospect of robust RWE evidence on safety and effectiveness of devices but also offer the possibility of nested study designs that can expedite patient recruitment at a lower cost than traditional clinical research.[14–16]

With growing recognition of the value of CRNs, there is a need to develop a consensus-based framework to evaluate them and the registries on which they are based. Our aim was to develop a robust framework to assess the maturity of registries and CRNs for device research and surveillance, to address increasing evidentiary needs of stakeholders. We defined the maturity of CRNs by how close they come to providing all the required information in an accessible, thorough, relevant, and reliable form. This framework will help to prioritize investment in systems and processes that are sustainable and that will supply the evidence needed for regulatory and other evaluations requested by stakeholders. We describe this framework, along with its evolution through two rounds of Delphi survey responses from a range of key stakeholders.

METHODS

The key domains of the framework were developed by the MDEpiNet Coordinating Centre in consultation with FDA and an expert group of collaborators from patient advocacy groups, academic, clinical, industry, and regulatory settings. The domains of the framework were based on a previous IMDRF report[17] that was led by a number of coauthors of that study. There are seven domains:

1. Promotion of unique device identification.
2. Improving data collection efficiency.
3. Advancing data quality for regulatory decision-making.
4. Considering TPLC research.
5. Establishing governance and ensuring sustainability.
6. Leveraging registries as quality systems.
7. Incorporation of patient-generated data and PROs.

In this study, we used the Delphi method for reaching consensus to develop and refine the framework from our initial design. The Delphi method was established by the RAND Corporation in 1964.[18] It was introduced to eliminate peer influence of traditional survey designs by using an anonymous platform to collect unbiased opinions. The technique employs multiple rounds of questionnaires until a target consensus is reached from a group of diverse participants. This method is used routinely by MDEpiNet to create core minimum data elements for studying various technologies[19–22] and is also used by our partner IDEAL (Idea, Development, Exploration, Assessment, Long-term study framework) group to develop guidelines for evaluation of new surgical techniques and complex therapeutic technologies.[23]

Using the Delphi method, we aimed to establish a framework that includes five levels of maturity for each of the seven domains. MDEpiNet Executive Operations Committee members, CRN leaders, and a range of stakeholders experienced in the field of device

research and surveillance using RWE were selected for the survey.

Two rounds of the Delphi survey were circulated to participants using the Weill Cornell Medicine's Qualtrics survey platform (https://weillcornell.az1.qualtrics.com/). Round 1 was carried out in July–August 2020 and round 2 in October–November 2020. First, the participants were asked to agree or disagree on each entire domain, as presented, together with its five levels of maturity. If the participants agreed on the domain as it was presented, they moved on to the next domain. However, if they disagreed on any detail of the domain or its five levels, they were presented with follow-up questions. The follow-up questions allowed participants to provide free-text comments on the text of the domain or any of its proposed five levels regarding their disagreement. In this way, consensus was assessed for each of the seven domains as well as their five levels.

The defined aim of the Delphi process was achievement of 80% consensus for all seven domains and their five levels. The lead investigators and registry experts (AS, DM-D, JLC, EWP, PG, and AB) reviewed the survey results and used the comments made by participants to propose changes to the text of the domains and their levels until the target of 80% consensus was reached when next reviewed by the Delphi participants. The responses of round 1 were reviewed to provide clarity on definitions or language without losing the meaning or the structure of the overall model. This guided revision of the framework for round 2 of the survey. Based on the responses from round 2, the framework was further revised to create the final version, which was circulated to the participants for final comments.

The one domain in which 80% consensus was not achieved was domain 3, data quality. To resolve this, an expert panel (JLC, EWP, and AS) was convened, which reviewed all the relevant comments by teleconference on 15 December 2020. The revised version of this domain was then presented to participants and committee members on 29 December 2020 via Zoom videoconference when target consensus level was achieved.

RESULTS

Fifty-two individuals were identified as experts and were invited to participate. Of the 52 invited, a total of 41 responded to round 1 of the survey (79.9% response rate). Six participants expressed 100% agreement in round 1, and so they were excluded from round 2. All the remaining 35 responded to round 2 (100%). There was, therefore, a total of 41 responses, which were evaluated for the final model development. The characteristics of the survey participants are summarized in table 1. There were 21 (51.2%) experts who represented clinical perspective, and 12 of these experts also had academic roles. Six (14.6%) additional experts primarily represented academic perspective. There was also representation from

Table 1 Characteristics of the Delphi survey participants (N=41)

Characteristics	Percentage (%)
Professional role*	
Clinical	51.2
Academic	14.6
Regulatory	17.1
Industry	9.8
Patient representative	7.3
Location	
USA	87.8
Europe	4.9
Asia	7.3
Sex	
Male	65.9
Female	34.1

*Participants can be identified as having multiple roles.

regulatory, industry, and patient stakeholder communities (table 1).

In round 1, only the TPLC domain achieved the target consensus (82.9%) (table 2). In round 2, the agreement level for each domain increased, such that all domains reached the 80% target for consensus, except the data quality domain, which achieved 75.6% agreement. Where there were disagreements, these tended to be heterogenous, without any common theme. The one exception was the data quality domain, in which there was disagreement about the level of detail and therefore the burden of auditing requirements. After an expert panel review, the team was able to resolve the disagreement and propose a modified approach of the data quality domain to reach the target consensus, which was then agreed on by the participants when the final framework was circulated for comment. Most importantly, each item (levels 1–5) of each domain in the framework received more than 90% agreement in round 2 (figure 1).

DISCUSSION

Our two rounds of Delphi responses achieved consensus for all seven domains of the framework (with subsequently agreed adjustment for one domain), each with five levels, designed to evaluate the maturity of CRNs and registries to support medical device evaluation.

This framework offers a means of assessing the maturity, or level of development, of registries and CRNs, whatever their origin or type, specifically with respect to their suitability for generating reliable RWE. This is important because such a wide range currently exists globally. Not all registries or CRNs were created for the purpose of generating research results. Some CRNs are based on

Table 2 Delphi survey results: % agreement and disagreement on coordinated registry network maturity framework

| Domains	Round 1 (N=41)			Round 2 (N=41)		
	Agreement	Disagreement		Agreement	Disagreement	
	All levels (%)	At least one level (%)	All levels (%)	All levels (%)	At least one level (%)	All levels (%)
Device identification	70.7	29.3	0.0	92.7	7.3	0.0
Efficiency	75.6	24.4	0.0	80.5	19.5	0.0
Data quality	61.0	39.0	17.1	75.6	24.4	2.4
TPLC	82.9	17.1	2.4	92.7	7.3	2.4
Governance and sustainability	73.2	26.8	7.3	87.8	12.2	0.0
Healthcare quality Improvement	78.0	22.0	4.9	85.4	14.6	0.0
Patient-generated data and PROs	56.1	43.9	2.4	85.4	14.6	0.0

The final version of the framework is shown in online supplemental appendix A1.
PRO, patient-reported outcome; TPLC, total product life cycle.

registries started by medical professional societies in response to transformational technologies such as transcatheter valve therapies.[24] Others leverage traditional registries developed by specialty societies (eg, Society for Vascular Surgery (SVS)) and a variety of integrated health systems, used for clinical care, quality improvement, billing, and also for collection of national statistics.[25 26] Our framework offers an understanding of the capability of any registry or CRN to provide information for relevant stakeholders in a standardized manner. It will promote harmonization of assessment of maturity across different disciplines and different health systems worldwide. The framework is intended as a dynamic model, with the capacity to evolve over time as new experiences accumulate within the data ecosystem.

An example of a CRN that has achieved maturity in most domains described by our framework is the Vascular Implant Surveillance and Interventional Outcomes Network (VISION) CRN. This CRN is successful in efficiently capturing device data for patients undergoing vascular surgery and interventional care. The CRN covers 40% of relevant hospitals across the USA, with over 90%

enrollment of patients and completion of case report forms complete. It has created a national repository of linked data sources to obtain long-term outcomes and has published a series of studies documenting the value of these data for quality improvement and for informing regulatory decisions (figure 2).[27–30] It also contributes to the International Consortium of Vascular Registries (ICVR) for analyses of device outcomes.[31 32] The CRN uses data from the Vascular Quality Initiative of the Society for Vascular Surgery, which was launched in 2003 to improve the quality, safety, and effectiveness and to reduce costs of vascular procedures.[26] As a quality improvement initiative, it conducts regular data audits and provides reports back to participating institutions, including outlier assessments. The VISION CRN has also recently launched a PRO data collection pilot with disease-specific and general health measures.

It should be emphasized that a CRN or registry does not need to have the highest score in all seven domains to be considered mature and useful. Application of maturity framework and the levels of maturity that it specifies can help registries and CRNs identify the gaps and
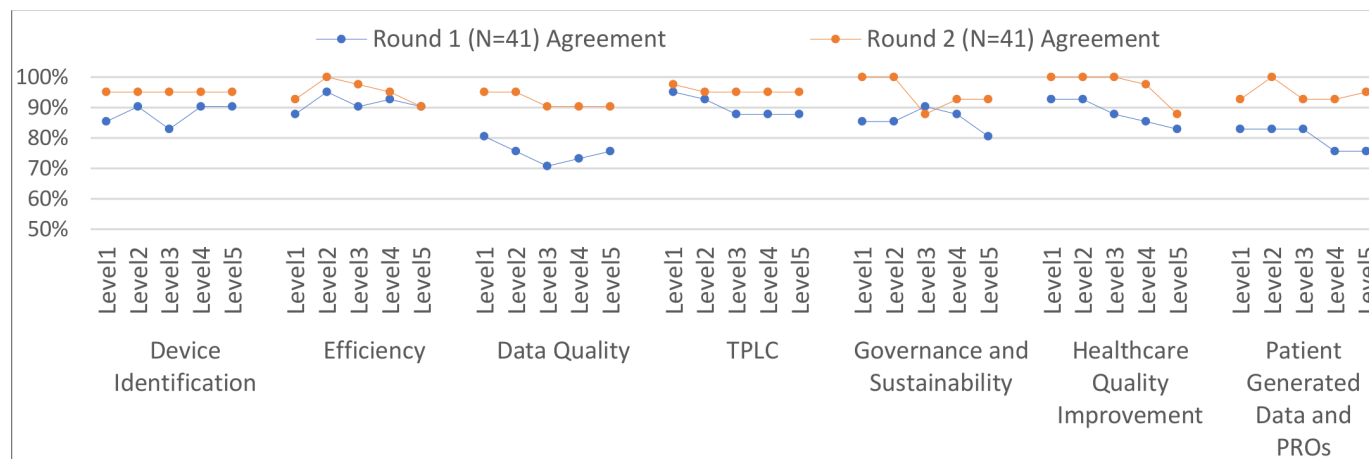
Figure 1 Delphi survey results: percent agreement on levels of maturity in each domain. PRO, patient-reported outcome; TPLC, total product life cycle.
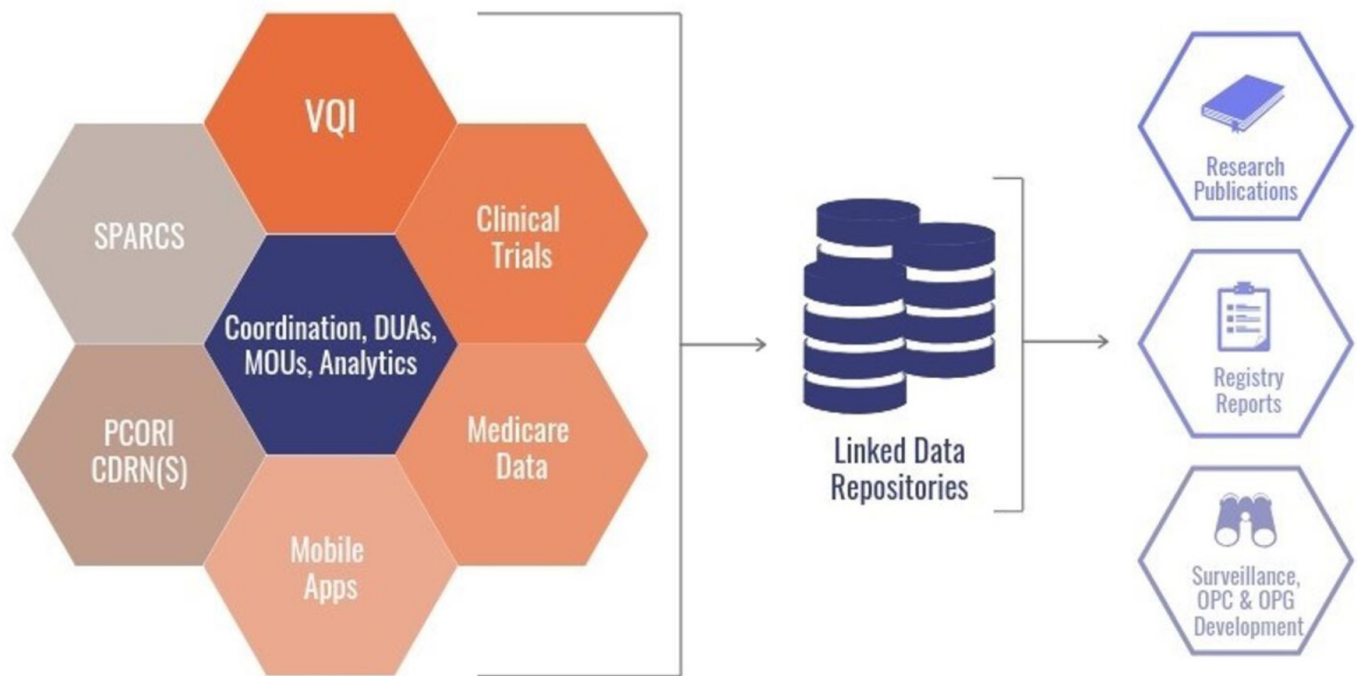
Figure 2 Vascular Implant Surveillance and Interventional Outcomes Network coordinated registry network. The center hexagon depicts the role of the MDEpiNet Coordinating Centre, and outer hexagons represent various data partners and data sources. CDRN, Clinical Data Research Network; DUA, data use agreement; MOU, memorandum of understanding; OPC, Objective Performance Criteria; OPG, Objective Perfomance Goals; PCORI, Patient-Centered Outcomes Research Institute; SPARCS, Statewide Planning and Research Cooperative System; VQI, Vascular Quality Initiative.

prioritize investments in data infrastructure and analytical processes, provided that their initial design has the potential for evolution. It is also important to understand that the framework is not intended as a system to produce an overall 'score' for any CRN or registry, but rather to assess each of its domains and then to take an overall perspective. What is important for any registry or CRN is its initial design, which needs to have the capacity for development, along the lines set out in the framework. This means involving all the key stakeholders in the initial development phase, including patients, professional societies, and manufacturers.

From the international perspective, there are emerging linked data networks that can become CRNs in Europe and Australia. In the UK, for example, there are well-established national registries, such as the National Joint Registry, that have been linked with routinely collected Hospital Episode Statistics, to study the risk of revision due to prosthetic joint infection following primary knee replacement.[33] The UK Transcatheter Aortic Valve Implantation registry also has experience linking with routine National Health Service and has provided risk outcomes of transcatheter aortic valve implantation from 2007 to 2012.[34] The UK Clinical Practice Research Datalink, with detailed information on 60 million patients from primary care providers (community-based), also provides huge potential for RWD studies, although specific device identification is challenging.[35] In Australia, population-based linked hospital morbidity and mortality data have been used to study age-stratified outcomes of surgical aortic valve replacement.[36]

Our framework creates opportunities for harmonization and global collaboration in the development and evolution of registries and CRNs because it offers a shared vision of the qualities required for them to provide reliable and useful RWE. International collaborations offer great potential for rapid acquisition of information about short-term and long-term safety and effectiveness of novel and established technologies, particularly those that are not commonly used in clinical practice. MDEpiNet has initiated international collaborations that are using registries and administrative datasets for device research and surveillance. Examples include the ICVR[37] and the International Consortium of Orthopaedics Registries.[38] Applying the CRN maturity framework to these systems will help make global collaborations increasingly more robust and useful.

CONCLUSIONS

Our maturity framework offers a consistent method for assessing the capacity of registries and CRNs to provide useful and reliable RWE about medical devices. It identifies gaps and guides their future development. It can be applied in any country or health system and, therefore, has value in enabling international collaborations.

APPENDIX A1: MATURITY FRAMEWORK

1. Promotion of unique device identification (UDI): the precise identification of medical devices is essential for evaluating the performance over time. Currently, most registries use manufacturer names, device names or billing codes for product identification, but this is mostly inadequate for unique product identification. Both regulators and MDEpiNet now advocate use of Unique Device Identification (UDI) system.[a] The FDA UDI rules require manufacturers to assign unique identifiers to their marketed devices and submit required device attributes to a UDI Database. In the U.S., the FDA's AccessGUDID, a public portal of the Global Unique Device Identification Database (GUDID), serves this purpose.[b] By providing a unique numeric or alphanumeric code for each device model and an identifier that includes the production information for that specific device (eg, serial number, manufacturing date), the UDI delivers the most accurate way to identify and track medical devices.

Device Identification domain describes the registry's ability to uniquely identify a device. Ideally, the UDI would be included; however, when unavailable, the registry should capture a combination of identifiers that enables unique identification of the device (eg, catalogue number, manufacturer, brand or generic name, device description).	Level 1 Early Learner	The registry or a linkable database in a CRN is capturing device information that is available under CPT, ICD, or other generic coding for the device-based procedure. [i]
	Level 2 *Making Progress*	The registry or a linkable database in a CRN is capturing device information using at least manufacturer and specific device names and leverages relevant CPT, ICD, or other generic coding system. [i]
	Level 3 Defined Path to Success	Building from level two achievements, the CRN has conducted large scale demonstration project to include manufacturer's product catalogue numbers or UDI that included at least five percent of annual patient enrollment.
	Level 4 *Well Managed*	The registry or a linkable database in a CRN is routinely capturing device information with manufacturer's product catalogue numbers or UDI that can identify devices and mapped to attributes/features needed for research and surveillance.
	Level 5 Optimised	The registry or a linkable database in a CRN is routinely capturing device information with UDI and mapping to attributes/features needed for research and surveillance. UDI information is seamlessly and efficiently integrated with the registry or CRN operations.

[i] Level 1 and level two achievements can be sufficient if only one device and few devices are on the market and if such coding would appropriately identify the device. In all other instances, catalogue numbers and ideally UDIs are required.

[a]Gross TP, Crowley J. Unique device identification in the service of public health. *The New England journal of medicine.* 2012;367(17):1583-1585.

[b]Unique Device Identification System. In: FDA, ed. *21 CFR § 16, 801, 803, 806, 810, 814, 820, 821, 822, 830.* Vol 0910-AG312013:58785-58828.

2. Improving data collection efficiency: Minimising the burden of data collection processes is crucial, to maximise data submission. Centres with advanced informatics are able to organise their clinical workflows to record data needed for registries in ways that reduce effort and so improve the completeness of data collection.[c] this kind of structured data capture minimises the number of staff needed for data collection and the time they need to spend. agreements about the core vocabulary and corresponding technical (database) representation allow integration of high-quality data into the processes of care; promotion of automated collection; lowering the burden of data collection; minimization of human error; and reduction of resource requirements. Efforts to reduce the burden of data collection and improve the quality of data include scanned capture of UDI on device labels and auto-population of key device attributes from AccessGUDID. AccessGUDID offers means to auto-populate fields such as manufacturer, brand, device size, and other standard fields needed for analysis. Finally, soliciting patient input and collecting data through innovative patient-facing applications enables inclusion of endpoints of interest, addressing patient preferences and gaining further efficiencies in data collection.

Efficiency domain describes the extent to which the registry is embedded in the healthcare quality improvement system so that data collection occurs as part of care delivery (ie, not overly burdensome, not highly complicated, not overly costly) and integrated with workflow of clinical teams. A key pre-condition for this domain is that the core minimum data process with key stakeholders is developed in order to define the CRF and the elements are clinically relevant and harmonised. This will ensure that reliable and relevant data elements with proper definitions are included in the data collection effort.	Level 1 Early Learner	Heavy burden of data collection with ad hoc data elements on a project basis but without agreement on clinically relevant core minimum data elements.
	Level 2 *Making Progress*	Clinically relevant core minimum data elements are established with key stakeholder input. Data collection is started but there is a heavy burden on data collectors (manual data entry with no automation).
	Level 3 *Defined Path to Success*	In addition to level two achievements, technologies are in place (eg, structured data extraction from EHRs; mobile apps) to reduce burden on data collectors, and a pilot project is completed on adoption of data and terminology standards that will enable exchanges between data information ecosystems (interoperability).
	Level 4 *Well Managed*	Technologies are in place (eg, structured data extraction from EHRs; mobile apps) to reduce burden on data collectors, and a multisite demonstration project is completed on adoption of data and terminology standards that will enable exchanges between data information ecosystems (interoperability).
	Level 5 Optimised	Technologies are in place (eg, structured data extraction from EHRs; mobile apps) for all core minimum data elements and a fully automated data collection for most core minimum data elements, and there is a full adoption and integration of data and terminology standard (assumes complete interoperability).

[c]Sanborn TA, Tcheng JE, Anderson HV, et al. ACC/AHA/SCAI 2014 health policy statement on structured reporting for the cardiac catheterization laboratory: a report of the American College of Cardiology Clinical Quality Committee. *J Am Coll Cardiol.* 2014;63(23):2591-2623.

3. Advancing data quality for regulatory decision-making: A key tenet of the CRNs construct is the development and adoption of discipline-specific core minimum data in collaboration with regulators. this includes reaching agreement on precise definitions of data elements. consecutive data collection and completeness (minimising missing or out-of-range values) are important in producing robust medical device evidence and CRNs strive to achieve adequate enrollment with complete records of the target population. Coverage (ie, regional, national, health system etc.) is another important quality measure; and adequate coverage of hospitals and community practices within the scope of the registry is important for evidence generalizability.

Data Quality domain focuses on relevance, coverage (scale), completeness of patient enrollment and data elements (records) at both baseline and follow-up, and accuracy verified by periodic audits (ideally annually or at least every 2 years). These four concepts take into account the relevance and reliability concepts outlined in the real-world evidence guidance issued by the Centre for Devices and Radiological Health at the FDA. A key pre-condition for this domain is that the registry core minimum data elements and research modules are defined in collaboration with key stakeholders. This will ensure relevance because data elements with proper definitions and key stakeholder input are included in the data collection efforts (see also TPLC domain). Coverage (scale) concept is related to extent of participation of sites that use particular a technology/device. Completeness concept is related to how complete the enrollment is at each site and the core minimum data (records). Accuracy is defined by the degree of matching of the CRN/registry data to the source documents.

Level	Description
Level 1 *Early Learner*	The coverage includes the pilot registry/ CRN with single or several site efforts that capture small patient populations (data completeness and other quality measures are not yet relevant).
Level 2 *Making Progress*	The coverage includes a large number of sites (large population) but mostly inadequate enrollment [ii] of patients but robust completeness [iii] of data elements (records). Plans are in place for conducting audits to assess and improve the data quality.
Level 3 *Defined Path to Success*	The coverage includes a large number of sites engaged (large population), there is adequate enrollment [ii] of patients and completeness [iii] of data elements (records). Plans for conducting and executing audits of data quality at least once with minimum* requirements.
Level 4 *Well Managed*	The coverage is at least regional or includes a large national health system with adequate enrollment [ii] of patients and completeness [iii] of data elements (records). Ongoing sequential audits with at least one audit completed with moderate* requirements.
Level 5 Optimised	The coverage is national with adequate enrollment [ii] of patients and completeness [iii] of data elements (records). Initiating routine audits with extensive* requirements (at least bi-annual). *Auditing requirements: Minimum includes verification of at least exposure (eg, device) and outcomes using a generalizable cohort; moderate includes verification of exposure (eg, device), outcomes and key risk factors using a generalizable cohort; and extensive includes verification of entire data collection forms using a generalizable cohort.

[ii] Greater than 80% regional, national, or major health system coverage might be adequate; [iii] Greater than 80% enrollment with complete records might be adequate.

4. Considering Total Product Life Cycle (TPLC) research: Generating evidence from the time of early adoption of technologies is an important priority to support attainment of startup funds. Registries for breakthrough technologies can be designed to include specific factors needed for evaluation of effectiveness (eg, Transcatheter aortic valve replacement (TAVR)); and to facilitate later transformation into a quality registry, by ensuring collection of minimum core data fields necessary for surveillance. A key issue is to not confuse the purpose of the registry with specific investigations that should be 'nested' within it: the latter can include collection of additional data elements. Using RWE in clinical trials is feasible, particularly in 'pragmatic trials' where patients and device operators included are broadly representative of the target population. To evaluate long-term outcomes, mature CRNs need to demonstrate robust linkage with relevant data sources that enable enhancement of data and longitudinal follow-up.[d e]

TPLC domain describes the total life cycle of a device and the notion that registries can serve as the infrastructure for conducting both clinical research and device surveillance at different stages of device evaluation. Registry core minimum data elements and research modules should ensure relevance of the collected data from stakeholder perspective (see also Data Quality domain). In addition, the use of registries may allow for a seamless integration of evidence generation at the point of care throughout the device life cycle. A critical aspect of lifecycle research is obtaining long-term outcome data with efficient methodology. This domain is aligned with FDA's TPLC vision.

Level	Description
Level 1 *EarlyLearner*	Developed a plan for conducting short-term or long-term clinical outcome studies (eg, direct follow-up or data linkages) and surveillance.
Level 2 *Making Progress*	Developed some capacity (eg, IT infrastructure system) for conducting short-term or long-term clinical outcome studies and surveillance.
Level 3 *Defined Path to Success*	Registry has experience with at least one short-term or long-term clinical study or surveillance during product lifecycle that assists regulatory decision making. However, it has limited capacity for analytics and burdensome/inadequate [iv] process to obtain long-term outcome data (eg, linking registry to EHRs or claims data) for research and surveillance.
Level 4 *Well Managed*	Registry has experience with at least one study during the product lifecycle that assists regulatory decision making. Developed sustainable capacity for analytics and an adequate [iv] process to obtain long-term outcome data (eg, linking registry to EHRs or claims data) for research and surveillance.
Level 5 *Optimised*	Registry has substantial experience (eg, three or more studies) that assisted regulatory decision making, has sustainable capacity for analytics, and an adequate [iv] process to obtain long-term outcome data (eg, linking registry to EHRs or claims data) for research and surveillance.

[iv] If direct follow-up is conducted, greater than 80% achievement might be adequate. When using data linkages, greater than 90% might be adequate.

[d]Columbo JA, Martinez-Camblor P, O'Malley AJ, et al. Long-term Reintervention After Endovascular Abdominal Aortic Aneurysm Repair. Ann Surg. 2019;July 8, 2019 - Volume Publish Ahead of Print - Issue - p.

[e]Columbo JA, Sedrakyan A, Mao J, et al. Claims-based surveillance for reintervention after endovascular aneurysm repair among non-Medicare patients. *J Vasc Surg.* 2019;70(3):741-747.

5. Establishing governance and ensuring sustainability: MDEpiNet emphasises strong governance and sustainability as essential issues for the CRNs. even if a CRN is mature in many domains, any registry that is solely funded as a pilot study or by a standalone manufacturer will cease to exist once the organisation has achieved its short-term goals. sustainability requires multiple stakeholders to buy into the value that is generated by the CRN. CRNs that are hosted by a professional society or health system, with multiple funding sources and transparent leadership and governance, are most likely to be sustainable in the long-term. MDEpiNet promotes creating a 'steering committee' as well as 'research and publication' and 'sustainability' subcommittees to engage stakeholders and to create multiple leadership opportunities for dedicated and enthusiastic experts. holding annual think-tanks or meetings with stakeholders helps to achieve alignment and priority setting for infrastructure and research. creating an atmosphere of collaboration and developing trust will enrich a CRN and is key to establish and sustain the continuous dialogue in supporting a learning (healthcare) system of medical device evaluation.

Governance and Sustainability domain describes the governance structure focusing on participation of major stakeholders enabling generalizable (regionally, nationally or health system wide) data collection and transparent governance*. The hosting organisations include professional societies, integrated health systems, payers, and various states. In addition, the ability for the registry to obtain major and diverse sources of funding is critical for sustainability. Registries and CRNs built by manufacturers for their own purposes are special instances that are not in scope of this domain.

Level 1 Early Learner	Absence of professional society/major health system/state endorsement, mostly pilot and project level governance.
Level 2 Making Progress	Absence of professional society/major health system/state endorsement. Reasonable funding is available (eg, support for a specific project at NIH R01 level or industry sponsorship at the same level).
Level 3 Defined Path to Success	Hosted by a professional society/major health system/state. Reasonable funding is available (eg, support for a specific project at NIH R01 level or industry sponsorship at the same level), establishing transparency in governance.
Level 4 *Well Managed*	Hosted by a professional society/major health system/state. Robust funding is available (eg, multi-year large scope projects funding in place at NIH centre grant level or multiple industry sponsorship at the same level), and governance is transparent.
Level 5 Optimised	Hosted by a major professional society/major health system, commitment to funding indefinitely (eg, renewable NIH centre grant level or multiple industry sponsorship at the same level), and governance is transparent.

*Transparent governance metrics include but are not limited to participation of major stakeholders and clear organisational structure with steering committee, subcommittees, and data access policies.

6. Leveraging registries as quality systems: Most healthcare enterprises participate in registries as tools for quality improvement. analyses of processes and outcomes from registries serve as feedback to inform the sites about conformance with guidelines, comparative patient outcomes, opportunities to improve care, and other critical strategic, administrative, and operational imperatives. Device use and outcomes are considered part of this function.[f] This infrastructure will enable medical device research and surveillance in the context of both the device and the device operator's performance. Lessons learnt from cardiology, cardiac surgery and vascular surgery registries can be very helpful for the evaluation and improvement of care.[g h i j] Sharing best practices in provider feedback, such as use of creative data visualisation techniques, can enhance clinician and hospital participation in quality improvement registries.

Healthcare Quality Improvement domain describes the registry process for quality improvement. The registry is a healthcare delivery improvement system or is evolving into one as device technologies are diffused into practice and need continuing evaluation (including outlier identification). The registry has established mechanisms to bring about beneficial change in healthcare delivery through stakeholder participation, ownership, and integration into the relevant healthcare systems.

Level 1 Early Learner	Registry does not have provider feedback benchmarking process and conducts limited device outlier assessments.
Level 2 Making Progress	Registry has more than one, and growing number of participants in provider feedback benchmarking process and conducts limited device outlier assessments.
Level 3 Defined Path to Success	Registry has initiated routine provider feedback for all participating sites. As part of that process, it is developing routine device outlier assessment.
Level 4 Well Managed	Registry has completed first major periodic feedback process. As part of the process, it has initiated device outlier assessment.
Level 5 Optimised	Registry has regular and ongoing (at least annually or similar) provider feedback in place and routinely includes device outlier assessment. Ideally, there is automation of quality process with advanced analytics and visualisation tools integrated with data collection.

[f]Sedrakyan A, Campbell B, Graves S, Cronenwett JL. Surgical registries for advancing quality and device surveillance. *Lancet (London, England)*. 2016;388(10052):1358-1360.

[g]Carroll JD, Edwards FH, Marinac-Dabic D, *et al*. The STS-ACC transcatheter valve therapy national registry: a new partnership and infrastructure for the introduction and surveillance of medical devices and therapies. *J Am Coll Cardiol.* 2013;62(11):1026-1034.

[h]Sedrakyan A, Campbell B, Graves S, Cronenwett JL. Surgical registries for advancing quality and device surveillance. *Lancet (London, England)*. 2016;388(10052):1358-1360.

[i]Shahian DM, Grover FL, Prager RL, et al. The Society of Thoracic Surgeons voluntary public reporting initiative: the first 4 years. *Ann Surg.* 2015;262(3):526-535; discussion 533-525.

[j]De Martino RR, Hoel AW, Beck AW, et al. Participation in the Vascular Quality Initiative is associated with improved perioperative medication use, which is associated with longer patient survival. *J Vasc Surg.* 2015;61(4):1010-1019.

7. Incorporation of *patient* generated data and PROs: Patient generated data and PRO collection is an important priority of the FDA and other regulators, for safety and efficacy in medical devices.[k] Patients can contribute is by serving as partners, participating in research and surveillance, and sharing their experience related to devices. Robust and comprehensive patient generated, and PRO data collection is possible when combined with use of mobile applications, advancement in EHR systems and linkages to EHRs and registries.[l]

The PRO measures should include collecting at least one general health and one disease- specific outcome measure. Centre for Devices and Radiological Health at the FDA defines the PRO as a measurement based on a report that comes directly from the patient (ie, study subject) about the status of a patient's health condition without amendment or interpretation of the patient's response by a clinician or anyone else.

Level 1 *Early Learner*	The CRN identified (ideally with patient engagement) and collaborated with stakeholders to define disease specific and general health validated PROs that meet regulatory guidelines.
Level 2 Making Progress	In addition to level 1, the CRN conducted a demonstration project of obtaining PROs and integrating within CRN infrastructure.
Level 3 Defined Path to Success	In addition to level 2, the CRN is able to seamlessly integrate PROs within CRN infrastructure using patient- facing applications.
Level 4 *Well Managed*	In addition to level 3, the CRN is routinely obtaining PROs using a consecutive and generalizable sample and using these for research and surveillance and has conducted at least one study using PROs for a benefits and harms assessment of technologies.
Level 5 Optimised	In addition to level 4, the CRN is routinely obtaining PROs on a large scale to allow benchmarking at the participating institutional level and has substantial experience of using PROs for a benefits and harms assessment of technologies.

[k]Value and Use of Patient Reported Outcomes (PROs) in Assessing Effects of Medical Devices. CDRH Strategic Priorities 2016- 2017 https://www.fda.gov/files/about20fda/published/Value-and-Use-of-Patient-Reported-Outcomes-28PROs29-in- Assessing-Effects-of-Medical-Devices.pdf. Accessed 04/09/2021.

[l]Wu AW, Kharrazi H, Boulware LE, Snyder CF. Measure once, cut twice--adding patient-reported outcome measures to the electronic health record for comparative effectiveness research. *J Clin Epidemiol*. 2013;66(8 Suppl):S12-20.

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