Medical Specialty Societies
An Emerging Source of Real-World Evidence

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For many conditions requiring specialty clinical care, the era of obtaining real-world evidence (RWE) insights from insurance claims is drawing to a close. Life sciences companies are developing treatments for increasingly smaller subsets of disease populations, increasing the information demands to define populations and characterize their course of illness. The data elements required to establish these patient populations, and demonstrate that new treatments improve those patients' outcomes relative to usual care, are rarely needed to substantiate payment for services in any current reimbursement model. Among the 14 oncology drugs approved by the FDA in 2015, patients indicated for nine drugs (alectinib, cobimetinib, daratumumab, dinutuximab, necitumumab, osimertinib, palbociclib, trabectedin, trifluridine/tipiracil) are impossible to identify solely from the use of insurance claims. Tumor biomarkers, histology, and the level of response observed from prior therapies are all missing from insurance claims and are needed to verify these medicines' treatment indications.

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Even when treatment-eligible patients can be identified from insurance claims, insights regarding clinical judgments and treatment outcomes are still missing from those claims. Mortality can only be crudely inferred by events preceding a patient's disenrollment, or by the infrequent case of in-hospital death. Progression is often inferred from insurance claims by the administration of a new line of therapy, but these data cannot discriminate between progression, toxicity, and patient preference as reasons for therapy discontinuation. New data sources are also required to analyze prognostic scores, performance status, and tumor attributes that imply specific treatment pathways.

The declining value of insurance claims for many RWE questions has exerted several forms of pressure on evidence for market access. It has prompted innovation in the ways that life sciences companies use randomized trial data (e.g., new simulation technologies, indirect and mixed treatment comparisons). It has also increased readiness to invest in observational studies that depend on primary data collection. But notably, it has also maintained pressure on locating healthcare data from other sources, such as electronic medical records (EMR), that may hold the level of clinical detail required for evaluation of today's treatments. The cost, flexibility, and repeated use benefits of healthcare databases such as EMRs hold continued appeal to those managing

constrained evidence generation budgets. Described below are the factors leading to increased availability of EMRs, incentives to improve EMR data quality, and the emerging role of medical specialty societies in aggregating EMR databases for RWE.

Expanded Adoption of Electronic Medical Records

EMR data sources have been available for RWE purposes in some European countries since the 1990s. The predecessor to the Clinical Practice Research Datalink has been publicly available since 1994, and practice registers have been available in the Netherlands through the PHARMO Institute since 1999. However, research-ready access to EMRs varies widely among European countries, and it remains heavily biased towards general practitioner records. Life sciences companies interested in exploring the benefits and risks of specialty care products have seen limited value from European EMR databases.

The availability of EMR records in the U.S. has increased dramatically due to business concerns and regulatory developments. The initial transition from practice management systems to EMRs was prompted by fears that the "Y2K" problem, the hard-coding of two-digit years in FORTRAN- and COBOL-programmed billing systems, would create fatal errors in providers' ability to invoice for services.

Some U.S. EMR companies aggregated data from their new customers for research purposes. Aggregated databases from general purpose EMR vendors such as Allscripts, Cerner, and General Electric have been used for peer-reviewed research in the life sciences. The collective experiences of using such databases have been mixed. While they provide access to content not typically available from other healthcare databases, many data elements were missing or unpopulated. EMR companies could sell systems to physician practices, but had little influence on the quality or completeness of data entry in those systems. Researchers increasingly sought information that was stored in unstructured documents, such as dictated clinician notes or laboratory reports. EMR vendors, however, lacked the incentive, authority, or technical capabilities to strip identifiers that could compromise patient privacy from those documents.

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In addition to general purpose EMR systems, some EMRs were developed for the needs of specific medical specialties. Among those, the EMRs for oncology practices were most likely to have their data aggregated for research purposes. Oncology databases sourced from Varian and Impac became available for research use, but bore many of the same challenges as those from general-purpose EMR databases. Some specialty EMR database providers made an effort to improve data entry quality, for their own business benefit as well as the benefit of researchers. McKesson's iKnowMed EMR system, originally developed by U.S. Oncology, enforced data entry checks and quality systems as a condition for getting access to group purchasing and drug ordering benefits. Most recently, Flatiron Health has committed to automated and manual enhancement of data for several different EMR brands to improve feedback for physician customers and to enhance the value of data for life science research.

Incentives for Improved EMR Data Quality

U.S. companies marketed EMRs not just as solutions to fixing Y2K problems, but also for improving population-based care. This marketing push, and perhaps some effective lobbying, inspired the U.S. government to incentivize their adoption in exchange for greater accountability for quality care. The 2009 American Reinvestment and Recovery Act contained provisions referred to as the Health Information Technology for Economic and Clinical Health Act (HITECH). HITECH offered payment incentives for EMR adoption as long as providers demonstrated "meaningful use" of non-billing features to assure high quality care processes in their practice.[1] The Centers for Medicare and Medicaid Services (CMS) gained authority in 2006, under the Tax Relief and Health Care Act (TRHCA), to reward voluntary physician quality reporting with increased physician reimbursements.[2] That program, now called the Physicians Quality Reporting System (PQRS), has gradually shifted its range of reporting options to favor use of EMR data. PQRS received additional support when the 2010 Affordable Care Act (ACA) authorized Medicare reimbursement penalties for those not participating in PQRS by 2015. The Medicare Access and CHIP Reauthorization Act of 2015 (MACRA) streamlined HITECH's EMR adoption incentives and TRHCA's PQRS reporting incentives into a Merit-Based Incentive Payment System (MIPS), which will begin in 2017.[3]

The legislative incentives for EMR use and quality reporting apply to physicians across medical specialties. This has increased the likelihood that data on real-world specialty care exist within the EMR databases of U.S. physician practices. However, obtaining ethical access to well-powered cohorts from these EMRs requires aggregation from their distributed locations, and also sufficient data processing to assure patient privacy and research validity.

Medical Specialty Societies Offer Support

Physicians can meet PQRS reporting requirements through participation in registries; CMS has established two models by which entities can form registries for submitting physicians' PQRS results. One of these models, called the Qualified Clinical Data Registry (QCDR), has gained favor among numerous medical specialty societies. U.S. medical specialty societies have increasingly taken on the challenge of aggregating specialty EMR records and applying for certification as QCDRs. The Council of Medical Specialty Societies (CMSS) has fostered this interest, sharing best practices through conferences and the publication of a registry primer.[4] The current list of QCDRs includes EMR-based registries affiliated with more than a dozen U.S. medical specialty societies.[5]

Given that PQRS reporting influences physicians' reimbursement rates under Medicare, medical societies can provide a substantial membership benefit by assisting practicing physicians with their EMR-based quality reporting. Most medical societies do not have the technical capabilities to extract or aggregate EMR records from distributed physician practices; these societies have outsourced extraction and aggregation tasks to technology vendors. Unlike the EMR databases aggregated by individual EMR companies, the task of aggregating EMRs for medical specialty societies requires merging data from multiple brands with dissimilar data models. PQRS measures are based on a Quality Data Model (QDM), first developed by the National Quality Forum and now jointly maintained by CMS and the Office of the National Coordinator for Health Information Technology.[6] While the QDM provides a target list of data elements that should be standardized, it provides little guidance to data aggregators on the database structure in which to arrange these elements from disparate EMR systems.

Aggregation vendors' technical support is often funded directly by the sponsoring medical society. A review of public information on the QCDR list and specialty society websites suggests that member physicians currently pay minimal or no fees for participation in their society's QCDR. The sponsorship and financial underwriting of the medical societies are substantial incentives for physicians to contribute EMR data into aggregated registries. A synopsis of several medical specialties, and their current state of research readiness, appear below.

The **American College of Cardiology (ACC)** has developed an increasing number of registries under the National Cardiovascular Data Registry® (NCDR) brand.[7] ACC maintains numerous hospital-based registries that depend on data collection forms. Their first outpatient registry, – Practice INNovation And Clinical Excellence (PINNACLE™) began in 2008, with its first PQRS reporting conducted in 2009.[8] Initial data collection was also performed using data collection forms, but ACC has incentivized EMR-based reporting through partnerships with a data extraction vendor and certification of export functions from EMR vendors. A functioning EMR has been a participation requirement since 2010, although the registry still extracts only a portion of participants' full EMR data.

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PINNACLE is the most research-ready of the medical specialty registries. ACC maintains a governance process to approve research applications. Approved applications are executed by a limited set of approved analytic centers, not by the research requestor. ACC publishes the PINNACLE data dictionary, a printed version of its data collection form, and a list of abstracts, manuscripts, and unpublished reports on studies that have used PINNACLE. The first peer-reviewed manuscript using PINNACLE data was published in 2010.[9]

The **American Academy of Ophthalmology (AAO)** began development of the Intelligent Research In Sight Registry (IRIS®) in 2014. IRIS was certified as a QCDR for PQRS reporting in 2016. Unlike ACC's PINNACLE, IRIS was conceptualized as an EMR aggregation registry from its inception. AAO states clear intentions to use the data for research purposes in its promotional materials. A case study of IRIS in the CMSS registry primer mentions pilot study contracts between AAO and external researchers.[4] AAO acknowledges in this same case study that broader support for external research depends on their development of a review infrastructure, slated for 2017. AAO has not yet published a data dictionary or other

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support materials that would inform potential applicants of the IRIS Registry's value for particular research questions.

The **American Academy of Neurology (AAN)** announced the formation of its Axon Registry™ in 2015.[10] By 2016, AAN announced that the Axon Registry had already been approved as a QCDR.[11] Like AAO's IRIS Registry, the Axon Registry was established as an EMR-sourced registry from its inception. AAN has established a Registry Committee and a Data Governance Committee with responsibilities for the Axon Registry, but has not published specific intentions to release data for external research, nor has it published supporting materials that could inform researchers of the Axon Registry's potential value.

The **American Society of Clinical Oncology (ASCO)** established CancerLinQ™ in 2012. ASCO developed a prototype CancerLinQ database in 2013, based on breast cancer patients from several cancer centers.[12] Development accelerated in 2015, when the enterprise was incorporated as a wholly owned subsidiary and a new executive team was hired to expand enrollment. The current model involves data extraction through participating practice EMRs, as with the other registries previously described.

CancerLinQ has been the most explicit of medical specialty society registries in terms of identifying its participating practices, which could inform how representative participating practices are of oncology practices as a whole.[13] CancerLinQ has also published its governance structure and its authority for re-use of data.[14,15] Although neither ASCO nor CancerLinQ have published details regarding current external research use of registry data, these publications provide more specific details about the potential for future data use than are available from other medical specialty registries. First, the current CancerLinQ framework maintains personal health identifiers (PHI) from contributing practices. CancerLinQ proposes separate database instances, some retaining PHI for use in CancerLinQ's role as a Business Associate for participants, and others stripped of identifiers for use as Limited Data Sets or De-Identified Data Sets as defined under the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule. Second, the scope of elements collected within CancerLinQ includes unstructured documents, with intention to use those documents for future analysis activities. CancerLinQ consulted an Institutional Review Board, which deemed that the scope of activities proposed for CancerLinQ participants was exempt under the healthcare operations clause of the HIPAA Privacy Rule. It is possible that future data uses may be considered beyond the scope of healthcare operations and may require ethics review.

Potential Advantages of Medical Specialty EMR Databases

As previously discussed, aggregated EMR databases in the U.S. have previously been accessed through commercial entities. Accessing similar records from a medical specialty society has several potential advantages to the commercial access model. First, commercial enterprises have usually obtained access to EMR records through purchasing or barter agreements. The cost or effort required to obtain these data must be passed along to researchers through data access or license fees. Medical specialty societies collecting EMR records for registries are also, in effect, bartering for data access. However, the magnitude of pass-through cost is likely to be much lower for medical societies than for commercial entities, as long as those societies are able to obtain data without payments to individual practices.

Second, the purpose of medical society EMR registries includes a built-in feedback loop that holds potential for improving the quality of data entry and consistency. QCDRs can show physicians which patients fail performance measures in ways not likely visible within the practice's EMR interface. Because better performance on PQRS measures leads to improved reimbursement, physicians have incentive to correct data entry for poorly-documented patients. Medical specialty societies are more directly involved in the development of PQRS measures than are commercial entities. The potential benefit is that EMR databases aggregated by those societies naturally lead to improved data entry quality. The Business Associate relationship that permits this feedback loop also depends on specialty societies' access to patient identifiers, which are usually stripped or encrypted prior to sharing of EMR data with commercial entities. Possession of identifiers increases the opportunity to link patient records with those in other care settings, potentially overcoming the disadvantages of researching patients in a single practice setting.

Finally, medical specialty societies maintain a stronger professional relationship with their physician members

than would commercial entities. The benefits of this relationship can be observed in the registry examples discussed above. Practices appear willing to contribute patient identifiers and content such as unstructured documents to these registries, which would be unlikely for commercially aggregated EMR databases. It is likely that member physicians would be more open to appeals from a specialty society to expand the level of engagement in externally sponsored research. Supplementing database studies with prospective data collection, or more precisely targeting recruitment for clinical trials, might become feasible uses of specialty society EMR databases in ways that commercial databases could not support.

Criteria for Viable Specialty Society EMR Databases

While EMR registries from medical specialty societies possess potential advantages, that potential must be realized before these registries hold value for external researchers. At present, the volume of research supported by these databases is small, limited to few medical specialties, and a subset of EMR data elements within those specialties. Several success factors will determine whether these EMR registries become useful RWE resources for the life sciences industry.

First, medical societies are in the business of serving their clinician members. They are not experienced at developing financial and operating models for the production of research-ready data. The registry examples previously described all appear to depend on external technology vendors to accomplish the initial steps of data extraction and aggregation. Additional functions of data curation, database documentation, inquiry support, and fulfillment must all be developed if specialty societies hope to support external research at any scale. The potential for unintended privacy exposure or processing errors that undermine data validity also require a robust set of quality management procedures. Such procedures are also not a core capability of medical societies. External interest in such data will be directly proportional to the quality, scale, and speed of access that result from a well-organized data production enterprise. Medical societies will most likely require external support to design and implement such operations.

Second, medical specialty societies who undertake EMR registries will face tension between their membership mission and the range of research interests from external parties. Governance structures must clearly identify the range of potential uses for registry data, so that participating practices maintain confidence in their continued participation. Beyond concerns about maintaining privacy, participating practices may not yet be prepared for uses of registry data that compare quality performance across practices, use financial information such as contracted rates or staffing costs, link patient records to care rendered outside the practice, or represent intrusions in the form of patient recruitment activities. The boards of medical specialty societies, populated with physician members, will need to demonstrate leadership in defining mutually acceptable uses that balance the interests of participants and research sponsors.

Finally, the incentives that have prompted societies to establish EMR registries must either remain in place, or be replaced by equally attractive incentives. As with most healthcare databases, research access to medical specialty registries is secondary to other business or regulatory functions. Should government incentives for EMR use be repealed or decreased, U.S. medical specialty societies would require additional reasons to underwrite registries, and members would need additional reasons to continue participating. Funding from external research sponsors can provide one such incentive for continuing registries, but benefits of that funding may be perceived differently by medical societies and their members. Efforts that inspire participants to a higher purpose, such as the Cancer Moonshot Initiative's urging to break down barriers to research collaboration in oncology, will likely need to be paired with incentives that meet the continued financial and business interests of participating specialty practices. However, under current incentives, medical specialty EMR registries hold increasing promise for obtaining real-world insights on specialty care.

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