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Demonstrating the Value of Outcomes in Echocardiography: Imaging-based Registries in Improving Patient Care

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INTRODUCTION

Echocardiography is one of the most commonly performed procedures for diagnosis, therapeutic guidance, and management of a large number of diseases. In 2010, echocardiography represented 11% of Medicare spending on imaging services, accounting for \$1.2 billion US dollars in cost, with roughly 25% of all Medicare Fee-for-service beneficiaries receiving one echocardiogram.^{1,2} With the passage of the Patient Protection and Affordable Care Act in 2010, there has been a rise in interest and participation in bundled payment and cost-sharing programs that shift the financial responsibility for maintaining care quality to the individual provider or group.³ Health care stakeholders including providers and groups are now facing mounting pressure to justify the added value of diagnostic tests, procedures, and other treatments that are provided to patients, deemed to be under their care. This is particularly the case with medical imaging, which has outpaced growth in other physicians services.¹ In response, the American Society of

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Echocardiography (ASE), American College of Cardiology, American Heart Association, and other cardiovascular societies have put forth appropriate use criteria (AUC) for diagnostic imaging, to create consensus about appropriate imaging that both payers and providers agree upon.⁴

While imaging services overutilization has been the primary focus of regulatory efforts, comparatively little attention has been given to the consequences of underutilization. In part, this bias towards overutilization in the published literature reflects the complexity of measuring underutilization. In an analysis of nationwide billing data from 2001–2011, billing codes for echocardiography were reported in only 8% of hospitalizations for acute myocardial infarction, cardiac dysrhythmia, acute cerebrovascular disease, heart failure, and sepsis, despite established echocardiography indications for these diagnoses, and demonstrated inverse association between echocardiography and inpatient mortality in this setting.⁵ While this study suggests that the burden of underutilization of imaging services may be large, it is difficult to discern if echocardiograms were undercoded or if the apparent protective benefit of echocardiography is due to less sick individuals surviving to receive an echocardiogram, rather than a function of improved diagnosis or treatment provided by echocardiography.⁶ Still, other studies have suggested a survival benefit to echocardiographic imaging. In an analysis of Olmsted County residents with clinical heart failure, only 63% of patients received an echocardiogram within 3 weeks of a heart failure diagnosis.⁷ This group had a 39% improved survival compared to those not receiving an echocardiogram.

While improved survival with echocardiography may reflect the bias of healthier individuals receiving an echocardiogram, and therefore, a causal effect of echocardiography on reducing mortality cannot be inferred at the present time, it is also plausible that echocardiography has a substantial benefit by improving diagnosis and appropriate treatment allocation. For example, the role of echocardiography in risk prediction for sudden death after acute myocardial infarction relies heavily on our understanding of the role of left ventricular ejection fraction in sudden death risk.⁸ Sudden death risk is integrally tied to systolic function, and treatment decisions regarding defibrillator placement are made based on this relationship. In this case, the value of imaging is to improve risk stratification and case selection, and while the optimal imaging technique for quantitation of systolic function is debated, there is broad agreement on the need for imaging.

More recent data have suggested that echocardiography may continue to be underutilized in certain circumstances. In a study of inpatients not undergoing echocardiography, 16% presented with conditions for which echocardiography was indicated.⁹ In another 2016 retrospective analysis of Commercial and Medicare insurers administrative claims data, only 17.5% of more than 67,000 patients with new onset heart failure received any testing for ischemic heart disease during the index hospitalization and only 27.4% at 90 days.¹⁰ Stress echocardiography was performed in only 7.8% of index hospitalizations and in only 14.3% by 90 days. While standard 2D transthoracic echocardiography was the most commonly utilized test, only 63.6% of patients presenting with new heart failure received an echocardiogram during the index hospitalization with only 72.9% receiving an echocardiogram within 3 months.¹⁰ Data from the Massachusetts General Hospital

evaluating surveillance for valvular heart disease have suggested that while 20% of providers can be considered over-utilizers of echocardiography, the problem of underutilization may be larger with 25% of providers considered under-utilizers relative to AUC recommendations.¹¹ Certain racial and demographic groups may be preferentially affected by underutilization. African American, female, older, and Medicaid patients may be less likely to receive appropriate echocardiographic surveillance for valvular heart disease.¹²

Yet does underperformance of echocardiograms in the setting of clear indications reflect underutilization? As it is currently not possible to interrogate the reasons for clinician behavior and ordering of an echocardiogram in a large dataset, it is difficult to say an echocardiogram was “underutilized” versus appropriately not utilized. Combined with the paucity of randomized clinical trials of echocardiography vs. no echocardiography for specific clinical indications, it is difficult, at the current time, to discern the direct health benefits conferred from echocardiography.

THE CASE FOR VALUE IN OUTCOMES

The Current State of Outcomes Research in Echocardiography

Faced with rising cost pressure and an increasing need to justify testing, imagers need new strategies to demonstrate the value of imaging. In particular, imagers need to demonstrate that imaging data impacts outcomes of relevance to patients and thereby justifies the cost and inconvenience of testing. In this setting, developing a robust infrastructure to carry out high quality outcomes research is of paramount importance to help understand the circumstances in which echocardiography is over- and under- utilized and the value of imaging towards improving patient care. In 2014, the American Society of Echocardiography Foundation convened a multi-stakeholder healthcare summit on the role of cardiovascular ultrasound in the emerging value-based payment model.¹³ Central to the goals of this summit which advocated for echocardiography as the “value choice” in cardiac imaging was the expansion of the role of echocardiography as a diagnostic tool through identification of how echocardiography impacts patient care.¹³

To date, while multiple studies have used echocardiographic findings (e.g. left ventricular ejection fraction, grade of mitral regurgitation, etc.) as outcomes,¹⁴ comparatively fewer studies have studied whether detection of these findings leads to actionable changes in clinical management and improved patient outcomes. Additionally, current normal values for echocardiography are largely based on deviations from the average values in a normal population, rather than risk of adverse outcomes.¹⁵ While large population studies of normal individuals have formed the basis of the current recommended normal values,^{16–21} very few (i.e. left atrial size, left ventricular sizes, and left ventricular systolic function) are tied to cutoff values that are prognostically significant.^{15,22} For example, the guideline recommended upper limit of normal for right atrial size is based on the distribution of right atrial size in a healthy, normal population, yet a moderately abnormal right atrial size does not necessarily equate to a moderately increased risk for clinical outcomes.

Moreover, what defines normalcy within clinical subgroups remains unclear. For example, while transmitral e'-velocity declines with age, the parameters that distinguish normal and

abnormal aging with regard to risk of heart failure hospitalization are unknown, or how to use this information to intervene so as to prevent hospitalization or improve prognosis. With aging of the population, the prevalence of valvular and structural heart disease is rapidly increasing and there is an urgent need to understand the implications of imaging findings and the optimal use of imaging to identify and manage disease.^{23,24} To the extent that further patient phenotyping with imaging provides incremental risk information that guides therapeutic management and leads to improved outcomes, the indications for imaging will continue to expand to the benefit of the patients we treat. From the patient's perspective, in addition to potential improvements in diagnosis and treatment, outcomes research in imaging may provide useful prognostic information and guide shared decision making. It may help to understand both over- and under-utilization of echocardiography and lead to improvements in evidence-based recommendations for appropriate imaging, based on patient-centric values. Efforts are already underway to evaluate whether normal chamber sizes differ across countries, regions, and cultures through the World Alliance of Societies of Echocardiography (WASE) Normal Values study, an international effort led by the ASE and ASE International Partners across 6 continents.²² Whether or not such differences, if identified, lead to measurable changes in outcomes to certain treatments remains uncertain, but such efforts are important first steps towards answering this question.

Methods for Capturing Outcomes

To determine if echocardiography is associated with improved outcomes, we first have to measure these outcomes and link them with imaging data. Sources of outcomes data include patient self-report (e.g. patient-reported quality of life measures), electronic health records, clinical trials, large registries and cohorts, and administrative billing data (Table 1). Additionally, mobile and wearable devices increasingly collect information on a patient's health status that may be valuable for research purposes.

Each of these data sources presents unique challenges and opportunities. For example, while short, well-validated, and reliable questionnaires exist to monitor a patient's symptoms and quality of life,²⁵ these outcomes have been proven difficult to capture in busy clinical practices where there are competing demands.²⁶ Electronic health records are a rich and granular sources of patient data, but even in large integrated health systems such as Veterans Administration hospitals, outcomes may be incompletely captured leading to biased estimates of risk. Similarly, although clinical trials represent the gold standard for evaluating the efficacy of an intervention due to the ability to control, via randomization, for unmeasured confounding and use of rigorously adjudicated clinical events, they may selectively enroll healthier individuals whose characteristics do not generalize to real world practice.²⁷ Large registries and cohorts may overcome many of the generalizability issues inherent in clinical trial enrollment. However, they rely on site participation, complete and accurate data entry, and enrollment of generalizable populations to provide accurate insights into outcomes.

Administrative billing claims may also provide information on clinical diagnoses and procedures performed during a given hospitalization but have unique advantages and disadvantages. For example, while national payer data, such as Medicare, allow for

outcomes to be captured from hospitalizations at sites other than that of the index echocardiogram (and thus may be more complete than outcomes captured locally), analysis of claims is limited in scope to those participating in a given insurance plan (e.g. Medicare Fee-for-service beneficiaries). To date, few integrated data repositories exist aggregating multi-channel claims such but access and completeness remain barriers to widespread use. Claims may be subject to errors in coding and incomplete capture of the number and severity of clinical comorbidities. Despite these issues, validated coding algorithms exist to capture clinically relevant outcomes with several more algorithms in development.^{28–31} Additionally, as claims reflect the actual hospital and provider reimbursements, they may be used to study cost of care and predictors of utilization. While death information can be captured through linkage of imaging data to the Social Security Death Master File or National Death Index, it is difficult to interpret results of studies analyzing death as the endpoint without detailed clinical records to identify interventions a patient may have received that could confound the underlying relationship under evaluation. Claims may enrich the set of outcomes available to researchers, such as procedures, medications, comorbidities, and non-death outcomes (e.g. stroke, heart failure hospitalization, myocardial infarction, etc.) but require careful validation work to ensure that the outcome being assessed is well captured by the set of individuals claims substituting for it.

Methods for Capturing Imaging Data and Linkage to Outcomes

As adverse outcomes may be relatively infrequent, large registries of aggregated imaging report data are needed to demonstrate an association between cardiac structural or functional variables and clinical outcomes. Moving beyond echocardiographic reports and traditional outcomes-research-based approaches, large databases of echocardiographic images stored in a common picture archiving and communications system (PACS) and linked to patient outcomes may also permit testing of novel machine learning methods to identify individuals at elevated risk of adverse outcomes. Using convolutional neural networks, a type of machine learning method that extracts information from raw images, computers have been trained to automatically recognize echocardiographic views better than board-certified echocardiographers,³² automate echocardiographic measurements with comparable accuracy to manually adjudicated ones,³³ and discriminate individuals on echocardiogram with certain cardiomyopathies with a high degree of success.³³ Whether these same approaches could be used to identify clinical risk (e.g. individuals with atrial fibrillation at high risk of stroke or poor prognosis prior to transcatheter interventions), remains to be tested.

Aside from large registries of images, there are a number of additional challenges to developing large multicenter databases of echocardiographic report data. First, there may be intrinsic variability in echocardiographic measurements related to non-standard views, variable image quality (due to non-uniform use of modern echocardiographs or patient-related factors), and physiologic parameters (e.g. heart rate, blood pressure). Second, there is site-variation in the acquisition and recording of echocardiographic data that make large-scale analyses more challenging.³⁴ While structured echocardiographic data fields are readily analyzable and linked to outcomes, variable definitions can differ across sites, requiring mapping of site-obtained variables to a common variable name. Many health systems report echocardiographic data in non-structured data formats that require manual

data extraction or use of natural language processing to extract the relevant report information. Regional and institutional variations in echocardiogram image and report quality may be difficult to standardize across sites. If data analysis is restricted to echocardiograms with adequate or good quality, this may introduce selection bias as those with adequate image quality may differ systematically from those that do not. In this setting, professional organizations such as the American Heart Association, American College of Cardiology, and American Society of Echocardiography and national oversight bodies such as the Intersocietal Accreditation Commission (IAC) have a central role at promoting standardization of image acquisition and reporting.

Third, inter-operability between major electronic health record systems and privacy restrictions continue to challenge sharing information between sites. Fourth, image report data may be appropriately missing if the underlying image quality is sufficiently poor so as to impede accurate interpretation, limiting the power for detecting true associations. Fifth, few large imaging registries collect DICOM image files given the complexity of obtaining and storing this information. Challenges to developing and using large image-containing registries include privacy concerns, the need for large image storage capacity, efficient retrieval of studies for analysis, extracting image elements from Digital Imaging and Communications in Medicine (DICOM) files, and the choice of what clips or still images to include or exclude. Vendor specific configurations in DICOM formatting or post-processing of images may create inter-vendor differences in echocardiographic parameters (e.g. global longitudinal strain) that may be difficult to harmonize across systems.³⁵ Moreover, these vendor-specific configurations create challenges for developing new software applications to extract image information from multiple sites where those sites do not share the same vendor. The costs of extracting and maintaining large databases of raw images have so far been a major barrier to routine incorporation of images in existing registries. However, as raw images are often needed to apply machine learning based approaches for automated image quantification and predictive analytics, both echocardiographic report and image data are necessary to extract the full value of information from an echocardiogram.

Even in circumstances where data collection is perfect, data privacy restrictions may limit data sharing across sites and the ability to link with outcomes data. For example, Medicare claims data may not be shared across sites to protect patient privacy, thus limiting claims access to those with specified contractual agreements (e.g. data use agreements) with Medicare for their use. Merging aggregated echocardiographic data with outcomes requires individual-level linkage to ensure that the individual who underwent a given echocardiogram is the same as experienced an outcome. While strategies exist for deterministic matching using minimal patient health information,^{36,37} most direct linkage strategies rely on patient identifiers such as medical record number, social security number, date of birth, name, or home address to serve as a unique key to connect individuals across datasets. Sites may be wary to share potentially discoverable patient information across sites or may do so under strict data use agreements that limit data access.

Unique Challenges to Outcomes Research in Echocardiography

Outcomes research in echocardiography presents a number of unique challenges. A patient's outcome may be determined by a given provider's response to the echocardiographic diagnosis, rather than the diagnosis itself. For example, while a correct wall motion abnormality diagnosis can lead to prompt treatment of an acute myocardial infarction and improved outcomes for the patient, the same correct diagnosis could lead to adverse outcomes if ignored by the ordering providers. Similarly, an incorrect diagnosis (e.g. false positive wall motion abnormalities, confusion between aortic stenosis continuous wave velocity profiles with that of mitral regurgitation) could lead to adverse outcomes if it leads to erroneous treatment or avoidance of the correct treatment. While it is therefore important to evaluate which treatments a patient received, it is more challenging to assess the impact of performance of an echocardiogram on clinical decision making. Likewise, non-cardiac findings, present in roughly 7.5% of trans-thoracic echocardiograms, could increase cost and potentially influence management.³⁸

Additionally, many other potentially confounding variables may be associated with cardiac structural or functional abnormalities and also related to outcomes, leading to false observed associations unless accounted for in the analysis. These variables can be broadly categorized into several domains (Table 2). While summary comorbidity measures such as the Charlson or Elixhauser comorbidity indices have been used for confounding adjustment in outcomes research,^{39,40} it is uncertain how many of the component variables of these summary measures are related to cardiac structure or function or how well these scores will work in the analysis of imaging data.

FORGING THE ROAD AHEAD

The creation of large multicenter registries of imaging data tied to outcomes is critically important for the advancement of outcomes research in echocardiography and improving clinical care. The ImageGuide Registry has taken a lead in this regard.⁴¹ Established in 2015 by the American Society of Nuclear Cardiology (ASNC), the ImageGuide Registry aims to track and improve the quality of patient care through understanding trends in imaging utilization, cardiac structure and function parameters, and the outcomes of imaged patients. In 2017, the American Society of Echocardiography partnered with ASNC to establish the ImageGuideEcho registry which collects aggregated echocardiogram reports across multiple sites and collates specific quality metrics, allowing sites to have timely feedback on their performance. As sharing of data and resources may involve significant investment of human and financial capital from an individual site, the ImageGuideEcho registry has been set up to improve value for sites by collecting and reporting back data on CMS Merit-Based Incentive Payment System (MIPS) performance measures that are required for meeting minimum reporting requirements.⁴¹ Additionally, participating laboratories receive benchmark reports to evaluate performance on these and other measures relative to normative data, which can be used to demonstrate appropriate use of cardiac imaging testing to payers, enhance patient care at a provider and laboratory-wide level, and improve lab efficiency. Globally, these measures can be used to develop normative data on lab quality, distributions of echocardiographic measurements within clinical subgroups (to evaluate departures from

these norms), and can drive further standardization of laboratory practice toward the goal of promoting adherence to best practices. As site participation in national registries (including the ImageGuideEcho registry) is often driven by financial consequences of non-participation or to highlight lab quality in public rankings of performance, the ability to aggregate, evaluate, and report lab quality allows participating sites an efficient means to collect measures required for public reporting and assess deficiencies in lab quality that might result in future financial penalties for subpar performance. Participation in the registry may also permit future site enrollment and participation in pragmatic clinical trials that identify participants for inclusion based on echocardiographic information.⁴² Additionally, strong industry backing and support has endowed the ImageGuideEcho registry with resources to collect and maintain such data for sites, payors, interested researchers, industry partners, regulators, and professional organizations. While this registry is in the beginning stages of development, long term plans include incorporation of outcomes data to track a patient along the continuum of care.

Internationally, the National Echocardiographic Database of Australia (NEDA) has taken a lead in developing solutions to overcome several of the aforementioned challenges and has already collected > 40 million aggregated echocardiogram reports across 14 clinical laboratories, linked to nearly 60,000 all-cause deaths over a median of 40 months.⁴³ Using a vendor-agnostic algorithm, back-ups of clinical studies are automatically uploaded to an Azure Cloud Server and variables names are transformed semi-automatically to meet a common NEDA variable definition. Filtering is applied to remove duplicate studies, merge identical patients, remove nonsensical values using range limiting tools, and assign a unique identifier, specific to each individual included. Once populated into the Master NEDA Dataset, data are inspected and cleaned using graphical and statistical tools to ensure data elements conform to standards and are within physiologic ranges, and are linked to Australian national death statistics. NEDA researchers have used this unique dataset to identify risk in pulmonary hypertension at an earlier cutoff than previously identified,⁴⁴ evaluate the risk of non-severe aortic stenosis, and evaluate the prognostic importance of different methods of ejection fraction calculation.⁴⁵ Additionally, they have developed automated systems for impute aortic valve area using other echocardiographic data without the need for left ventricular outflow tract measurements with plans to further utilize artificial intelligence in other applications.⁴⁶ Applying these automated data upload and quality filters to existing datasets may improve the amount and types of imaging data aggregated, and reduce the costs and barriers to acquisition.

Additionally, local databases may be useful to exploit rich electronic health record data. At Beth Israel Deaconess Medical Center, we have linked a database of 271,618 echocardiograms performed on 135,792 unique individuals over an 18-year period to death information from the Social Security Death Master File. There were a total of 26,163 deaths that occurred during this time period, allowing for more than adequate power to evaluate associations between cardiac structural and functional variables and risk of death. Additionally, we have linked 96,975 (71.4%) of those individuals over the same time period to complete 100% Medicare Fee-for-service inpatient and outpatient claims from 2003–2016. Recent efforts at Massachusetts General Hospital have resulted in a multi-institutional linkage of echocardiography databases, including demographic and limited outcomes data,

which have enriched the diversity, power, and generalizability of analyses with echocardiographic data. Additionally, these large site-specific datasets may serve as data seeds for multicenter federated data networks such as Sentinel, PCORNet, and the NIH Collaboratory, many of which are already linked to CMS claims, which aggregate electronic health record data including diagnoses, procedures, laboratory results, and other testing across participating sites with data sharing agreements.⁴⁷ There has already been significant public investment in creation of these datasets, yet all lack imaging data elements, and sharing of site-specific echocardiographic data may overcome this critical deficiency. Important to all types of imaging registries is the urgent need for standardization of imaging metadata and variable definitions across sites. Here, the American Society of Echocardiography, European Association of Cardiovascular Imaging, and other international professional bodies can provide leadership by convening a committee to provide consensus definitions of echocardiographic variables under a common data model.

In summary, despite seemingly surmountable barriers, outcomes research in echocardiography remains critically important, and with improvements in technology and data analytics, there is perhaps no better time than the present for building the infrastructure to do such essential work. If, however, we malign the narrative of overuse as an arbitrary obstruction to care, we ignore both the real external pressure for accountability and the opportunity to find metrics tied to improvements in patient outcomes that could be widely implemented in place of existing measures of performance. An improved understanding of the relationship of cardiac structure and function to outcomes could improve the ability of new guidelines to reflect real-world practice, aligning with patient-centric outcomes rather than consensus agreement. The ability to identify how outcomes differ in amongst clinical and imaging subgroups, may lead to more specific and tailored recommendations, targeted towards a specific risk group. Moreover, widespread adoption of this approach could lead to substantial, measurable improvements in patient health and refinements in the diagnostic and prognostic abilities of echocardiography.

With support for the creation of large multicenter registries linked to outcomes, we hope to expand upon existing data resources with the goal of creating unique and collaborative resources to understand the importance of structural and functional perturbations identified by echocardiogram to clinical care. It is our hope that continued efforts to link imaging data to outcomes may provide new indications for echocardiography in clinical management and help precision medicine efforts to tailor therapeutic strategies to the optimal patients, demonstrating the value and importance of imaging to patient management.

CONCLUSIONS

The increased utilization of non-invasive cardiac imaging has resulted in national efforts to curtail its growth. The value of imaging can be demonstrated through its impact on patient outcomes. To do so requires a concerted effort to aggregate imaging studies across sites and to link them to measurable clinical outcomes that matter to patients and payors. Ongoing efforts to do so will lead to optimization of diagnostic strategies, changing indications for echocardiography, and an overall improvement in patient outcomes.

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ABBREVIATIONS:

AUC	Appropriate Use Criteria
ASE	American Society of Echocardiography
ASNC	American Society of Nuclear Cardiology
CMS	Centers for Medicare and Medicaid Services
IAC	Intersocietal Accreditation Commission
PACS	Picture Archiving and Communications System
DICOM	Digital Imaging and Communications in Medicine
WASE	World Alliance of Societies of Echocardiography
NEDA	National Echocardiographic Database of Australia

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Table 1:

Sources of Outcome and Echocardiographic Data

	Outcomes Data	Echocardiographic Data
Data Source	Advantages/Disadvantages	Advantages/Disadvantages
Patient self-report	<ul style="list-style-type: none"> Well-validated and reliable questionnaires available. Difficult to capture in practice. 	<ul style="list-style-type: none"> Patient self-report of imaging data is not validated and likely biased by recall.
Electronic Health Records	<ul style="list-style-type: none"> Detailed patient information (e.g. diagnoses, testing, treatments). Outcomes may be incompletely recorded or captured. Challenging to extract information. Privacy concerns involving data access and sharing across sites. 	<ul style="list-style-type: none"> Predominant source of large aggregated imaging data Site-variation in acquisition and recording of data Frequently includes non-structured data Variables may require mapping across sites Interoperability and privacy concerns limit sharing across sites Frequent missing data
Clinical Trials	<ul style="list-style-type: none"> Gold standard for evaluation of efficacy. Detailed, adjudicated outcomes. May lack generalizability and expensive to conduct. 	<ul style="list-style-type: none"> Imaging data often adjudicated at central core labs May lack generalizability and expensive to conduct Limited number of subjects with echocardiograms and limited data obtained from images
Registries or Cohort Studies	<ul style="list-style-type: none"> May enroll generalizable, “real-world” populations. Relies on site participation, complete and accurate data entry, and inclusion of generalizable populations. 	<ul style="list-style-type: none"> Large echocardiographic databases (e.g. ImageGuideEcho registry) in development May enroll generalizable, “real-world” populations. Relies on site participation, complete and accurate data entry, and inclusion of generalizable populations. Variables collected may differ by site
Administrative Billing Claims	<ul style="list-style-type: none"> Capture of outcomes across-sites. Cost and billing data included. Few repositories of multi-payor claims. Subject to coding errors and incomplete capture of number and severity of comorbidities. 	<ul style="list-style-type: none"> Claims for echocardiograms contain cost and billing data. Limited information on imaging variables Few repositories of multi-payor claims. Subject to coding errors and incomplete capture of number and severity of comorbidities.
Mobile or Wearable Technology	<ul style="list-style-type: none"> Provides near-continuous or continuous physiologic information. Few metrics are validated against clinical outcomes. Proprietary control limits access to data. 	<ul style="list-style-type: none"> None currently available for echocardiography
National Health/ Vital Status Repositories	<ul style="list-style-type: none"> Source of death information across sites (e.g. National Death Index or Social Security Death Master File) 	<ul style="list-style-type: none"> None currently available for echocardiography

	Outcomes Data	Echocardiographic Data
Data Source	Advantages/Disadvantages	Advantages/Disadvantages
	<ul style="list-style-type: none">• Comprehensiveness and data quality varies	

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Table 2:

Domains of Potential Confounding Variables in Outcomes Research

Domain	Examples of Variables in Each Domain
Demographics	Age, sex, race, country of origin
Clinical comorbidities	Myocardial infarction, diabetes mellitus, atrial fibrillation, hypertension
Imaging variables	Left ventricular systolic function and chamber dimensions, degree of hypertrophy, estimated pulmonary artery systolic pressure
Socioeconomic	Income, education, occupation, presence of health insurance, neighborhood of residence
Functional	Frailty, disability, completion of ADLs/IADLs, frequent falls, need for assistive durable medical equipment
Health behaviors	Smoking, diet, physical activity, illicit drug use
Acuity of underlying condition	Principal diagnosis, physiologic stability
Perceptions	Health-related quality of life and overall health status, cultural and religious beliefs, preferences around treatment

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