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Measuring Frailty in Health Care Databases for Clinical Care and Research

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Considering the increasing burden and serious consequences of frailty in aging populations, there is increasing interest in measuring frailty in health care databases for clinical care and research. This review synthesizes the latest research on the development and application of 21 frailty measures for health care databases. Frailty measures varied widely in terms of target population (16 ambulatory, 1 long-term care, and 4 inpatient), data source (16 claims-based and 5 electronic health records [EHR]-based measures), assessment period (6 months to 36 months), data types (diagnosis codes required for 17 measures, health service codes for 7 measures, pharmacy data for 4 measures, and other information for 9 measures), and outcomes for validation (clinical frailty for 7 measures, disability for 7 measures, and mortality for 16 measures). These frailty measures may be useful to facilitate frailty screening in clinical care and quantify frailty for large database research in which clinical assessment is not feasible.

Key Words: Frailty, Healthcare administrative claims, Electronic health records

INTRODUCTION

Frailty is a clinical state resulting from age-related changes in multiple physiologic systems and accumulation of diseases that reduces patient ability to maintain homeostasis in response to stressors.[1] Frailty is common in older adults, affecting one in every 10 community-dwellers[2,3] and one in every two nursing home residents,[4] and is associated with increased risks of death (relative risk [RR], 1.6–6.0), disability (RR, 1.8–2.8), institutionalization (RR, 2.6–24.0), and falls (RR, 1.2–2.4).[1] Health care costs for older adults with frailty increase by up to 2-fold compared to those in their non-frail counterparts,[5,6] mainly due to inpatient care, post-acute care, and care for potentially preventable conditions.[7,8] Given the considerable clinical and societal consequences of frailty in the ever-growing aging population, assessment of frailty in clinical and population settings offers valuable opportunities for prevention and treatment through efficient use of evidence-based interventions and resources.[9-11]

Several validated tools are available to measure frailty,[12-15] which can be selected based on the purpose (screening, diagnosis, or monitoring response to interventions), setting (emergency department, inpatient, outpatient, or public health), and available resources (trained staff to perform self-report vs. objective assessment).[16] Although simple clinical assessment tools[17-19] and online calculators are available,[20] frailty assessment typically requires clinical assessment in the form of a survey[21-23] or objective assessments of physical performance[24-27] conducted by a clinician (e.g., geriatrician) or trained health care professional. However, routine adoption of the frailty concept for clinical care or public health practice is variably slow across health systems in different countries,[11] in part due to a lack of time and resources for assessment.[28,29] To overcome these barriers, there is a growing interest in the measurement of frailty using ubiquitous health care databases such as administrative claims data and electronic health records (EHRs), which are by-products of health care encounters and transactions between health care providers and health plans. Administrative claims data contain diagnosis codes, health service codes, and prescription drug data obtained from a large population of health plan members but lack detailed clinical information such as vital signs, physical examination findings, and diagnostic test results. In contrast, EHR provide clinical information not available in administrative claims data; however, much of the information is unstructured (e.g., narrative clinical notes) and may be discontinuous due to patients receiving care at multiple health systems using different EHR systems.[30] Nonetheless, frailty scores derived from health care databases ("database-derived frailty measures") hold promise for population-level frailty screening as well as health services and outcomes research in frail older adults who are under-represented in clinical trials.[31]

This review summarizes the latest advances in frailty measurement in health care databases, mainly administrative claims data and EHR, as well as the potential applications for clinical care and research. Frailty measures requiring in-person surveys or evaluations are beyond the scope of this review. The outline is as follows: (1) literature search; (2) general approaches to frailty measurement in health care data; (3) frailty measurement in administrative claims data; (4) frailty measurement in EHR; (5) considerations in developing a database-derived frailty measure; (6) potential applications of database-derived frailty measures; (7) areas of uncertainty; and (8) conclusions.

LITERATURE SEARCH

A literature search was conducted in PubMed using the Medical Subject Headings, "frailty" AND ("administrative claims, healthcare" OR "electronic health records" OR "Medicare"), and their variations in the title field. Additional filters were applied, including publication date, January 1, 2001, to December 31, 2019, and "aged, 65+ years". This search yielded 50 articles. Risk scores derived from health care databases that aimed to predict mortality or hospitalization were not considered as frailty measures, although they may also be correlated with frailty.[32,33] From the search results, 10 reviews or commentaries; 9 articles using frailty measures not derived from health care databases; and 8 articles not reporting development, validation, or application of database-derived frailty measures were excluded. The initial search was supplemented by an additional 29 articles from the references of the included articles. Finally, 52 articles informed this review.

GENERAL APPROACHES TO FRAILTY MEASUREMENT IN HEALTH CARE DATA

Health care databases generated primarily for health care service administration, care quality assessment, and clinical care delivery generally do not contain sufficient information to derive clinically validated measures of frailty.[12-15] Therefore, frailty measures[24-27] requiring clinical assessment (e.g., gait speed, grip strength, physical activity, or cognitive function) cannot be directly calculated. In the absence of sufficient clinical information, researchers attempted to measure frailty using demographic information, diagnosis codes, or health service codes available in health care databases. The approach to developing a frailty measure depended on the availability of a dataset containing a reference standard measure of frailty and methods to select diagnosis and health service codes in health care databases (Fig. 1).

Clinical Knowledge-Driven Selection

Health care providers and researchers with expertise in aging and frailty select diagnosis codes or health service codes based on prior research and clinical knowledge. These codes may include diseases (e.g., pressure ulcer, failure to thrive, or history of falls), symptoms or signs (e.g., fatigue, muscle weakness, abnormality of gait), and health services (e.g., hospital beds, walking aids, or transportation services) commonly reported or used by older adults with frailty.[31] Frailty has been defined as the presence of any code within a pre-specified period (e.g., 12 months), while its absence assumes that the condition does not exist. This approach is straightforward and does not require a dataset containing a reference standard measure of frailty. It generally offers high specificity and low sensitivity but underestimates frailty prevalence. Alternatively, researchers have quantified frailty by counting the number of different codes in a pre-specified period and deriving a deficit-accumulation frailty index[34] using these codes as health deficits. For example, a person with 10 of 40 pre-specified codes within a 12-month period is assigned a frailty index of 0.25 (= 10/40). The deficit-accumulation approach allows measurement of severity rather than all-or-none classification and choice of a threshold to achieve high sensitivity or high specificity depending on the purpose. Notably, a deficit-accumulation frailty index calculated mainly from diagnosis codes seems to have a narrower range of values (99^{th} percentile 0.4–0.5)[35] than that for a frailty index calculated from clinical assessment (99^{th} percentile 0.6–0.7).[36]

Data-Driven Selection without a Reference Standard

When a dataset with a reference standard frailty measure is not available, researchers have tried to define frail individuals in the dataset by cluster analysis.[37] Cluster analysis is an unsupervised learning technique that classifies individuals into groups of similar nature in terms of measured characteristics in the dataset such as diagnosis codes, hospital days, and total costs during a pre-specified period. After examining the characteristics of the groups derived from cluster analysis, one of the groups (i.e., the group with a

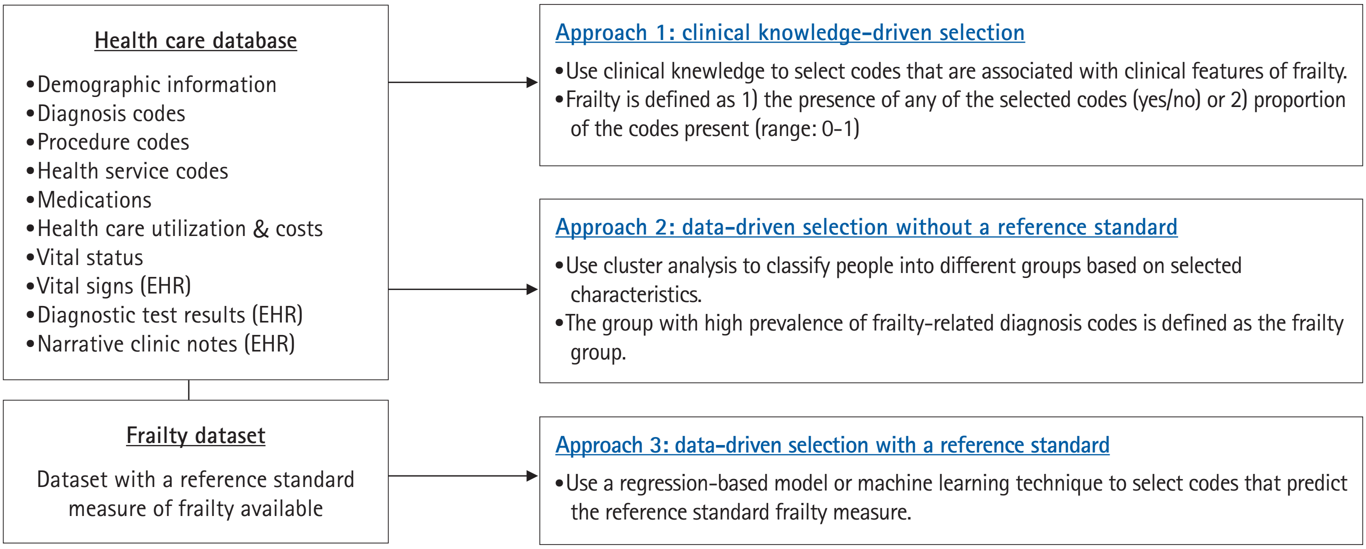

Fig. 1. Approaches to developing a frailty measure in health care databases. Prior research applied three general approaches to develop a frailty measure for health care databases. When a dataset containing information on a reference standard measure of frailty was not available, frailty was measured using diagnosis and health service codes selected based on clinical knowledge (approach 1) or cluster analysis using diagnosis codes, hospital days, and total costs (approach 2). When a dataset with a reference standard measure of frailty was available, a variable selection method (e.g., penalized regression or machine learning technique) was used to select diagnosis and health service codes to measure frailty (approach 3). EHR, electronic health records.

high number of diagnoses indicative of frailty) can be designated as the frailty group. However, cluster analysis can be computing-intensive for large datasets and may not yield the same grouping in different datasets. Gilbert et al.[37] tried to overcome this limitation by conducting cluster analysis in a subset of a large hospital administrative dataset and developing a logistic regression model to predict frailty group membership based on diagnosis codes. The predicted probability from this logistic model can be used to assign individuals to the frailty group from the entire dataset. While this approach identifies frail individuals without requiring a dataset with a reference standard frailty measure, determining the number of groups in the cluster analysis and designating a single frailty group may be subject to interpretation. Moreover, frail individuals may not be classified exclusively into a single group (e.g., frail people with cancer and frail people with heart disease may be classified into different groups despite similar levels of frailty).[38]

Data-Driven Selection with a Reference Standard

If a population-based dataset containing information on a reference standard frailty measure (e.g., frailty phenotype or deficit-accumulation frailty index) and administrative claims data is avaiable, specific codes can be selected against the reference frailty measure (also known as supervised learning). Several variable selection algorithms have been applied— e.g., stepwise regression,[39,40] penalized regression,[39,41] or tree-based algorithms.[39] More flexible "black-box" machine learning algorithms such as random forest and gradient boosting, provide limited or marginal advantages over regression-based algorithms in predictive performance.[39] Under this approach, the first step is variable selection and estimation of weights (in regression models) to optimize predictive performance against a reference standard measure of frailty in a training dataset. The model derived from the training dataset is evaluated in a hold-out testing dataset or via cross-validation. This method can select codes that are positively (e.g., degenerative disease of the central nervous system) or negatively (e.g., vaccination) associated with frailty. It provides better predictive performance of frailty and adverse health outcomes than counting the number of codes or calculating a deficit-accumulation frailty index directly from the codes.[41]

FRAILTY MEASUREMENT IN ADMINISTRATIVE CLAIMS DATA

Table 1 summarizes 16 frailty measures for administrative claims data. Of these, 12 measures were developed for the United States Medicare[8,39-48] or Veterans Affairs[49,50] claims databases, including two proprietary measures; namely, the Johns Hopkins Adjusted Clinical Groups Frailty Indicators[43] and JEN-Frailty Index,[45,46] two were developed for the Canadian claims databases,[51,52] and two were developed for the United Kingdom hospital claims data-

Table 1. Frailty measures for administrative claims data

	Author (y)	Database/population (study year)	Outcomes		Predictors
			Development	Validation	
Clinical knowledge-driven selection	Lunney et al.[42] (2002)	Medicare database (USA) - Medicare 0.1% sample (1993–1998)[42]	Not applicable	None	Presence (yes/no) of any of 11 conditions based on ICD diagnosis codes
	Abrams et al.[43] (2003)	Medicare database (USA)[43] - HMO in Israel (2008)[54] - Major non-cardiac surgery, emergency general surgery, orthopedic surgery patients in Canada (2002–2014)[80-83]	Not applicable	Vulnerable Elders Survey Mortality Complications Discharge disposition Costs	Presence (yes/no) of any of 10 conditions based on ICD diagnosis codes (Johns Hopkins Adjusted Clinical Groups)
	Chrischilles et al.[44] (2014)	Medicare database (USA) - Acute MI patients (2007–2008)[44] - Kidney cancer patients (2000–2009)[84]	Not applicable	Mortality Cardiac catheterization Complications Costs	Presence (yes/no) of any or ≥ 2 of 16 conditions based on ICD diagnosis and HCPCS codes
	JEN Associates[45,46] (2008)	Medicare database (USA)[45,86] - Spouses of AD patients (2001–2005)[85] - National Long-Term Care Survey (2004)[60] - Medicare 5% sample (2011–2014)[61]	Not applicable	Mortality NH admission Costs Disability	Count of the number of 13 conditions present based on ICD diagnosis codes (JEN-Frailty Index)
	Hope et al.[47] (2015)	Medicare database (USA) - ICU patients (2004–2008)[47]	Not applicable	Mortality	Presence (yes/no) of nursing facility claims or 11 conditions based on ICD diagnosis codes
	Soong et al.[53,87] (2015)	Inpatient claims database, England - HES database (2005–2013)[53,87]	Not applicable	Mortality Discharge disposition Readmission	Presence (yes/no) of any of 9 conditions based on ICD diagnosis codes
	Joynt et al.[8] (2017)	Medicare database (USA) - Medicare 20% sample (2011–2012)[7,8]	Not applicable	Costs	Presence (yes/no) of ≥ 2 of 12 conditions based on ICD diagnosis codes and HCPCS codes (specified by Kim and Schneeweiss)[31]
	Orkaby et al.[49] (2018)	VA claims database (USA) - National sample (2002–2012)[49]	Not applicable	Mortality	Proportion of 31 health deficits present based on ICD diagnosis, CPT, and HCPCS codes
	McIsaac et al.[51] (2019)	Administrative claims database (Canada) - Major non-cardiac surgery (2002–2015)[51,88]	Not applicable	Mortality Discharge disposition	Proportion of 30 health deficits present based on ICD diagnosis codes, drugs, assistive device codes, and living environment (preoperative Frailty Index)
Data-driven selection without a reference standard	Gilbert et al.[37] (2018)	Inpatient claims database, England - HES database (2005–2013)[37] - Hospital cohorts[37]	Frailty cluster (from cluster analysis)	Mortality Prolonged hospitalization Readmission Frailty phenotype Deficit-accumulation FI	Includes 109 ICD diagnosis variables
Data-driven selection with a reference standard	Rosen et al.[50] (2000)	VA claims database (USA) - Long-term care (1996–1997)[50,89]	Disability	Disability	Includes 13 conditions based on ICD diagnosis codes
Data-driven selection with a reference standard	Dubois et al.[52] (2010)	Prescription claims database (Canada) - PRISMA cohort (2001–2005)[52]	Functional status score	Mortality Disability Hospitalization NH admission	Includes 11 prescription drug categories
	Davidoff et al.[40] (2013)	Medicare database (USA) - MCBS cohort (2001-2005)[40] - HRS cohort (2008-2010)[56] - SEER-Medicare cohort (1999–2007)[90,91]	Disability	Mortality Disability Frailty phenotype Deficit-accumulation FI	Includes sex, Medicaid enrollment, number of office visits, 8 health care visit types, 3 health care services, 9 procedures, 6 DMEs, and 2 imaging tests based on CPT and HCPCS codes, and geographical regions

(Continued to the next page)

Table 1. Continued

Author (y)	Database/population (study year)	Outcomes		Predictors
		Development	Validation	
Faurot et al.[48] (2015)	Medicare database (USA) - MCBS cohort (2006)[48] - Medicare beneficiaries with or without influenza vaccination (2007–2008)[62] - ARIC cohort (2011–2013)[58] - MarketScan Medicare (2013)[63] - HRS cohort (2008-2010)[56]	Disability	Mortality Disability Falls Mobility impairment Frailty phenotype Deficit-accumulation FI Costs	Includes age, sex, race, and 23 conditions based on ICD diagnosis, CPT, or HCPCS codes
Segal et al.[39,55] (2017)	Medicare database (USA) - CHS cohort (1992–1993/1997)[39] - NHATS cohort (2000)[55] - Medicare TAVR cohort (2011-2015)[64] - HRS cohort (2008-2010)[56]	Frailty phenotype	Mortality Disability Hospitalization Fracture NH admission Frailty phenotype Deficit-accumulation FI	Includes age, sex, race, Charlson Comorbidity Index, past hospitalization, and 16 conditions based on ICD diagnosis codes
Kim et al.[41] (2018)	Medicare database (USA) - MCBS cohort (2006–2007/2011–2012)[41] - HRS cohort (2008–2010)[56,57]	Deficit-accumulation FI	Mortality Disability Hospitalization SNF stay NH admission Falls Frailty phenotype Deficit-accumulation FI	Includes 52 ICD diagnosis variables, 25 CPT variables, and 16 HCPCS variables

AD, Alzheimer disease; ARIC, Atherosclerosis Risk in Communities; CHS, Cardiovascular Health Study; CPT, Current Procedural Terminology; DME, durable medical equipment; FI, frailty index; HCPCS, Healthcare Common Procedure Coding System; HES, Hospital Episode Statistics; HMO, health maintenance organization; HRS, Health and Retirement Study; ICD, International Classification of Diseases; ICU, intensive care unit; MCBS, Medicare Current Beneficiary Survey; MI, myocardial infarction; NH, nursing home; NHATS, National Health and Aging Trends Study; PRISMA, Program of Research to Integrate Services for the Maintenance of Autonomy; SEER, Surveillance, Epidemiology, and End Results; TAVR, transcatheter aortic valve replacement; VA, Veterans Affairs.

base.[37,53] Database-derived frailty measures varied widely in terms of development approaches (clinical knowledge in nine measures, cluster analysis in one measure, and reference standard measures in six measures), number of variables included (nine to 109 variables), target populations (general vs. specific disease populations), and validation outcomes (clinical frailty assessment, functional status, mortality, health care utilization, or costs). Only seven of 16 measures have been compared against a clinical frailty assessment[37,54-59] and seven measures have been tested for disability[50,52,56,57,60] or nursing home admission.[45,52,57,60]

The comparative performance of database-derived frailty measures has not been well studied. In an analysis of Medicare Current Beneficiary Survey data, implementation of a deficit-accumulation frailty index using commonly used diagnosis codes or health service codes showed lower correlation with a reference standard frailty index and was less predictive of mortality than a frailty measure developed using a least absolute shrinkage and selection operator (LASSO) regression.[41] A recent study compared four Medicare claims-based frailty measures—Davidoff index,[40] Faurot index,[48] Segal index,[39] and Kim index[41]—for the ability to measure frailty phenotype, deficit-accumulation frailty index, and activities-of-daily-living dependency (requiring another person's help to perform daily activities). Of the four measures, the Kim index showed higher C statistic for frailty phenotype (0.78 vs. 0.73–0.74) after age and sex adjustment, as well as age and sex-adjusted partial correlation with a deficit-accumulation frailty index from clinical assessment (0.55 vs. 0.18–0.32).[56]

These frailty measures have been applied to define population subgroups by frailty levels,[61] reduce confounding by frailty in examining the association between influenza vaccination and mortality,[62] estimate health care costs attributed to frailty, [63] and improve mortality prediction after transcatheter aortic valve replacement.[64]

FRAILTY MEASUREMENT IN EHR

Table 2 summarizes five frailty measures for EHR. Four measures were developed for three United States regional EHR systems[65-68] or the Veterans Affairs EHR database,[69] while the e-Frailty Index was developed for the United Kingdom primary care practices,[35] which was later implemented in a primary care EHR system in Australia.[59] Clinical knowledge-based selection was used for four mea-

Table 2. Frailty measures for electronic health records

	Author (y)	Database/population (study year)	Outcomes		Predictors
			Development	Validation	
Clinical knowledge-driven selection	Clegg et al.[35] (2016)	Primary care EHR database (UK) - ResearchOne database (2008–2016)[35,70,75] - THIN database (2008–2013)[35,73] - CPRD database (2001–2009)[71,72] Primary care EHR database, Australia - A primary care clinic[59]	Not applicable	Mortality Hospitalization NH admission Fracture Frailty phenotype	Proportion of 36 health deficits present based on Read codes (codes for diagnosis, procedure, disability, and social circumstances) and polypharmacy
	Lekan et al.[65] (2017)	A tertiary-care hospital EHR database (USA) - Inpatients (2010–2011)[65,66]	Not applicable	Mortality Readmission SNF stay	Includes 16 biopsychosocial factors including 4 laboratory tests
	Anzaldi et al.[67] (2017)	A regional health system EHR database (USA) - Medicare ACO enrollees (2011–2013)[67]	Not applicable	Geriatric syndromes identified using diagnosis codes and text phrases	Mention of "frailty" in clinical notes
	Pajewski et al.[68] (2019)	A regional health system EHR database (USA) - Medicare ACO enrollees (2014–2016)[68]	Not applicable	Mortality Falls Health care utilization	Includes 54 health deficits based on diagnosis codes, smoking status, vital signs, laboratory tests, and functional status
Data-driven selection without a reference standard	Shao et al.[69] (2017)	VA EHR database (USA) - Heart failure patients (2010)[69]	Topics generated from clinical notes	Mortality Hospitalization	Includes 53 topics generated from clinical notes

ACO, accountable care organization; CPRD, Clinical Practice Research Datalink; EHR, electronic health records; NH, nursing home; SNF, skilled nursing facility; THIN, The Health Improvement Network; VA, Veterans Affairs.

sures while data-driven selection without a reference standard was used for one measure. A natural language processing method to explore unstructured clinic notes was applied for two measures.[67,69]

Of these measures, the e-Frailty Index has been most widely used in the United Kingdom primary care EHR database to describe frailty trajectories before dying,[70] examine the effect measure modification of systolic blood pressure and mortality relationship by frailty,[71] predict fractures and mortality after fractures,[72] and assess de-intensification for diabetes and hypertension treatment regimens among older adults with frailty.[73]

CONSIDERATIONS IN DEVELOPING A DATABASE-DERIVED FRAILTY MEASURE

Database-derived frailty measures use different types of data (e.g., diagnosis, procedure, and health service codes) collected over a pre-specified period, ranging from 6[39] to 36[49] months. Because some claims datasets record information according to a unique coding system specific to each country (e.g., Current Procedural Terminology codes and Healthcare Common Procedure Coding System codes in the United States and Read codes in the United Kingdom), the choice of datasets can affect the transportability of the frailty measures. The length of the assessment period during which codes are measured may affect the accuracy of capturing certain chronic conditions. Chronic conditions that are less likely recognized or coded by general practitioners (e.g., dementia and incontinence) may require a longer assessment period than acute conditions (e.g., acute myocardial infarction) or well recognized chronic conditions (e.g., hypertension and diabetes). A longer assessment period to calculate a frailty measure reduces the amount of follow-up data available for the main analysis.

Frailty measures developed from health care databases tend to rely on diagnoses, whereas clinical frailty assessment relies more on functional status and physical performance, factors rarely available in health care databases. Health service codes indicating clinical encounter types (e.g., home visits) and use of durable medical equipment (e.g., hospital beds or wheelchairs) seem to be important to capture functional impairment or poor physical performance, which differentiates frailty measures from comorbidity indices.[57] However, including demographic characteristics in the frailty model lessens its ability to explain variation in frailty beyond demographic variables.[56]

Once a frailty measure is developed, the key step is its validation against a reference standard measure of frailty. Given the lack of consensus on frailty definitions,[12] prevalent activities-of-daily-living dependency can be used as an alternative outcome for validation.[40,48,56,60] However, information on a reference standard frailty measure or activities-of-daily-living dependency is not always available. Many database-derived frailty measures were tested for mortality prediction rather than for frailty itself. Although frailty is associated with mortality, it is unclear how these frailty measures can be differentiated from mortality prediction models.

Another consideration is that coding systems or coding practices may change over time or vary across geographical regions. In the United States, the International Classification of Disease system transitioned from the 9th to 10th revisions in October 2015. New billing codes are generated for new procedures and health care services and some codes are retired each year. Coding practice may be influenced by the likelihood of reimbursement for health care services, which may differ across health care systems or countries. Therefore, the performance of claims-based frailty measures should be evaluated periodically in more contemporary datasets and before application to a different health care system or country.

Lastly, the development of a frailty measure from EHR may require restricting the population to those with high rates of data completeness within an EHR system to avoid bias due to health information outside the EHR system.[30] A predictive algorithm is available to identify those with high rates of completeness.[74]

POTENTIAL APPLICATIONS OF DATABASE-DERIVED FRAILTY MEASURES

Frailty measures calculated from health care databases can be useful to measure frailty and study health outcomes of older adults with frailty in clinical care and research (Table 3).

Clinical Care

Database-derived frailty measures can be used to screen older adults for frailty in a health care system or a health plan. Because database-derived frailty scores generally have C statistics ranging from 0.65 to 0.75 for frailty phenotype and correlation coefficients of 0.2 to 0.6 against a deficit-accumulation frailty index,[37,39,56] they are unlikely to replace bed-side clinical frailty assessments. Frailty measures are useful to predict adverse health outcomes. In particular, the Kim index performed better than a comorbidity index for the prediction of disability, mobility impairment, recurrent falls, and skilled nursing facility days in the Medicare population.[41,57] However, an e-Frailty Index >0.19, a threshold for frailty, had a positive predictive value of 0.11 for death in the next 3 months among primary care patients in the United Kingdom. These results suggest that, although a database-derived frailty measure may be a strong predictor in a population, it cannot be interpreted deterministically for an individual (this issue also exists for a clinical frailty assessment).[75] Nonetheless, they can be useful as a routine screening test to identify individuals requiring additional detailed assessment and individualized care management.[76] A cut-off point for positive screening can be determined according to percentile distributions (e.g., top 5% percent), sensitivity and specificity for frailty state (e.g., 90% sensitivity to detect frailty phenotype), or pre-defined clinically relevant thresholds (e.g., ≥ 0.20 according to a deficit-accumulation frailty index) after considering clinical contexts (e.g., outpatient, inpatient, or preoperative screening) and available resources for detailed assessment and care management.

Research

Database-derived frailty measures provide vast opportunities for clinical research in older populations. These measures can be used to efficiently screen individuals for enrollment in a clinical trial of interventions for frailty. In database studies to evaluate treatment effects in older adults, treated individuals may differ in frailty levels from untreated individuals, which leads to confounding. Such bias can be reduced by adjusting for a frailty measure, although residual confounding may persist.[62] In choosing a frailty measure for confounding adjustment, a measure that does not include demographic variables may be more effective than a measure that includes them.[56] Moreover, frailty can be an effect measure modifier. The benefits and risks of a treatment may vary by frailty status—e.g., a hypnotic drug increases the risk of hip fracture more in less frail older adults than frailer ones who are totally dependent.[77] Evaluation of treatment effect heterogeneity by frailty in health care databases may provide real-world evidence to guide individualized treatment choice based on frailty assessment in older adults who are typically excluded from clinical trials. In some clinical trials that enrolled frail individuals yet lacked frailty assessment, frailty levels at trial baseline can be estimated by linking trial data to administrative claims data or EHR and applying database-derived frailty measures. Such secondary analyses of existing clinical trial data may generate hypotheses for future trials.

AREAS OF UNCERTAINTY

Few studies to date used a database-derived frailty measure as an

Table 3. Potential applications of database-derived frailty measures and areas for future research

Areas	Applications	Caveats/areas for future research
Clinical care	Screen for frail individuals requiring detailed evaluation and care management in a health care system or health plan Predict the risk of adverse health outcomes (frailty measures are more useful than comorbidity measures for the prediction of disability, mobility impairment, falls, and SNF days).	Database-derived frailty measures are acceptable yet imperfect; thus, they are unlikely to replace clinical assessment. Seeking health care during acute illness or functional decline may lead to overestimation of the frailty level (informed presence bias). Further improvement in frailty measurement may be possible by including clinical assessment datasets (e.g., MDS or OASIS in the United States Medicare database) or EHR clinic notes.
Research	Efficiently screen for frail individuals to enroll in a clinical trial Adjust for case-mix (confounding) by frailty in evaluating the effect of medical treatment or outcomes among health care systems Evaluate the treatment effect heterogeneity by frailty in analysis of health care databases or clinical trial datasets (by linking clinical trial data to claims data for estimation of frailty level)	Responsiveness and MCID of database-derived frailty measures remain to be investigated. The assessment period used to calculate a frailty measure ranges from 6 to 36 months. The optimal period is not known. Residual confounding may exist even after adjusting for case-mix by using a database-derived frailty measure. Usefulness of EHR data may depend on the health information technology infrastructure and completeness of documentation.

EHR, electronic health records; MCID, minimal clinically important difference; MDS, Minimum Data Set; OASIS, Outcome and Assessment Information Set; SNF, skilled nursing facility.

outcome (i.e., change in frailty level over time) to evaluate the treatment effect. The responsiveness of a frailty measure to improvement or deterioration of health status and the minimal clinically important change have not been well studied. Diagnosis codes, which comprise a large proportion of the database-derived frailty measures, tend to be carried over visits and accumulate over time in administrative claims data or EHR, causing increased frailty score. Since older adults are more likely to seek medical care during acute illness or functional decline (informed presence bias[78]), the estimated frailty level may be affected by the effect of acute illness and frailty progression may be recorded more often than improvement. Furthermore, in health care databases, the information needed to estimate frailty is obtained over time as opposed to clinical trials wherein information is obtained from a discrete assessment visit (e.g., baseline or follow-up visit). Therefore, the assessment periods may overlap between outcome frailty and baseline frailty, making the two measures highly collinear. For these reasons, the utility of a database-derived frailty measure as a treatment outcome remains uncertain.

Information on functional status or physical performance is often recorded in health care databases. In United States Medicare data, the Minimum Data Set records clinicians' assessments of functional status among nursing home patients. The Outcome and Assessment Information Set contains information on patient outcomes for individuals receiving home care. In EHR, cognitive function and physical function are documented in clinical notes by primary care physicians, specialists (e.g., geriatricians, neurologists, and psychiatrists), physical therapists, or occupational therapists. In the absence of routine assessment, these documentations tend to be inconsistently available or for a subset of patients in specific clinical contexts (e.g., after a fall event, hospitalization, or major surgery), which may not represent an individual's usual state of health. A recent study by Kharrazi et al.[79] showed that the prevalence of geriatric syndromes was underestimated when only claims and structured EHR data were analyzed; natural language processing of unstructured EHR data substantially improved detection by 1.5-fold for dementia, 3.2-fold for falls, 18.0-fold for malnutrition, and 455.9-fold for lack of social support. While these findings are promising, the contribution of unstructured EHR data for case identification depends on the health information technology infrastructure and completeness of documentation by health care providers.[79] How to best combine clinical information with administrative claims data or structured EHR data requires further investigation.

CONCLUSIONS

The use of a database-derived frailty measure offers new opportunities to facilitate frailty screening in clinical care and quantify frailty for large population-based database research in which clinical assessment is not feasible. Several database-derived frailty measures have been validated for use in administrative claims data and EHR, with some key differences (Fig. 2): target population (16 ambulatory, 1 long-term care, and 4 inpatient), data source (16 claims-based and 5 EHR-based measures), length of the assessment period (6 to 36 months), data types required for calculation (diagnosis codes required for 17 measures, health service codes for 7 measures, pharmacy data for 4 measures, and other additional

Frailty Measure by Health Care Database	Population	Data Source	Assessment Period (Months)	Types of Data Needed for Calculation				Existing Data on Validation		
				Diagnosis	Health Services	Pharmacy	Others	Clinical frailty	Disability	Mortality
US Medicare										
Lunney (2002)	Ambulatory	Claims	12	X						
Abrams (2003)	Ambulatory	Claims	12	X				X		X
Chrischilles (2013)	Ambulatory	Claims	12	X	X			X		
Davidoff (2013)	Ambulatory	Claims	12		X		X	X	X	X
JEN Associates (2014)	Ambulatory	Claims	12	X					X	X
Hope (2015)	Ambulatory	Claims	12	X				X		
Faurot (2015)	Ambulatory	Claims	8	X	X		X	X	X	X
Joynt (2017)	Ambulatory	Claims	12	X						
Segal (2017)	Ambulatory	Claims	6	X			X	X	X	X
Lekan (2017)	Inpatient	EHR	12	X			X	X		
Anzaldi (2017)	Ambulatory	EHR	24	X						
Kim (2018)	Ambulatory	Claims	12	X	X			X	X	X
Pajewski (2019)	Ambulatory	EHR	24	X		X	X	X		
US Veterans Affairs										
Rosen (2000)	Long-term care	Claims	6	X				X		
Shao (2017)	Ambulatory	EHR	12	X				X		
Orkaby (2018)	Ambulatory	Claims	36	X	X			X		
UK/England										
Soong(2015)	Inpatient	Claims	24	X				X		
Clegg (2016)	Ambulatory	EHR	12	X	X	X	X	X		X
Gilbert (2018)	Inpatient	Claims	24	X				X		X
Canada										
Dubois (2010)	Ambulatory	Claims	6	X				X		
McIsaac (2019)	Inpatient (surgical)	Claims	36	X	X	X	X	X		

Fig. 2. Considerations in choosing a database-derived frailty measure. EHR, electronic health records.

information for 9 measures), and outcomes against which a frailty measure was validated (clinical frailty assessment for 7 measures, disability for 7 measures, and mortality for 16 measures). This summary can serve as a guide to choosing a database-derived frailty measure that suits specific objectives and databases at hand.

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CONFLICT OF INTEREST

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