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Measuring Frailty Using Claims Data for Pharmacoepidemiologic Studies of Mortality in Older Adults: Evidence and Recommendations

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Abstract

Purpose—Geriatric frailty is a common syndrome of older adults that is characterized by increased vulnerability to adverse health outcomes and influences treatment choice. Pharmacoepidemiologic studies in older adults that rely on administrative claims data are limited by confounding due to unmeasured frailty. A claim-based frailty score may be useful to minimize confounding by frailty in such databases. We provide an overview of definitions and measurement of frailty, evaluated the claim-based models of frailty in literature, and recommend ways to improve frailty adjustment in claims analysis.

Methods—We searched MEDLINE and EMBASE from inception to April 2014, without language restriction, to identify claim-based multivariable models that predicted frailty or its related outcome, disability. We critically appraised their approach, including population, predictor selection, outcome definition, and model performance.

Results—Of 152 reports, three models were identified. One model that predicted poor functional status using health care service claims in a representative sample of community-dwelling and institutionalized older adults showed an excellent discrimination (C statistic, 0.92). The other two models that predicted disability using either diagnosis codes or prescription claims alone in institutionalized or frail adults had limited generalizability and modest model performance. None of the models have been applied to reduce confounding bias in pharmacoepidemiologic studies of drug therapy.

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Conclusions—We found little research conducted on development and application of a claim-based frailty index for confounding adjustment in pharmacoepidemiologic studies in older adults. More research is needed to advance this innovative, potentially useful approach by incorporating the expertise from aging research.

INTRODUCTION

Pharmacoepidemiologic studies of mortality in older adults using administrative claims data are mainly criticized for their limited ability to capture important clinical information and prognostic factors that are available to physicians who make treatment decisions.¹ Physicians are more likely to withhold treatments to patients who have limited life expectancy or high vulnerability to treatment-related adverse events. As a result, incomplete measurement and adjustment for such patient characteristics can result in confounding bias. For example, vaccinations were less likely to be given to patients who had long-term hospitalizations or skilled nursing stays.² Users of lipid-lowering agents, non-steroidal anti-inflammatory drugs, and glaucoma drugs were healthier and had lower mortality than non-users among older adults.^{3–5} The protective association persisted after adjusting for age, sex, and comorbidities.^{3,5} This suggests that some important prognostic factors were not captured in claims data.

Frailty as an unmeasured confounder

One such prognostic factor that is increasingly recognized by physicians is frailty. A frail older person is typically described as a “slow, weak, and thin” person who appears older than one’s chronologic age. In the geriatrics and gerontology literature, frailty is defined as a state of increased vulnerability and reduced ability to recover homeostasis after a stressful event, thereby leading to adverse outcomes, such as falls, disability, delirium, and mortality.^{6–11} It typically results from accumulated impairments in multiple physiologic systems.⁷ Frail patients are at higher risk of treatment-related adverse events due to their reduced physiologic reserve and limited adaptability to a stressful event. As a result, physicians are more likely to use a lower intensity or avoid treatments that may cause serious adverse events and discontinue treatments that may not result in immediate benefits in order to minimize polypharmacy. Several recent practice guidelines even beyond the geriatrics field recommend considering frailty and assessment of risks and benefits in treatment choice in older adults.^{12–18} A differential use of various medical and surgical interventions by frailty status has been well documented in observational studies that reflect real-world clinical practice (Table 1). How strongly frailty influences treatment choice varies across the types of treatment and associated risks. For instance, the prevalence difference in frailty was larger for high-risk interventions (e.g. chemotherapy and warfarin) than for low-risk interventions (e.g. statin). This difference may be more pronounced in the oldest old population, up to 50% of whom are frail.¹⁹ As such, modification of treatment according to frailty status result in confounding bias in pharmacoepidemiologic studies in older adults.

In addition, some emerging evidence suggests that frailty may predict older patients who are more likely to harm from chemotherapy or surgical procedures.^{20,21} On the other hand, the

association between sleep medications and hip fracture among nursing home residents was greater in those with mild frailty (who were ambulatory and had more opportunities to fall) than those with severe frailty (who were almost non-ambulatory).²² This reflects that the safety profile of a treatment may depend on frailty status. Therefore, frailty can be an effect modifier in studies of treatment effectiveness and safety in older adults.

Measurement of frailty

How to operationalize the concept of frailty for research and clinical practice has been a hot topic of geriatrics and gerontology research in the past decade.⁹ In research, the *frailty phenotype*⁷ and the *frailty index*¹¹ are most widely used among several validated frailty models.²³ The *frailty phenotype*, proposed by Fried et al., is constructed on the biological cycle of frailty that consists of shrinking, weakness, exhaustion, slowness, and low physical activity.⁷ The *frailty index*, proposed by Mitnitski et al., counts the number (or proportion) of health deficits from a pre-specified number (usually 30) of symptoms, signs, diseases, test abnormalities, and disability in physical, psychological, and social domains.¹¹ The *frailty phenotype* requires very specific information from self-report and geriatric assessment, whereas the *frailty index* places few restrictions on the type and number of individual components to define frailty (Table 2). Because of its flexibility in choosing individual items, the *frailty index* has been successfully applied to various population-based surveys, cohorts, and patient databases that did not contain the same components of health deficits as the original database where it was initially developed.²⁴ This is an important advantage of the *frailty index* that may be useful in developing a claim-based frailty score. In clinical practice, most physicians recognize frailty based on information from a combination of sources, which include observation of the overall appearance (“eyeball” test), review of comorbidities, medications, and ADL disability, and examination of mobility and muscle strength.^{7,25}

In administrative claims data, most of the components that are used to determine frailty are not available or incompletely measured. Thus, two individuals with the same age and seemingly similar comorbidity profile in claims data may have a considerably different level of frailty and mortality risk. Individuals who are near the end of life with advanced frailty may have fewer encounters with health care system, which further limits our ability to capture their health status completely and similarly to those with more encounters. Moreover, there is no specific International Classification of Diseases (ICD) code for frailty. Although physicians commonly consider frailty before recommending treatments, they do not reliably document manifestations of frailty in medical records or submit relevant ICD codes (e.g. abnormality of gait, cachexia, debility, exhaustion, fall, failure to thrive, fatigue, loss of weight, pressure ulcer, senility, or muscle weakness).

The relationship of frailty, disability, and comorbidity and relevance to confounding adjustment

The inter-relationship among frailty, disability, and comorbidity is complex and untangling these overlapping concepts may be difficult.^{9,26} Disability is defined as difficulty in performing basic or instrumental activities of daily living (ADLs) and viewed as a consequence of frailty and comorbidities.²⁶ In general, individuals with high burden of

comorbidities are more likely to become frail and disabled. Nonetheless, it is important to recognize that frailty can identify patients at high risk for poor outcomes who otherwise may not be identified as such based on comorbidity and disability. In the Cardiovascular Health Study, 27% of frail older adults in the community did not have major comorbidities or disability (Figure).⁷ Frailty was associated with 1.3 to 2.2-fold elevated risk of worsening disability, hospitalization, and mortality, independently of comorbidities and disability.⁷ This suggests that adjusting for comorbidities and disability may result in residual confounding by frailty. The magnitude of this bias will depend on the prevalence difference in frailty between treated and untreated patients as well as the association between frailty and the outcome of interest that is not captured by comorbidities or disability.

Existing approaches that may reduce unmeasured confounding by frailty

To date, much progress has been made in risk adjustment methods using summary scores of measured confounding, such as propensity scores or disease risk scores.^{27–30} The impact of unmeasured confounding by surrogates of frailty (e.g. disability, cognitive and physical function impairment) has been assessed by a sensitivity analysis using an independent dataset and the confounder-outcome associations from the literature.^{31–34} If a subset of claims data is linked to a validation dataset that contains frailty measures, propensity score calibration or reweighting can be applied to reduce confounding by frailty.^{35,36} These methods require an external data source with frailty measures. In the absence of such external data, a self-controlled design or an active comparator design can be useful. High-dimensional propensity score analysis^{37,38} that adjusts for proxies (which may be associated with frailty) and instrumental variable analysis³⁷ may also reduce unmeasured confounding by frailty under some untestable assumptions. In a study of conventional versus atypical antipsychotic use on mortality in nursing home residents, high-dimensional propensity score and instrumental variable analyses resulted in the effect estimates similar to those when additional clinical data, including manifestations of frailty, were adjusted for.³⁷

Claim-based frailty score as an alternative approach

As an alternative approach, a frailty score can be developed and validated from claims data. Although geriatricians and gerontologists have developed several models of frailty for clinical and research use,^{23,39} little effort has been made to translate these models into pharmacoepidemiologic studies. A successful adaptation of these models of frailty for claims data has a great potential to improve the validity of pharmacoepidemiologic studies in older adults. In the following sections of this review, we critically evaluated the existing claim-based models of frailty in the literature and proposed how to develop and validate a claim-based frailty score for pharmacoepidemiologic studies.

METHODS

We identified claim-based models of frailty in the literature by searching MEDLINE and EMBASE from inception to 4/30/2014, using the following key terms and their variations: *frailty*, *disability*, *activity of daily living*, *vulnerability*, *bias*, *confounding*, *case mix*, *risk adjustment*, and *administrative claims database*. We also searched the reference lists of included papers. Since functional impairment and disability are manifestations of frailty, any

papers that reported a multivariable model to predict frailty or disability using claims data were included. In each paper, we examined data source, population characteristics, outcome definition, predictors, and model performance (calibration and discrimination) in the derivation and validation samples.

RESULTS

Of 152 citations identified in literature search, we found three claim-based multivariable models^{40–43} that predicted frailty or disability in older adults (Table 3). These models varied widely with respect to population source, outcome definition, type of predictors, and model performance. Rosen et al. analyzed the national Veterans Affairs database of long-term care residents to develop a model that used 13 diagnostic categories to predict worsening disability in three basic ADLs over six months.^{40,41} The model was limited by moderate discrimination (C statistic 0.68–0.70) and uncertain generalizability to females and community-dwelling non-veterans. In a random community-based sample of frail older Canadians identified by a postal screening questionnaire, Dubois et al. developed an index that predicts a summary disability score that consists of basic and instrumental ADLs, mobility, communication, and mental function, based on prescription claims for 11 conditions.⁴² However, the overall model fit was poor ($R^2 = 0.12–0.16$) and its generalizability to non-frail older adults remains uncertain. The index by Davidoff et al. overcomes most limitations of the earlier indices by using a nationally representative sample of both community-dwelling and institutionalized Medicare beneficiaries.⁴³ Instead of using diagnosis codes or prescription claims, this index used health care service claims (e.g. types of visits, procedures, durable medical equipment) that are both positively and inversely associated with poor functional status. Poor functional status was an approximation of the Eastern Cooperative Oncology Group performance status from basic and instrumental ADLs, strength, stamina, and exercise. This outcome definition seems to overlap with some components of *frailty phenotype* (weakness, slowness, and low physical activity). Although the discrimination (C statistic 0.92) and calibration of this index were excellent, they might have been overestimated due to the inclusion of individuals who are already institutionalized or on hospice care for terminal illness. None of the three identified models have been applied to reduce confounding bias in pharmacoepidemiologic studies of a drug treatment.

DISCUSSION

To date, we found very little research conducted on development and application of a claim-based frailty score in pharmacoepidemiologic studies. Two models that were developed from institutionalized or already frail individuals had limited generalizability to the general population of older adults in the community.^{40–42} Only the model by Davidoff et al. that was developed from a representative population of older adults seemed useful for pharmacoepidemiologic studies.⁴³ Nonetheless, these models focused on predicting disability rather than the accepted definitions of frailty from aging research. Measuring frailty is attractive, because it can identify high-risk older patients even when they are not considered high risk based on comorbidities and disability as well as those who are more likely to benefit (or harm) from a treatment.^{20,21} In the following paragraphs, we propose

two potential approaches to develop a claim-based frailty score that incorporate insights from geriatrics and gerontology research.

Approach 1: Deriving the *frailty index* directly from claims database

Given the challenges in measuring individual components to define the *frailty phenotype* from claims data, we believe that creating a *frailty index* with diagnosis and procedure codes from claims data (as “health deficit”) may be feasible and offer some advantages over the *frailty phenotype*. The flexibility in choosing individual items for the *frailty index* can allow selection of pre-specified list of claims in the database at hand, as long as a sufficient number of claims are selected to cover multiple physiologic systems and their prevalence increases gradually with age (without saturating too early). In addition, the health deficits required to construct the *frailty index* may differ between community-dwelling and institutionalized populations. For instance, the prevalence of hearing loss gradually increases with age in community-dwelling older adults; but the prevalence reaches almost 100% in institutionalized older adults. When counted as a health deficit, hearing loss does not help discriminate the health risk in institutionalized populations. Therefore, it can be included in the *frailty index* only for community-dwelling population. Another advantage is that the *frailty index* provides better discrimination in predicting the risk of adverse outcomes than the *frailty phenotype*.^{44,45} While the *frailty phenotype* may be clinically appropriate to identify vulnerable patients for interventions and monitor the change in individual components over time, the *frailty index* is more suitable for the purpose of confounding adjustment in pharmacoepidemiologic studies of mortality.

Approach 2: Gold-standard-driven development of a claim-based frailty score

As an alternative to deriving the *frailty index* directly from claims database, we can build a multivariable model that uses claims to predict a “gold standard” frailty (either the *frailty phenotype* or the *frailty index*) that is defined from in-person assessment. Below we describe steps to develop and evaluate a claim-based frailty score (Table 4).

The first step is to find a database that has both claims data and in-person assessment that is needed to define a “gold standard” frailty. A few population-based epidemiologic studies of aging that have been linked to claims data can be valuable data sources (e.g. Adult Changes in Thought Study, Cardiovascular Health Study, Health and Retirement Study, Longitudinal Study of Aging, and National Long-Term Care Survey) (Study main websites were provided in Table 4). Electronic health records (EHR) are a potentially useful source to capture frailty in a real-world population that can be linked to claims. EHR contains clinical data (laboratory, pharmacy, radiology, and physician orders), and narrative clinical notes (medical history, symptoms, and clinical reasoning behind treatment decision making) that are difficult to obtain from claims data. However, there are challenges in measuring a “gold standard” frailty from EHR. As mentioned earlier, most physicians do not use one of the accepted models of frailty but rely on their subjective assessment (“eyeball” test). Although there are a few clinical prediction models based on EHR data,^{46–48} how to create an EHR-based frailty score remains to be determined. Selective availability of certain clinical data, complex patterns of health care system use and difficulties in mining information from narrative clinical notes pose several technical and analytical challenges, such as missing data

problems⁴⁹ and differential ascertainment or misclassification of confounders. Routine use of clinical templates and advances in natural language processing programs may mitigate these challenges in the future.

The next step is to define a “gold standard” frailty using detailed clinical information in the surveys, epidemiologic cohorts, or EHR. Although both the *frailty phenotype* and *frailty index* can be used, we recommend modeling the *frailty index* that has better discrimination than the *frailty phenotype* in predicting the outcome risk. Once a “gold standard” frailty is defined, a wide range of claims that are measured within a time frame (e.g. 1 year) – diagnoses, prescriptions, and health care service claims – need to be considered. Based on our understanding about the clinical phenotype or underlying biology of frailty, we should consider certain predictors *a priori*, such as diagnosis codes, durable medical equipment claims, and nursing or personal care service claims that characterize frail patients (Table 4). In addition to these claims, we need to include claims that are negatively associated with frailty. As shown by Davidoff et al.,⁴³ some health care services (e.g. ambulance, upper gastrointestinal tract endoscopy, and minor skin procedures) are more utilized by frail patients, while preventive services (e.g. screening and vaccination) are less utilized.

The performance (calibration and discrimination) of the derived claim-based frailty score needs to be evaluated in an independent hold-out sample, or using cross-validation or bootstrap resampling to avoid overestimation of model performance. The criteria for a successful frailty measure have been proposed in terms of content validity, construct validity, and criterion validity.⁵⁰ According to the criteria, a successful frailty measure should be dynamic (changes over time), include multiple determinants, and replicate some of the known relationships with age (more common in advancing age), gender (more common in women), and adverse clinical outcomes (fall, hospitalization, institutionalization, home health service use, and mortality). Finally, a validated claim-based frailty score should be applied to reduce confounding bias in a known example of a treatment that has substantial confounding by frailty.

Areas of uncertainty

First, it may be useful to examine the inherent characteristics of a claim-based frailty score. It is important to study the optimal length of period to capture claims data for development of a claim-based frailty score and the sensitivity of the score to reflect changes in clinical frailty over time. Second, it is unknown which of the two approaches we outlined leads to better confounding adjustment. This can be assessed by comparing C statistics between the derived frailty scores. Third, when the frailty score, comorbidity score, and disability score are created using the same claims database, it is unclear whether the claim-based frailty score can provide additional prognostic information beyond existing confounding summary scores (e.g. comorbidity score, disease risk score, or propensity score). Lastly, the transportability of a frailty score developed from one population to similar populations in different databases that might have different health care utilization and practice patterns should be evaluated. This may be less problematic with our first proposed approach, that is, deriving the *frailty index* directly from claims data using a pre-selected list of health deficits

available in that particular claims database. Our second approach, however, needs validation in independent databases.

CONCLUSIONS

As observational data remain a major source of comparative effectiveness research in older adults, there is a critical need to advance methods to adjust for confounding bias by frailty by incorporating the accumulated expertise from geriatrics and gerontology research. Among different operationalized definitions of frailty used in clinical practice, we believe that the *frailty index*, the count of health deficits in multiple physiologic systems, is more promising for the purpose of confounding adjustment. A claim-based frailty score should consider including certain *a priori* list of diagnoses and health care service claims that characterize frail patients, as well as consider additional diagnoses, prescriptions, and health care service claims that are either positively or negatively associated with the frailty. More research is needed to evaluate the performance and transportability of claim-based frailty scores in different databases and additional reduction in confounding bias beyond existing methods.

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Figure. The Relationship Among Frailty, Comorbidity, and Disability in the Cardiovascular Health Study (Reprinted with permission⁷)

Percents listed indicate the proportion among those who were frail ($n = 368$), who had comorbidity and/or disability, or neither. Total represented: 2,762 participants who had comorbidity and/or disability and/or frailty. n of each subgroup indicated in parentheses. ⁺Frail: overall $n = 368$ frail participants. ^{*}Comorbidity: overall $n = 2,576$ with 2 or more out of the following 9 diseases: myocardial infarction, angina, congestive heart failure, claudication, arthritis, cancer, diabetes, hypertension, chronic obstructive pulmonary disease. Of these, 249 were also frail. ^{**}Disabled: overall $n = 363$ with an ADL disability; of these, 100 were frail.

Table 1

Examples of Differential Use of Medical and Surgical Treatments by Frailty Status

Treatment or Target Condition	Treatment Options	Frail patients N (%)	Non-frail patients N (%)
Aortic stenosis (Bainey et al.) ⁵¹	Total sample (mean age: 82 years)	68 (100)	85 (100)
	Surgical aortic valve replacement	6 (9)	27 (32)
	Transcatheter aortic valve replacement	32 (47)	26 (31)
	Medical treatment	30 (44)	32 (37)
Bisphosphonate (Sambrook et al.) ⁵²	Total sample (mean age: 83 years)	326 (100)	1675 (100)
	Bisphosphonate	2 (1)	76 (5)
	No bisphosphonate	324 (99)	1599 (95)
Chemotherapy for breast cancer (Aaldriks et al.) ⁵³	Total sample (mean age: 76 years)	28 (100)	27 (100)
	4 cycles of chemotherapy	18 (64)	21 (78)
	< 4 cycles of chemotherapy	10 (36)	6 (22)
	Total sample (mean age: 77 years)	194 (100)	112 (100)
Coronary artery disease (Purser et al.) ⁵⁴	Coronary artery bypass surgery	23 (13)	21 (19)
	Percutaneous coronary intervention	70 (38)	59 (53)
	Medical treatment	91 (49)	32 (28)
	Total sample (age: 77 years)	147 (100)	1518 (100)
Statin (Gnjidic et al.) ⁵⁵	Statin	53 (36)	659 (43)
	No statin	94 (64)	859 (57)
	Total sample (mean age: 83 years)	130 (100)	77 (100)
Warfarin for atrial fibrillation (Perera et al.) ⁵⁶	Warfarin	30 (23)	53 (69)
	No warfarin	100 (77)	24 (31)

Table 2

Measurement of Frailty in Geriatrics and Gerontology Research

	Measurement of Frailty Phenotype ⁷	Measurement of Frailty Index ¹¹
Core features of frailty⁵⁰	<ul style="list-style-type: none">• Increased vulnerability and reduced ability to recover homeostasis after a stressful event• Changes over time• Includes impairments in multiple physiologic systems• More common in advanced age, women, and related to disability• Predict adverse outcomes (e.g. falls, disability, delirium, and mortality)	
Operationalization	<p>Frailty is quantified as the presence of the following characteristics:</p> <ol style="list-style-type: none">1 Shrinking: unexplained weight loss > 10 pounds in the last year2 Weakness: gender- and body mass index-specific grip strength in the lowest 20%3 Exhaustion: self-report of exhaustion4 Slowness: gender- and height-specific time to walk 15 feet in the lowest 20%5 Low physical activity: gender-specific physical activity level (kcal) per week in the lowest 20% <p>Frailty is defined if 3 of the following items are met; pre-frail if 1 or 2 of the items are met.</p>	<p>Frailty is quantified as the number (or proportion) of health deficits from a pre-specified number of items (at least 30) of any symptoms, signs, diseases, test abnormalities, and disability that satisfies the following criteria:</p> <ol style="list-style-type: none">1 Health deficits should be acquired, increase with age, and predict adverse outcomes.2 Health deficits should not saturate prematurely in the population (should not be present in almost all participants in the population). <p>Although it is used as a continuous variable, the cutoff of 0.20 or 0.25 has been used.</p>
Advantages	<ul style="list-style-type: none">• Require only 5 items• Better clinical translation: targeted interventions and monitoring for each item are possible.	<ul style="list-style-type: none">• Few restrictions on individual items required• Allows finer discrimination of outcome risk than the <i>frailty phenotype</i>
Disadvantages	<ul style="list-style-type: none">• Specific individual items required• Allows only broad discrimination of outcome risk	<ul style="list-style-type: none">• Require at least 30 items• Less clear clinical translation

Table 3

Prediction Models of Frailty and Disability Based on Claims Data

Author (Year)	Model Development			Model Performance	
	Population	Outcome Definition	Predictors	Derivation Cohort	Validation Cohort
Rosen (2000; 2001) ^{40,41}	Derivation sample: All long-term care residents in the Veterans Affairs system, US, in 1996	Worsening disability, defined as 2 points increase in ADL dependence index (range: 3–15), derived from eating, toileting, and transferring over 6 months	Diagnosis codes for the following conditions: Pressure ulcer Terminal illness	Characteristics: N=15,639 Mean age: 72 years Male: 96% Outcome: 15%	Characteristics: N=13,723 Mean age: NR Male: NR Outcome: NR
	Validation sample: All long-term care residents in the Veterans Affairs system, US, in 1997		Hemiplegia/quadruplegia Multiple sclerosis Pulmonary disease Congestive heart failure Arthritis Cancer Alzheimer's disease Dementia other than Alzheimer's disease Parkinson disease Seizure disorder Substance-related disorder	Discrimination: C-statistic: 0.70 Calibration: H-L GOF: $P=0.10$ Predicted/observed risk Decile 1: 2%/3% Decile 5: 14%/13% Decile 10: 32%/33%	Discrimination: C-statistic: 0.68 Calibration: H-L GOF: $P=0.02$ Predicted/observed risk Decile 1: 2%/3% Decile 5: 14%/14% Decile 10: 29%/29%
Dubois (2010) ⁴²	Derivation sample: A random sample of frail community-based older adults, Canada	Functional Autonomy Measurement System score (0–87 points), derived from ADL, IADL, mobility, communication, and mental function	Prescription claims for the following conditions: Anxiety and sleep disorders Vascular disease Diabetes Cardiac diseases Mental disorders Anemia Respiratory illness Severe pain Neurologic condition Behavior problems Hyperlipidemia	Characteristics: N=1,000 Mean age: 83 years Male: 38% Outcome: 19 points	Characteristics: N=402 Mean age: 83 years Male: 38% Outcome: 20 points
	Validation sample: Same as derivation sample (a random split of the total population)				

Author (Year)	Model Development			Model Performance	
	Population	Outcome Definition	Predictors	Derivation Cohort	Validation Cohort
Davidoff (2013) ⁴³	<p>Derivation sample: A representative sample of community-based and institutionalized Medicare beneficiaries</p> <p>Validation sample: Same as derivation sample (a random split of the total population)</p>	Functional status (poor versus good), derived from ADL, IADL, strength, stamina, and exercise	<p>Health care service claims in the following categories:</p> <ul style="list-style-type: none"> E&M / other visits Nursing home visit Dermatology E&M visit Neurology E&M visit Rheumatology E&M visit Chiropractic Home visit Hospice visit Minor procedures Skin Ambulatory procedures Musculoskeletal Preventive services Screening Immunization/vaccination Major procedures Cardiovascular Colectomy Orthopedic – other Durable medical equipment Bath and toilet aids Wheelchairs Hospital bed Enteral and parenteral Medical / surgical supplies Other Imaging 	<p>Goodness of fit: $R^2 = 0.16$</p> <p>Characteristics: N=7,394 Mean age: 78 years Male: 39% Outcome: 9%</p> <p>Discrimination: C-statistic: 0.92 Using the cutoff 0.11, Sensitivity: 0.81 Specificity: 0.92 PPV: 0.50 NPV: 0.98</p> <p>Calibration: N=7,394; $P=0.32$ Mean age: 78 years Male: 39% Outcome: 9%</p>	<p>Goodness of fit: $R^2 = 0.12$</p> <p>Characteristics: N=7,394 Mean age: 78 years Male: 38% Outcome: 9%</p> <p>Discrimination: C-statistic: NR Using the cutoff 0.11, Sensitivity: 0.79 Specificity: 0.92 PPV: 0.48 NPV: 0.98</p> <p>Calibration: N=7,394; NR Mean age: 78 years Male: 38% Outcome: 9%</p>

Model Development				Model Performance	
Author (Year)	Population	Outcome Definition	Predictors	Derivation Cohort	Validation Cohort
			Imaging / procedures – heart including cardiac catheter		
			Standard imaging – nuclear medicine		
			Other		
			Ambulance		
			Electrocardiography monitoring and cardiovascular stress tests		
			Endoscopy		
			Upper gastrointestinal		
			Sigmoidoscopy		
			Colonoscopy		
			Medicaid enrollment		
			Region of country		
			Count of E&M office visits		
			Sex		
Abbreviations: ADL, activity of daily living; E&M, evaluation and management; H-L GOF, Hosmer-Lemeshow goodness-of-fit test; IADL, instrumental activities of daily living; NR, not reported.				Discrimination: Using the cutoff 0.11, Sensitivity: 0.81 Specificity: 0.92 PPV: 0.50 NPV: 0.98	Discrimination: Using the cutoff 0.11, Sensitivity: 0.79 Specificity: 0.92 PPV: 0.48 NPV: 0.98
				Calibration: H-L GOF: $P=0.32$	Calibration: H-L GOF: NR

Table 4
Recommendations for Development and Evaluation of a Claim-Based Frailty Score

Recommendations	
Database	<p>Consider population-based epidemiologic studies of aging that have claims and detailed clinical or survey data. Below are some examples:</p> <ul style="list-style-type: none"> • Adult Changes in Thought Study (http://www.grouphealthresearch.org/capabilities/clinic/clin_std.html#act) • Canadian Study of Health and Aging (http://www.csha.ca) • Cardiovascular Health Study (https://chs-nhlbi.org) • Health and Retirement Study (http://hrsonline.isr.umich.edu) • Longitudinal Studies of Aging (http://www.cdc.gov/nchs/isoa.htm) • National Long-Term Care Survey (http://www.nltes.aas.duke.edu) <p>Consider linking claims data to electronic health records.</p>
Population	Develop claim-based frailty scores separately for community-dwelling population and institutionalized population.
Definition of “gold standard” frailty	<p>Use the <i>frailty index</i> as a “gold standard” than the <i>frailty phenotype</i> for the purpose of confounding adjustment.</p> <p>Determine a pre-specified list (30) of health deficits (symptoms, signs, diseases, test abnormalities, and disability) in multiple physiologic systems available in database.</p> <p>Construct the “gold standard” <i>frailty index</i> as proportion of deficits.</p>
Development of claim-based frailty score	<p>Determine a time frame in which potential predictors are measured (e.g. 1 year).</p> <p>Consider the following <i>a priori</i> list of ICD-9-CM diagnosis codes and HCPCS codes that represent clinical manifestations of frail patients.</p> <ul style="list-style-type: none"> • Abnormality of gait: 781.2 • Abnormal loss of weight and underweight: 783.2 • Adult failure to thrive: 783.7 • Cachexia: 799.4 • Debility: 799.3 • Difficulty in walking: 719.7 • Fall: V15.88 • Malaise and Fatigue: 780.7 • Muscular wasting and disuse atrophy: 728.2 • Muscle weakness: 728.87 • Pressure ulcer: 707.0, 707.2 • Senility without mention of psychosis: 797 • Durable medical equipment (cane, walker, bath equipment, commode): E0100, E0105, E0130, E0135, E0140, E0141, E0143, E0144, E0147-E0149, E0160-E0171 • Nursing or personal care services: T1000-T1005, T1019-T1022, T1030, T1031 <p>Consider additional diagnosis codes, prescription claims, and health care service claims to identify predictors that are either positively or negatively associated with the “gold standard” frailty.</p>

Recommendations	
Evaluation of claim-based frailty score	Validate the performance of a claim-based frailty score against the “gold standard” definition of frailty in an independent hold-out sample, cross-validation, or bootstrap resampling.
	Test the associations with the following clinical outcomes that are known to be associated with frailty:
	<ul style="list-style-type: none">• Fall-related injury (including fracture)• Hospitalizations• Institutionalizations• Home health service use• Mortality
Assess the effectiveness of using claim-based frailty score (e.g. restriction, stratification, matching) on bias reduction using a known example of a treatment that has substantial confounding by frailty.	

Abbreviations: HCPCS, Healthcare Common Procedure Coding System; ICD-9-CM, the International Classification of Diseases, Ninth Revision, Clinical Modification