Research and Applications

Using elastic nets to estimate frailty burden from routinely collected national aged care data

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Received 15 August 2019; Revised 31 October 2019; Editorial Decision 21 November 2019; Accepted 25 November 2019

ABSTRACT

Objectives: To (1) use an elastic net (EN) algorithm to derive a frailty measure from a national aged care eligibility assessment program; (2) compare the ability of EN-based and a traditional cumulative deficit (CD) based frailty measures to predict mortality and entry into permanent residential care; (3) assess if the predictive ability can be improved by using weighted frailty measures.

Materials and Methods: A Cox proportional hazard model based EN algorithm was applied to the 2003–2013 cohort of 903 996 participants for selecting items to enter an EN based frailty measure. The out-of-sample predictive accuracy was measured by the area under the curve (AUC) from Cox models fitted to 80% training and validated on 20% testing samples.

Results: The EN approach resulted in a 178-item frailty measure including items excluded from the 44-item CD-based measure. The EN based measure was not statistically significantly different from the CD-based approach in terms of predicting mortality (AUC 0.641, 95% CI: 0.637–0.644 vs AUC 0.637, 95% CI: 0.634–0.641) and permanent care entry (AUC 0.626, 95% CI: 0.624–0.629 vs AUC 0.627, 95% CI: 0.625–0.63). However, the weighted EN based measure statistically outperforms the weighted CD measure for predicting mortality (AUC 0.774, 95% CI: 0.771–0.777 vs AUC 0.757, 95% CI: 0.754–0.760) and permanent care entry (AUC 0.676, 95% CI: 0.673–0.678 vs AUC 0.671, 95% CI: 0.668–0.674).

Conclusions: The weighted EN and CD-based measures demonstrated similar prediction performance. The CD-based measure items are relevant to frailty measurement and easier to interpret. We recommend using the weighted and unweighted CD-based frailty measures.

Key words: frailty, penalized regression, statistical learning, survival, geriatrics

INTRODUCTION

Frailty is a prevalent syndrome in older individuals accessing aged care services and is a key determinant of their health outcomes and

service utilization.¹ The importance of the identification and appropriate measurement of frailty for patient care is ubiquitously recognized in clinical practice.¹ However, how to best measure it is

an ongoing debate, and, increasingly, the effect of frailty on clinical and epidemiological research is recognized as a priority. While the most commonly used instrument for frailty assessment in the medical literature is the Physical Frail Phenotype,² numerous tools exist including over 67 instruments that were developed to collect frailty data directly from individuals and at least 17 others exploiting existing data to estimate frailty.^{3–20}

In 2016, 5.8% of Australians over the age of 65 years received residential aged care support.²¹ While estimates from small studies suggest that 4% to 59% of these older individuals are likely frail,^{22–24} population-based estimates are not available. As every older Australian that accesses government-subsidized aged care services must undergo an eligibility assessment through the Aged Care Assessment Program (ACAP) before obtaining services, a clear opportunity exists to derive frailty information from these assessments. In the 2017/18 financial year, 186 128 eligibility assessments were performed in Australia.^{25,26}

The purpose of this study was to: (1) use statistical learning to derive a frailty measure from the ACAP; (2) compare the ability of statistical learning based and traditional cumulative deficit based frailty measures^{27,28} to predict all-cause mortality and entry into permanent residential care services events; and (3) assess if the predictive ability of these frailty measures can be improved by using their weighted versions.

MATERIALS AND METHODS

Study design, setting, and data sources

A retrospective cohort study was conducted using data from the National Historical Cohort of the Registry of Senior Australians (ROSA).^{29,30} In brief, Historical ROSA is a deidentified cohort of individuals assessed for or receiving aged care services in Australia between 2003 and 2014, and it has linked information on aged care service utilization and mortality obtained from the Australian Institute of Health and Welfare (AIHW) National Aged Care Data Clearinghouse. In this study, linked data from the Aged Care Assessment Program (ACAP), residential aged care service utilization, and National Death Index datasets were used. The ACAP dataset was used to characterize the cohort and identify items to enter the frailty measures described.³¹ Health conditions in the ACAP dataset are coded according to the modified International Statistical Classification of Disease and Related Health Problems-Tenth Revision-Australian Modification (ICD-10-AM), which ensured comparison of conditions to the Australian Bureau of Statistics 4-digit code used for the Survey of Disability Ageing and Carers.³¹ Conditions are reported if they have an impact on the person's need for assistance with activities of daily living and social participation, and they are advised to be recorded when decided by a suitably qualified medical professional.^{31,32}

Population

Individuals 65 years old and older who had a first-time aged care eligibility assessment between 07/01/2003 and 06/30/2013 and of non-Aboriginal or Torres Strait Islander descent were included. Individuals were evaluated based only on their first aged care eligibility assessment. The cohort was followed up until 06/30/2014, yielding a minimum 1 year of follow-up for the entire cohort, with median follow-up of 3.85 years (95% CI: 3.83–3.86).

Frailty estimation

During an aged care eligibility assessment, 193 health conditions, signs, and symptoms and 11 functional limitations can be recorded

for each individual. Combined, there are 204 possible items, which were included in the development of the frailty measures in this study (Supplementary Table 1). The 2 data-driven approaches used to estimate frailty were:

Cumulative deficit index approach

Deficits were selected out of the 204 possible items if they satisfied the Searle et al criteria,²⁸ which require that: (1) deficits were associated with health status; (2) their prevalence generally increased with age; (3) their prevalence was not too high; (4) deficits covered a broad range of physiological systems; and (5) deficits were collected on a routine basis. Specifically, the items retained encompassed several physiological areas, had a deficit prevalence between 1% and 80%, and < 5% were missing data and expected to have increasing prevalence with age conditional on the survival bias. In this approach, some items were aggregated to create a single indicator when several similar conditions existed. For example, multiple types of cancer were aggregated to create a single binary indicator for the presence of cancer.

This approach led to a frailty index with 44 items, consisting of 8 activity limitations, 24 health conditions, and 12 signs and symptoms. For each item, the presence of the deficit was counted as 1 whereas the absence was counted as 0. The cumulative deficit frailty scores were estimated by dividing the sum of item indicators by the number of items in the frailty measure (ie, 44) leading to a possible range of scores from 0 to 1.0. The weighted version of the cumulative deficit frailty scores was constructed by summing item indicators multiplied by the coefficient estimates from the penalized version of a Cox proportional hazard model,³³ with the penalty set to 0.

Elastic net approach

For an elastic net-based frailty measure, items were selected using the elastic net regularized (penalized) regression approach³⁴ assisted by the 10-fold cross-validation. Penalized regression methods belong to a specific domain of statistical learning and have been referred to as machine learning algorithms in frailty estimation literature.^{5,8} All 204 individual (no aggregation) items from the aged care eligibility assessment were used. Items were included in the frailty measure as suggested by the maximum of the cumulative/dynamic nearest neighborhood-based area under the receiver operator characteristic curve (AUC) estimates from a Cox regression model,^{35–37} averaged across cross-validation attempts.

This approach led to a frailty measure with 178 items, consisting of 11 activity limitations, 140 health conditions, and 27 signs and symptoms (Supplementary Table 1). The unweighted and weighted versions of the elastic net based frailty scores were constructed in the same way as cumulative deficit based frailty scores. The weights for the elastic net-based measure were the coefficients from the fitted elastic net model corresponding to the one underlying the choice of 178 items to enter the measure. For an in-depth description of frailty scores estimation, see Supplementary S1.

Outcomes of interest

The main outcomes of interest in this study were all-cause mortality and entry into permanent residential aged care services within 1 year after individuals' first aged care eligibility assessments. For the all-cause mortality outcome, individuals were censored at the end of follow up (06/30/2014). For the entry into permanent residential aged care services outcome, individuals were censored at the end of follow-up or if they died.

Table 1. Population characteristics and frailty score distribution by estimation approach, overall and by training and testing samples

Characteristic	All				Training sample				Testing sample			
Total N (%)	903 996 (100%)				723 197(80%)				180 799(20%)			
Males	349 226				279 114				70 112			
Females	554 770				444 083				110 687			
Age, mean (SD)	82.1 (7.01)				82.05(7.01)				82.06(7.01)			
Deceased at 06/30/2013, N (%)	555 519 (61.5%)				443 950 (61.4%)				111 569(61.7%)			
Entered permanent residential aged care at 30/6/2013, N (%)	867 945 (96.0%)				694 488 (96.0%)				173 457(95.9%)			
Frailty score range, % ^a	FS _{CD}	FS* _{CD}	FS _{EN}	FS* _{EN}	FS _{CD}	FS* _{CD}	FS _{EN}	FS* _{EN}	FS _{CD}	FS* _{CD}	FS _{EN}	FS* _{EN}
[0.0, 0.2)	5.96	1.84	4.88	6.63	5.95	1.40	4.87	4.15	5.99	3.57	4.94	16.6
[0.2, 0.4)	29.9	43.4	18.0	73.9	30.0	42.9	18.0	74.39	29.78	45.4	17.8	72.0
[0.4, 0.6)	33.9	46.7	38.7	18.5	33.9	47.6	38.7	20.44	34.02	43.1	38.7	10.9
[0.6, 0.8)	26.5	7.95	30.5	0.92	26.5	8.01	30.5	0.99	26.48	7.68	30.6	0.61
[0.8, 1.0]	3.71	0.14	7.91	0.03	3.71	0.13	7.91	0.03	3.72	0.18	7.90	0.02

Abbreviations: FS_{CD}, Frailty Score Cumulative Deficit; FS*_{CD}, Frailty Score Weighted Cumulative Deficit; FS_{EN}, Frailty Score Elastic Net; FS*_{EN}, Frailty Score Weighted Elastic Net; SD, Standard Deviation.

^aNormalized frailty scores.

Validation and comparison of frailty measures

We consider weighted and unweighted frailty measures obtained from the cumulative deficit and elastic net approaches, 4 measures overall. To enable a direct comparison of the 4 frailty measures, their resulting frailty scores were normalized so that they are all in the interval from 0 to 1 (Supplementary S2). The frailty measures were validated based on Kaplan-Meier analysis by plotting survival curves for the cumulative probability of survival and not entering into residential aged care, using incremental values of the frailty scores (0.2-unit increments). The ability of the frailty measures to predict all-cause mortality and entry into permanent residential aged care within 1 year was assessed based on the AUC from the time-dependent receiver operating characteristic curves.^{34,35} The entire dataset was randomly subdivided into 80% training sample and 20% testing sample, with the latter used exclusively for assessment of the out-of-sample prediction. The models were trained on the training sample and tested on the testing sample.

To compare weighted versus unweighted frailty measures in terms of hazard prediction, Cox proportional hazard models that included sex and (log) age as a base, plus either weighted or unweighted frailty scores as a predictor variable, were fitted to the training datasets, and log hazards were predicted from the testing dataset. The weighted and unweighted frailty scores were assessed based on their ability to assign higher hazard to people actually experiencing an all-cause mortality event within 1 year and lower hazard to people remaining alive over the entire study period being followed up for at least 1 year. Predicted individual log hazards were averaged for groups of individuals with the same number of observed frailty items. To assess the difference in hazards predicted from the models with weighted and unweighted frailty scores, mean predicted log hazard values were plotted against the numbers of observed frailty items.

Sensitivity analysis

The ability of the frailty measures to predict all-cause mortality within 3 and 5 years and entry into permanent care within 6 months were also examined. All findings are consistent (data not shown) with the 1-year estimates presented.

RESULTS

Our cohort of 903 996 individuals was randomly subdivided into the training (N = 723 197, 80%) and the testing (N = 180 799, 20%) cohorts, the latter being used for prediction evaluation only. At the end of the study period (06/30/2014), 555 519 (61.5%) individuals were deceased and, out of the 867 945 eligible, 480 081 (55.3%) had accessed permanent residential aged care during the study period (Table 1).

A 178-item elastic net based frailty measure was created from applying the elastic net algorithm. Item selection was motivated by the weighted rather than unweighted frailty measure since the later reached maximum 10-fold cross-validation AUC value for only 8 items (Supplementary Table 1). Most of 178 selected items were contained in 44 items of the cumulative deficit-based frailty measure (Supplementary Table 2) with some exceptions. In particular, the elastic net algorithm failed to retain urinary tract infections, musculoskeletal conditions, neurological conditions (cerebral infraction, transient ischemic attacks, delirium), and emotional or speech symptoms while including Down's syndrome, spina bifida, congenital deformities, and infections.

All 4 frailty measures demonstrated increasing mortality (Figure 1) and entrance into permanent residential care (Figure 2) probability for higher frailty score estimates. The weighted versions of both elastic net and cumulative deficit frailty measures outperform their unweighted versions in their ability to identify the subjects experiencing the events at higher levels of frailty (Table 2).

For 1-year all-cause mortality prediction, the unweighted versions of elastic net (FS_{EN} AUC 0.641, 95% CI: 0.637–0.644) and cumulative deficit (FS_{CD} AUC 0.637, 95% CI: 0.634–0.641) based frailty measures demonstrated similar performance (Figure 3). For the entry into permanent residential aged care services event prediction, the unweighted version of the elastic net (FS_{EN} AUC 0.626, 95% CI: 0.624–0.629) and cumulative deficit (FS_{CD} AUC 0.627, 95% CI: 0.625–0.63) approaches also performed similarly (Figure 3).

The weighted versions of both frailty measures outperform their unweighted versions in terms of predictive ability, with the weighted elastic net based frailty measure outperforming the cumulative deficit based measure statistically, but not necessarily practically, for both 1-year all-cause mortality (AUC 0.774, 95% CI: 0.771–0.777

Figure 1. Kaplan-Meier curves and a number-at-risk table corresponding to normalized frailty score bands for the all-cause mortality event. Analysis based on the $N = 723\,197$ training sample. Due to the large sample sizes, the confidence intervals for the unweighted FS_{CD} and FS_{EN} are too narrow to be visible. 95% confidence intervals are visible in grey shade for the top 2 strata of the weighted FS_{CD}^* and FS_{EN}^* . The vertical line indicates 1-year follow-up. No censoring events were recorded in the number-at-risk table before 1-year follow-up, since all individuals were followed up for at least 1 year.

vs AUC 0.757, 95% CI: 0.754–0.760) and entry into permanent residential aged care services (AUC 0.676, 95% CI: 0.673–0.678 vs AUC 0.671, 95% CI: 0.668–0.674), [Figure 3](#).

When used within a model, the weighted frailty scores demonstrated better performance as compared to unweighted scores in predicting hazards of an adverse event ([Figure 4](#)).

DISCUSSION

In this study, we applied an elastic net algorithm to construct a frailty score from routinely collected aged care eligibility assessment

data and compared it to the traditional cumulative deficit approach to frailty estimation. Elastic net is a statistical learning technique that leads to interpretable outcomes and produces coefficients that can be used as weights for individual items entering a frailty measure. The obtained elastic net-based frailty scores were compared to the cumulative deficit frailty scores on the basis of their ability to identify individuals with higher 1-year risk of mortality and entry into permanent residential aged care services. Unweighted and weighted versions of elastic net and cumulative deficit-based frailty scores were considered. While all approaches confirmed that less frail individuals are more likely to survive and not enter permanent

Figure 2. Kaplan-Meier curves and a number-at-risk table corresponding to normalized frailty score bands for the entry into permanent residential care event. Analysis based on the $N = 694\,488$ training sample. Due to the large sample sizes, the confidence intervals for the unweighted FS_{CD} and FS_{EN} are too narrow to be visible. 95% confidence intervals are visible in grey shade for the top 2 strata of the weighted FS_{CD}^* and FS_{EN}^* . In the case of FS_{EN}^* , the confidence intervals do overlap. The vertical line indicates 1-year follow-up. All the censoring events in the number-at-risk table before 1-year follow-up correspond to death since all individuals were followed up for at least 1 year.

residential aged care services within 1 year from the time their frailty score was measured, the weighted versions demonstrated a better precision of identifying individuals experiencing a higher risk of these adverse events. In our study, the weighted frailty measures performed better than their unweighted versions, both statistically and most likely practically, with the practical value to be determined from the prospective application. An example of the value of applying a weighted versus unweighted frailty measure would be identification of people who are of an immediate need for aged care

intervention while redirecting the rest to less cost-intensive intervention options.

Several recent studies have used statistical modeling and machine learning techniques for developing frailty measures.^{3,5,8,12,13,18,19} Sternberg et al³ suggested a computerized method to estimate a binary frailty status based on the already collected health records and concluded that, within a logistic regression model, the resulted frailty estimates lead to a statistically significant prediction of emergency department visits, hospitalization, and mortality. There were

Table 2. Cumulative survival probability and cumulative 1 - probability of entering into permanent residential aged care by frailty score range by estimation approach

Frailty score range	Survival probability, (95% CI)				Probability of not entering PRAC, (95% CI)			
	FS _{CD}	FS _{CD} [*]	FS _{EN} [*]	FS _{EN}	FS _{CD} [*]	FS _{EN} [*]	FS _{EN}	FS _{EN} [*]
[0.0-0.2)	0.91 (0.91-0.92)	0.97 (0.97-0.97)	0.92 (0.91-0.92)	0.97 (0.97-0.97)	0.87 (0.87-0.87)	0.88 (0.88-0.89)	0.88 (0.88-0.89)	0.89 (0.88-0.89)
[0.2-0.4)	0.85 (0.85-0.86)	0.92 (0.92-0.92)	0.87 (0.87-0.87)	0.87 (0.86-0.87)	0.72 (0.72-0.73)	0.76 (0.76-0.76)	0.76 (0.76-0.76)	0.69 (0.68-0.69)
[0.4-0.6)	0.79 (0.79-0.79)	0.75 (0.74-0.75)	0.81 (0.81-0.81)	0.53 (0.53-0.54)	0.64 (0.63-0.64)	0.57 (0.57-0.58)	0.65 (0.65-0.66)	0.47 (0.47-0.48)
[0.6-0.8)	0.73 (0.73-0.73)	0.41 (0.40-0.41)	0.75 (0.74-0.75)	0.16 (0.15-0.16)	0.57 (0.57-0.57)	0.43 (0.43-0.44)	0.59 (0.59-0.59)	0.40 (0.38-0.42)
[0.8-1.0]	0.63 (0.62-0.63)	0.20; (0.17-0.22)	0.64 (0.64-0.65)	0.07 (0.05-0.12)	0.46 (0.46-0.47)	0.35 (0.31-0.40)	0.51 (0.51-0.52)	0.32 (0.23-0.44)

Abbreviations: CI, Confidence Interval; FS_{CD}, Frailty Score Cumulative Deficit; FS_{EN}, Frailty Score Elastic Net; FS_{EN}^{*}, Frailty Score Weighted Cumulative Deficit; FS_{EN}^{*}, Frailty Score Weighted Elastic Net; PRAC, Permanent Residential Aged Care.

also studies comparing machine (statistical) learning guided to cumulative deficit motivated frailty measures.^{18,19} In particular, Song et al¹⁸ compared a frailty measure generated from an artificial neural network with a frailty measure obtained with the cumulative deficit approach. The authors concluded that the machine learning based measure had a better performance in predicting mortality. Song et al¹⁹ compared several machine learning methods applied to frailty scores construction, also in terms of predicting mortality. The authors regarded the resulted measures as “weighted frailty indices” and concluded that machine learning based approaches performed better as compared to a traditional unweighted cumulative deficit approach. Relevant to our analysis, none of the authors directly compared weighted and unweighted approaches to frailty measure construction.

More recently, Segal et al⁵ constructed a frailty score from the health records obtained from the Cardiovascular Health Study. The authors used a literature review and expert advice to identify candidate items to enter their frailty measure. After attempting several machine learning methods, the authors applied a logistic regression-based adaptive least absolute shrinkage and selection operator (LASSO) approach to identify the best linear combination of variables capable to predict mortality, time to mortality, number of hospital admissions, and entry into permanent residential aged care. The authors retained a 21-item frailty measure, which included age and sex. Kim et al⁸ also applied LASSO regression for selecting variables for a frailty measure based on the routinely collected Medicare Current Beneficiary Survey data. The authors concluded that the 52-item frailty score they retained had performance similar to a comorbidity index when predicting mortality, but a better performance for predicting disabilities or recurrent falls.⁸

While Segal et al⁵ and Kim et al⁸ used a penalized regression approach similar to the one we applied in our study, there are limitations in these later studies that we believe we successfully addressed in our investigation. Firstly, in order to select relevant items to enter frailty measures, the authors applied the LASSO-based cross-validation on multivariate versions of the candidate models. While this approach allowed selecting the best linear combination of the variables to predict adverse events, the outcomes say little about the predictive ability of the selected variables after they are combined (ie, collapsed) into a univariate frailty measure. In contrast, we searched for a variable combination that best predicts an adverse event (all-cause mortality) after they were collapsed into a univariate frailty score. In fact, we found that predictive ability of a frailty score can rise or fall dramatically, depending on which item last entered the score (Supplementary eFigure 1 or interactive Supplementary iFigures 1-4). Secondly, the authors applied a special case of penalized regressions with the LASSO penalty, while we investigated the entire range of penalties from Ridge to LASSO within the elastic net method. Even though we objectively concluded that the predictive ability of a frailty measure is maximized under the LASSO penalty, we had no reason to expect this in advance and documented this numerical analysis result through the AUC surfaces presented in Supplementary eFigure 1, and interactive Supplementary iFigures 1-4.

Finally, and most importantly to our results, previous studies did not compare the unweighted frailty scores with their weighted versions while, in most cases, the weights were directly available from applying the methods. Xie et al,³⁸ in a review of 49 frailty measures reported in the literature, identified that only 3 of them applied weights to individual items.³⁹⁻⁴¹ The authors pointed out that not using weights is 1 of the gaps in frailty measures construction. Indeed, it is hardly reasonable to give equal importance to comparatively minor health conditions and symptoms, such as dizziness, and

Figure 3. Areas under the receiver operator characteristic curves for the mortality (left panel) and entrance into permanent residential care (right panel) events. The base model contains sex and age variables. The rest of the models contain base model variables plus a univariate frailty score.

major life-threatening health burdens, such as diabetes or cancers. It has already been suggested that weighted frailty measures perform better in predicting adverse outcomes as compared to their unweighted versions.^{41,42} In our study, we directly compared 2 alternative unweighted versions of a frailty measure with their weighted versions and concluded that weighted frailty scores perform substantially better in adverse events prediction.

Rockwood and Mitnitski⁴³ commented on the clinical value of weighted versus unweighted frailty measures. The authors pointed out that while a weighted score can perform better in predicting adverse events, weighting limits generalizability, which in the authors' opinion has the "greatest value." Having agreed with this argument, we still would like to reinforce that it is not known whether the benefits brought with generalizability of an unweighted frailty measure can justify the reduction of precision in clinical decision-making from not using weighted frailty measures.

It is reasonable to use weighted and unweighted frailty measures in parallel. A more traditional, easy-to-interpret unweighted frailty index can be used for clinical assessments by providers, while its weighted version could be used for analytical and prediction purposes within statistical models and machine learning algorithms. In our evaluation, we demonstrated that weighted frailty scores can predict the hazard of an event more precisely when used within a model—on average assigning higher hazard to individuals actually experiencing an event and lower hazard to event-free individuals. Weighted scores, compared to unweighted, almost uniformly lead to higher predicted hazard for true positive individuals (ie, the individuals who were actually deceased within 1 year), while predicting lower hazard for true negative individuals (ie, the individuals who stayed alive until the end of the observation period). The predicted hazard of mortality increases with the number of observed frailty items, once again confirming the validity of the frailty measures.

Frailty is a state of increased vulnerability to adverse outcomes associated with decreased physiological reserve and diminished re-

sistance to stressors.²⁸ In the elastic net approach suggested above, the resulted frailty measure was built with respect to a single adverse outcome, which in our study was all-cause mortality. In practice, a scope of adverse outcomes is more diverse, and our elastic net approach remained blinded to any alternative possibilities. While it is possible to define an algorithm simultaneously selecting items with respect to a set of several adverse outcomes (a multivariate response approach⁴⁴), to the best of our knowledge, such an attempt has never been implemented. Moreover, there is no reason to expect that items selected with such a multivariate response approach would perform better when compared to a frailty measure built using the cumulative deficit approach. In our study, when the predictive performance of the elastic net based approach was assessed with respect to an alternative adverse outcome (entry into permanent residential aged care services), the predictive performance of a more complex elastic net based frailty score became nearly identical to the broader less complex cumulative deficit-based measure.

In our study, the elastic net approach had good agreement with the cumulative deficit approach in selecting the items entering the frailty measures. However, the elastic net algorithm did not discard some items which did not meet criteria outlined by Searle et al²⁸ and, hence, were not included in the cumulative deficit-based measure. For example, Down's syndrome and diarrhea were selected with elastic nets, while the prevalence of these are clearly not expected to increase with age, contradicting one of the selection criteria outlined by Searle et al.²⁸ Adding to that, the elastic net approach failed to select items that are considered to be important to frailty measurement, such as falls, urinary tract infection, certain musculoskeletal conditions, neurological conditions, and emotional or speech symptoms. Moreover, without explicit instructions, the elastic net algorithm was not capable of determining sex-specific conditions, such as prostate cancer. In the cumulative deficit approach, this latter issue was effectively addressed by aggregating

Figure 4. Weighted versus unweighted performance in predicting all-cause mortality and staying alive. Predicted mean log hazards, with 95% confidence intervals, plotted against the observed numbers of frailty items. *Top Left panel:* Elastic net based predicted mean log hazard of all-cause mortality for people actually deceased within 1 year of follow-up. *Top Right panel:* Elastic net-based predicted mean log hazard of all-cause mortality for people who stayed alive over the study period and followed up for at least 1 year. *Bottom Left panel:* Cumulative deficit-based predicted mean log hazard of all-cause mortality for people actually deceased within 1 year of follow-up. *Bottom Right panel:* Cumulative deficit-based predicted mean log hazard of all-cause mortality for people who stayed alive over the study period and followed up for at least 1 year.

cancer items into a single indicator. While the penalized regression approach can be partially guided by accounting for associations between explanatory variables,^{45,46} the fact that an unguided elastic net-based algorithm remains oblivious to frailty relevance and biological specifics of candidate items is a major limitation of the method.

The items used for the measures we created are part of a mandatory aged care eligibility assessment that, since 2005, all Australians must undergo when seeking aged care subsidies from the Australian government, making this a true population study.²⁵ We recognize that some existing conditions may not be reported as a part of the assessment, since a condition has to cause people disability and limitation and be diagnosed by a suitably qualified

medical professional. Furthermore, only a maximum of 10 health conditions can be recorded at the time of the eligibility assessment. Therefore, it is possible that for someone with significant chronic and acute conditions, less serious conditions may not have been recorded. We have investigated this limitation and determined that there is a low proportion of individuals (~3%) expected to have a number of health conditions exceeding 10, and that would not impact their frailty estimation in a significant way. Finally, it is possible that the variables in our study can include incorrect values, missing values, and miscoding—all due to the nature of the data used. We attempted to minimize these issues by conducting comprehensive logic checks and cleaning of the existing data prior to undertaking this analysis.

The strengths of our study include the minimum attrition of our cohort and, therefore, low likelihood of a selection bias. We also have the cohort's complete government subsidized aged care service records, which is used to determine their entry into permanent residential aged care, matched to the National Death Index records. As a result, our analysis was applied to the large exhaustive subpopulation of older people entering the aged care system in Australia, covering an estimated 6.5% of the population in Australia over the age of 65 years old. Furthermore, the aged care eligibility assessments from which the information on these frailty measures were derived are part of a systematic and comprehensive eligibility assessment program established in 2003 which all Australians that access aged care subsidies for residential aged care must undergo. This assessment is performed by trained assessors or teams of assessors that include clinicians, social workers, or other types of skilled care providers.

CONCLUSION

Both elastic net- and cumulative deficit-based frailty measures can successfully predict 1-year all-cause mortality and entry into permanent residential care services events. The unweighted elastic net- and cumulative deficit-based frailty measures have nearly equivalent performance with respect to predicting these events. The weighted versions of the same frailty measures can predict the events substantially better, with the predictive ability of the elastic net-based measure maximized under the LASSO regularization. The elastic net approach has led to a more complex measure that includes a number of items irrelevant to frailty, excluding several essential items known to be frailty-related. On this ground, we recommend the cumulative deficit frailty measure, both weighted and unweighted versions, for practical use in the Australian aged care sector.

FUNDING

This work was supported by the South Australian Government through the Department for Innovation and Skills (2017–2021).

AUTHOR CONTRIBUTIONS

MM and MCI designed the study. MCI and SW were responsible for data acquisition. MM analyzed the data and wrote the initial draft of the manuscript. JK, RV, SW, and MCI were involved in interpretation of the analysis outcomes. All authors critically revised the manuscript for intellectual content and approved the final version. MM attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

SUPPLEMENTARY MATERIAL

[Supplementary material](#) is available at Journal of the American Medical Informatics Association online.

ACKNOWLEDGMENT

We would like to acknowledge the Healthy Ageing Research Consortium Investigator Team and the Registry of Senior Australians (ROSA) South Australian Health and Medical Research Institute (SAHMRI) Research Team for ensuring the success of the ROSA and support with this study. We also acknowledge the South Australian Government who provide us with support

(2017–2021) through the Department for Innovation and Skills, and the Australian Institute of Health and Welfare (AIHW) for the provision of the raw data used in the ROSA.

CONFLICT OF INTEREST STATEMENT

None declared.

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