Primary Care Prognostic (PCP) Index of 11-Year Mortality Risk: Development and Validation of a Brief Prognostic Tool

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BACKGROUND: Healthcare providers use a life expectancy of at least 5 to 10 years in shared clinical decision-making with older adults about cancer screening, major surgeries, and disease prevention interventions. At present, few prognostic indexes predict long-term mortality beyond 10 years or are suited for use in primary care settings.

OBJECTIVE: We developed and validated an 8-item multidimensional index predicting 11-year mortality for use in primary care.

DESIGN, SETTING, AND PARTICIPANTS: Using data from the Singapore Longitudinal Ageing Studies (SLAS), we developed a Primary Care Prognostic (PCP) Index for predicting 11-year mortality risk in a development cohort (n = 1550) and validated it in a geographically different cohort (n = 928).

MAIN MEASURES: The PCP Index was derived from eight indicators (body mass loss, weakness, slow gait, comorbidity, polypharmacy, IADL/BADL dependency, low albumin, low total cholesterol, out of 25 candidate indicators) using stepwise Cox proportional hazard models.

KEY RESULTS: In the developmental cohort, the mortality hazard ratio increased by 53% per PCP point score increase, independent of age and sex. Across risk categories, absolute risks of mortality increased from 5% (score 0) to 67.9% (scores 7–9), with area under curve (AUC = 0.77 (95% CI 0.73–0.80)). The PCP Index also predicted mortality in the validation cohort, with AUC = 0.70 (95% CI 0.64–0.75).

CONCLUSIONS: The PCP Index using simple clinical assessments and point scoring is a potentially useful prognostic tool for predicting long-term mortality and is well suited for risk stratification and shared clinical decision-making with older adults in primary care.

KEY WORDS: older adults; prognosis; mortality; frailty; malnutrition.

J Gen Intern Med 36(1):62–8
DOI: 10.1007/s11606-020-06132-2

Electronic supplementary material *The online version of this article (https://doi.org/10.1007/s11606-020-06132-2) contains supplementary material, which is available to authorized users.*

Received May 7, 2020
Accepted August 11, 2020
Published online August 20, 2020

INTRODUCTION

In aging populations, escalating numbers of older adults in need of medical care present formidable healthcare challenges.[1, 2] Individualized management of older adults requires clinicians to consider patients' life expectancy in making shared clinical decisions regarding chronic disease management, major surgeries, and cancer screening.[3] However, few prognostic indexes predict long-term mortality (beyond 10 years) in community-living older adults or can be easily used in primary care.

Current prognostic indexes face a number of issues that limit their application across a wide cross-section of patient groups and clinical settings.[4–8] Tools developed from hospital-based administrative data sets require information that are not routinely available or relevant in the primary care setting. Indexes based on multiple demographic, lifestyle, and behavioral risk, and disease variables are less relevant in older populations because predictors such as smoking, obesity, and chronic diseases are less important in the oldest old.[9, 10] While the Multidimensional Prognostic Index (MPI) has shown good predictive accuracy for mortality risk,[11] it requires a standard Comprehensive Geriatric Assessment (CGA) which is time-consuming and not practical in primary care settings.

Multidimensional tools which use items such as age, gender, instrumental activities of daily living, comorbidities, mood, cognitive function, and nutritional status have shown good predictive validity for 3 to 5 years, but have not been tested over longer time periods.[8, 12–16] Using data collected from community-dwelling older adults in the Singapore Longitudinal Ageing Studies (SLAS-1), we used a range of simple questionnaire, performance-based and blood indicators of health and functional status of older adults that are commonly used in primary care outpatient settings to develop a brief primary care prognostic index for predicting 11-year mortality risk in older adults. An 11-year mortality risk index was developed as few studies have evaluated long-term mortality risks of prognostic indices in population-based cohorts over periods longer than 5 or 10 years. This is important because

current guidelines do not recommend some preventive interventions such as cancer screening when life expectancy is less than 10 years.[17]

METHODS

Study Cohort

Data was collected from an observational population-based cohort study of older adults, aged ≥ 55 years in Singapore, with mortality follow-up from 1 September 2003 to 31 December 2014. Full details are previously described.[18] Briefly, between 1 September 2003 and 31 December 2005, a whole area population of 2804 older adult residents in a dozen adjoining precincts in the South-East Region of Singapore were invited to participate in the study. Informed consent was obtained, and the study was approved by an institutional review board. At recruitment, questionnaires were administered using face-to-face interviews conducted by research nurses at the participants' homes. Clinical measurements and blood draws were performed at a local study site center.

Development and Validation of the PCP Index

The derivation of the PCP Index used a cohort of 1550 participants who were recruited from one defined geographical area during the period from 1 September to 31 December 2004. Our validation cohort[19] was based on another cohort of 928 subjects who were recruited from a different residential area from 1 January 2005 to 31 December 2005.

A total of 25 performance-based and laboratory indicators of health and functional status of older adults were considered. (The full details for each measure are provided in Supplementary Table S1.) These indicators were selected for ease of collection in primary care settings and have been shown to predict mortality in older populations.[20–45]

All-Cause Mortality Follow-up

The follow-up vital status and date of death of the participants from baseline up to 31 December 2014 was determined by using the participants' unique National Registration Identity Card (NRIC) number matched to the National Death Registry. Two-hundred and forty-three participants died from 15,340 person-years of observation during a follow-up period of 11 years.

Statistical analysis

Cox regression models of time to event data, censored at the date of death or on 31 December 2014, and Kaplan-Meier plots of survival, with testing for proportional hazard assumptions and estimates of hazard ratios (HR) and 95% confidence intervals (95% CI), were used to derive predictors of 11-year mortality. In the development cohort, we used a two-stage approach. We first identified variables that significantly predicted mortality in initial multivariable models in groups (NSI nutritional indicators, blood biomarkers, physical functional indicators, and other clinical and functional indicators) which also included age and sex. Variables significantly predicting mortality in each of the initial models were placed into a final stepwise multivariable model, along with age and sex. Forward stepwise elimination, backward stepwise elimination, and backward elimination were all tested, yielding the same results.

Using weights (rounded to the nearest integer) derived from regression coefficients, setting the lowest coefficient a score of 1, a weighted summed score was derived to create the PCP Index. The summed scores across indicators range potentially from 0 to 10. The performance of the PCP Index's categorical levels: low (0–1), medium (2, 3), high (4, 5), and very high (6+) risk in predicting mortality risks were evaluated with HR estimates adjusted for age and sex. Discrimination of the model was assessed by receiver operating characteristic (ROC) curves and Harrel's C-statistics for mortality. We validated the PCP Index by comparing the predicted mortality from the development cohort to the observed mortality in the validation cohort. All analyses were performed using SAS 9.2 (SAS Institute, Inc., Cary, NC).

RESULTS

Characteristics of Development Cohort Subjects

The mean age of participants in the development cohort (n = 1550) was 66.4 (SD 7.8). Sixty-two percent were women. Twenty-three percent had less than 6 years of formal education and were either single, divorced, or widowed. Forty percent had 3 or more comorbidities and 29% required assistance in either IADL or BADL (Table 1). During the 11 years of follow-up, 243 (15.7%) participants died, from a total of 15,340 person-years of observation.

Development Cohort

Table 2 shows the mortality HR of association with the 25 individual indicators in separate models for clinical and functional indicators, physical functioning indicators, and nutritional indicators, controlling for age and sex. Four of the 11 NSI questionnaire indicators (inability to prepare meals or feed oneself, poor dentition, or oral issues causing difficulty eating, low intake of fruits or vegetables, take 3 more different drugs a day), and all blood, physical, clinical, and functional indicators, except low physical activity and depression, significantly predicted mortality independently of other indicators in their respective classes.

Table 3 shows the results when these significant indicators were entered simultaneously as candidate variables in the final

Table 1 Baseline Characteristics of Participants in Development and Validation Cohorts

	Development cohort	Validation cohort	*P* value
No. of subjects	1550	928	
Female sex	964 (62.2)	600 (64.7)	< 0.001
Age	66.4 ± 7.8	65.4 ± 7.1	< 0.001
Less than 6 years of education	364 (23.5)	103 (11.1)	< 0.001
Single, divorced or widowed	366 (23.6)	263 (28.3)	< 0.001
Comorbidity (≥ 3)	629 (40.6)	427 (46.0)	< 0.001
Lived alone	94 (6.1)	88 (9.5)	< 0.001
Body mass index, kg/m^2	23.5 ± 3.6	23.7 ± 3.5	0.28
Overweight or obese	189 (12.2)	139 (15.0)	0.049
Albumin (g/L)	41.8 ± 3.4	42.8 ± 2.9	< 0.001
Lymphocytes (per mm^3)	2034 ± 599	1900 ± 542	< 0.001
Total cholesterol (mmol/L)	5.46 ± 0.95	5.45 ± 0.97	0.81
Food intake indicators			
Physically unable to shop, cook and/or feed myself	51 (3.3)	9 (1.0)	< 0.001
Take 3 or more different drugs a day	366 (23.6)	251 (27.1)	0.056
Tooth or mouth problem causes difficulty eating	105 (6.8)	23 (2.5)	< 0.001
Few fruit or vegetables (less than 2 portions per day)	149 (9.6)	54 (5.8)	0.001
Illness/condition changes kind/amount of food eaten	639 41.2	366 39.4	0.38
Fewer than 2 meals eaten per day	46 (3.0)	11 (1.2)	0.004
Few milk products (less than once a day)	1093 (70.5)	419 (45.2)	< 0.001
Alcohol 3 or more drinks almost every day	57 (3.7)	24 (2.6)	0.14
Money not enough to buy needed food	48 (3.1)	5 (0.5)	< 0.001
Eat alone most of the time	234 (15.1)	127 (13.7)	0.34
Unintended loss/gain10lbs/4 kg last 6 months	63 (4.1)	24 (2.6)	0.053
Blood nutritional indicators			
Anemia (< 12 Female, < 13 Male)-WHO criteria	236 (15.2)	103 (11.1)	0.004
Albumin L4 40g/L	535 (34.5)	192 (20.7)	< 0.001
Low total cholesterol < 4.14 mmol/L	116 (7.5)	75 (8.1)	0.59
Low lymphocyte count < 1200/mm3	79 (5.1)	68 (7.3)	0.023
Physical functional indicators			
Weakness: unable to rise from chair (arms folded)	352 (22.7)	134 (14.4)	0.000
Poor gait: POMA gait score ≤ 8	67 (4.3)	12 (1.3)	0.000
Shrinking: BMI < 18.5 or weight loss[1]	151 (9.7)	67 (7.2)	0.032
Exhaustion	168 (10.8)	46 (5.0)	0.000
Low physical activity[2]	339 (21.9)	311 (33.5)	0.000
Frail (Score: 3 to 5)	67 (4.3)	16 (1.7)	0.000
Clinical indicators			
Comorbidity (3 or more medical conditions)[3]	629 (40.6)	427 (46.0)	0.000
IADL or BADL disability (Y/N)[4]	449 (29.0)	155 (16.7)	0.000
Polypharmacy (6 or more drugs)	170 (11.0)	94 (10.1)	0.51
Cognitive impairment (MMSE)	234 (15.1)	55 (5.9)	0.000
Depression: GDS ≥ 10	63 (4.1)	18 (1.9)	0.004

[1]*At least 5% of body weight or 10 pounds (4.5 kg) in the last 6 months or 3 kg (6.6 pounds) in the last 3 months*
[2]*Self-report: "None" for participation in any moderate to heavy physical activity (walking or recreational or sports activity)*
[3]*Hypertension, lipid abnormality, diabetes, stroke, myocardial infarction, atrial fibrillation, heart failure, major eye disorder, end-stage renal failure, asthma, chronic obstructive lung disease, arthritis, hip fracture, mental illness, dementia, neurodegenerative diseases, cancer, other chronic diseases*
[4]*Unable to perform any of one or more IADL or BADL without assistance*

model using backward and forward stepwise selection procedures. The final reduced model includes eight independent predictors of mortality, with HR ranging from 1.5 to 2.5. Two indicators are laboratory findings (low albumin and low total cholesterol), 5 are physical indicators (height loss, weakness, slow gait, functional disability), and 2 clinical indicators (multiple comorbidities and polypharmacy). The prognostic index scores ranged from 0 to 9, mean (SD) of 2.1(2.0). There was a stepwise increase in mortality, from 5% for those with a score of 0 to 68% among those with a score of 7–9, with distinct survival trajectories; these differences persisted over the 11 years of follow-up (Fig. 1). The area under the ROC (AUC) was 0.77 (95% CI 0.73-0.80), compared with the corresponding area under the ROC for age, which was 0.73 (0.70–0.77). An index combining the PCP Index with age did not significantly increase the AUC (0.78, 95% CI 0.74–0.80).

Validation Cohort

The mean age of participants in the validation cohort ($n = 928$) was 65 years, 64% were women. Eleven percent had less than 6 years of formal education and 28.3% were either single, divorced, or widowed. Forty-six percent had 3 or more comorbidities and 16.7% required assistance in either IADLs or BADLs (Table 1). During 9 years of follow-up, 86 participants died, from a total of 8342 person-years of observation.

The PCP Index scores in the validation cohort were lower than in the development cohort; the highest PCP Index score category (6–10) had no participants with scores greater than 6. The mortality rates increased from 3.0 per 100 person-years among those with PCP Index score of 0 to 35.7 per 100 person-years among those with the highest PCP Index score of 6 (Table 4). The PCP Index showed good accuracy in discriminating between those who died and those who

Table 2 Multivariable Models of Nutritional, Blood, and Clinical Indicators Predicting Mortality Risks in Development Cohort ($N = 1550$)

Frailty indicators	Multivariable Cox regression models			
	B	SE	HR (95% CI)	*P* value
Model 1: Nutritional intake indicators				
Unable to shop, cook and/or feed myself	1.175	0.269	3.24 (1.91–5.48)	< 0.0001
Takes 3 or more different drugs a day	0.542	0.141	1.72 (1.30–2.27)	< 0.0001
Difficulty eating	0.511	0.204	1.67 (1.12–2.49)	0.012
Few fruit or vegetables: < 2 portions per day	0.461	0.188	1.58 (1.10–2.29)	0.014
Illness changes the kind/amount of food eaten	0.028	0.137	1.03 (0.79–1.35)	0.836
Fewer than 2 meals eaten per day	0.248	0.315	1.28 (0.69–2.37)	0.430
Few milk products (less than once a day)	0.083	0.148	1.09 (0.81–1.45)	0.573
Alcohol 3 or more drinks almost every day	0.104	0.316	1.11 (0.60–2.06)	0.742
Inadequate money to buy needed food	− 0.070	0.322	0.93 (0.50–1.75)	0.828
Eats alone most of the time	0.132	0.169	1.14 (0.82–1.59)	0.434
Unintended loss/gain 4 kg last 6 months	− 0.075	0.316	0.93 (0.50–1.72)	0.811
Model 2: Laboratory indicators				
Anemia: < 12 female, < 13 male—WHO criteria	0.526	0.151	1.69 (1.26–2.28)	0.001
Albumin < 40 g/L	0.480	0.130	1.62 (1.25–2.08)	< 0.001
Low total cholesterol < 4.14 mmol/L	0.938	0.173	2.55 (1.82–3.59)	< 0.001
Low lymphocyte count < 1200/mm^3	0.633	0.217	1.88 (1.23–2.88)	0.004
Model 3: Physical functional indicators				
Weakness: Chair rise (lowest 20%)	1.254	0.140	3.50 (2.66–4.62)	0.000
Poor gait: POMA gait score ≤ 8	0.770	0.199	2.16 (1.46–3.19)	0.000
Low BMI (< 18.5) or weight loss[1]	0.481	0.180	1.62 (1.14–2.30)	0.008
Exhaustion	0.394	0.169	1.48 (1.06–2.07)	0.020
Low physical activity[2]	0.109	0.146	1.11 (0.84–1.48)	0.455
Model 4: Clinical and other functional indicators				
IADL or BADL disability (Y/N)[3]	1.018	0.134	2.77 (2.13–3.60)	0.000
Comorbidity (3 or more medical conditions)[4]	0.510	0.146	1.66 (1.25–2.22)	0.000
Polypharmacy (6 or more drugs)	0.509	0.169	1.66 (1.19–2.32)	0.003
Cognitive impairment	0.523	0.137	1.69 (1.29–2.21)	0.000
Depression	0.184	0.261	1.20 (0.72–2.01)	0.481

Hazard ratio was controlled for age and sex included as covariates in the models
[1]*At least 5% of body weight or 10 pounds (4.5 kg) in the last 6 months or 3 kg (6.6 pounds) in the last 3 months*
[2]*Self-report: "None" for participation in any moderate to heavy physical activity (walking or recreational or sports activity)*
[3]*Unable to perform any of one or more IADL or BADL without assistance*
[4]*Hypertension, lipid abnormality, diabetes, stroke, myocardial infarction, atrial fibrillation, heart failure, major eye disorder, end-stage renal failure, asthma, chronic obstructive lung disease, arthritis, hip fracture, mental illness, dementia, neurodegenerative diseases, cancer, other chronic diseases*

survived, with C-statistic of 0.70 (Table 5). There was reasonably close agreement between the observed mortality in the development and validation cohorts for various levels of risk.

In addition, we tested a 6-item version of the PCP Index which did not require blood measures (potential range of scores 0 to 8) which has an AUC of 0.75, with predicted probabilities of mortality ranging from 5.7% (score = 0) to 78.3% (score = 7–8). (See Supplementary Table S2.)

DISCUSSION

We developed and validated a prognostic index using a simple point scoring method that can be used by primary care providers to stratify older adults on their risk of 11-year mortality. The index predicted 11-year mortality independently of age and sex, spanned a wide range of absolute mortality from 5 to 68%, with uniformly wide

Table 3 Independent Risk Factors for 11-Year Mortality in the Development Cohort: Multivariable Cox Regression Final Selection Model ($N = 1238$)

PCP Index Indicators	*B*	SE	HR (95% CI)	Points
BMI < 18.5 or weight loss[1]	0.501	0.181	1.650 (1.158–2.352)	1
Weakness: unable to rise from chair (arms folded)	0.922	0.148	2.515 (1.880–3.363)	2
Poor gait: POMA gait score ≤ 8	0.505	0.201	1.657 (1.119–2.455)	1
Comorbidity (3 or more medical conditions)[2]	0.375	0.151	1.456 (1.083–1.956)	1
Polypharmacy (6 or more drugs)[3]	0.378	0.171	1.460 (1.044–2.041)	1
IADL or BADL disability (Y/N)[4]	0.720	0.142	2.055 (1.556–2.714)	2
Low Albumin (< 40 g/L)	0.533	0.130	1.704 (1.320–2.199)	1
Low total cholesterol < 4.14 mmol/L	0.483	0.177	1.620 (1.145–2.292)	1

[*]*Hazard ratio was controlled for age and sex included as covariates in the models*
[1]*At least 5% of body weight or 10 pounds (4.5 kg) in the last 6 months or 3 kg (6.6 pounds) in the last 3 months*
[2]*Hypertension, lipid abnormality, diabetes, stroke, myocardial infarction, atrial fibrillation, heart failure, major eye disorder, end-stage renal failure, asthma, chronic obstructive lung disease, arthritis, hip fracture, mental illness, dementia, neurodegenerative diseases, cancer, other chronic diseases*
[3]*Oral medications, not including vitamins or supplements*
[4]*Unable to perform any of one or more IADL or BADL without assistance*

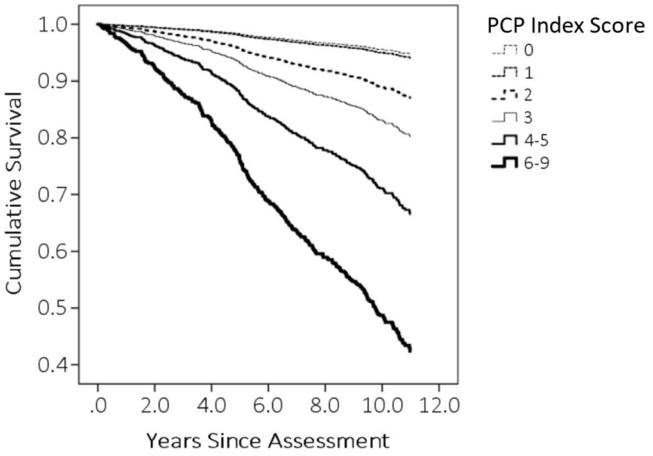

Figure 1 Kaplan-Meier survival of quartile risk groups over 11 years of follow-up.

separation across the different risk groups. The PCP Index predicted mortality in the validation cohort nearly as well as it did in the development cohort. The performance of the PCP Index compares favorably with that of other prognostic indexes that are also proposed for use by primary care providers for risk stratification of community-living older adults.[13–16] Studies have reported that functional status adds modestly to mortality prediction in primary care beyond age, sex, and comorbidities.[15, 16] Our study differs from previous studies by exploring a greater number of different and high-prevalence functional indicators for predicting mortality in the model development. Our index differs by using physical and functional indicators of frailty and malnutrition and provides estimates of mortality over 11 years, longer than other studies.

Older patients with high mortality risk over 5 to 10 years may benefit from closer monitoring and targeted interventions to improve life expectancy and quality of life. This is because the PCP Index is distinctively based on measures of physical frailty and malnutrition and identifies older adults who are pre-frail/frail and/or at-risk of malnutrition (or malnourished) with high mortality risks. These conditions have a high prevalence in older populations[46, 47] and should be monitored and treated.[48] The PCP Index may thus be used in older patients for holistic management of malnutrition and frailty which may improve quality of life and survival. Additionally, the PCP Index may also be a useful tool in healthcare policy and epidemiological studies for risk adjustment in the evaluation of quality of care, medical effectiveness, and patient care outcomes among healthcare organizations.

Our study has several limitations. First, the validation cohort was younger, was better educated, had higher income, and was better housed than the development cohort and few had the highest PCP scores. Among the strata present, the PCP Index performed nearly as well as the development index. Secondly, the AUC for our index was only slightly higher than using age alone as the predictor of mortality. Interestingly, our index was independent of age and can be used as an additional clinical marker for providers in clinical decision-making. Third, the study was performed using only elderly Chinese residents. Whether it would perform as well in other countries and other ethnicities needs to be studied. Finally, the index was developed from community-living older adults; it may not be generalizable to populations in hospitals or nursing homes. Further studies should also be conducted to determine how the PCP Index compares with other prognostic indices and to determine its validity in populations with longer or shorter life expectancies.

Study strengths include using physical, nutritional, and functional indicators that are standard clinical measures that can be easily performed in primary care settings. The PCP Index measures take no longer than 10 min to complete.

Table 4 PCP Index Calibration: Mortality Rates According to Risk Score in the Development and Validation Cohorts

Score	Development cohort				Validation cohort		
	Deaths	At risk	%	HR* (95% CI)	Deaths	At risk	%
Per point				1.53 (1.45–1.61)			
Score							
0	19	382	5.0	1 (referent)	9	297	3.0
1	20	361	5.5	1.12 (0.60–2.10)	22	285	7.7
2	31	257	12.1	2.54 (1.43–4.50)	13	123	10.6
3	40	214	18.7	4.05 (2.35–6.99)	16	102	15.7
4	41	127	32.3	7.62 (4.42–13.1)	7	54	13.0
5	26	84	31.0	7.24 (4.01–13.1)	9	29	23.1
6	28	69	40.6	11.2 (6.23–20.0)	10	28	35.7
7+	38	56	67.9	22.6 (13.0–39.3)			
C-statistic			0.77 (0.73–0.80)	0.70 (0.64–0.75)			
Risk quartiles							
0–1	39	743	5.2	1 (-)	31	582	5.3
2–3	71	471	15.1	2.49 (1.68–3.69)	29	225	12.9
4–5	67	211	31.8	4.23 (2.79–6.43)	16	82	20.7
6–9	66	125	52.8	7.34 (4.73–11.4)	10	28	35.7
C-statistic			0.76 (0.72–0.79)	0.66 (0.60–0.73)			

**Sex and age-adjusted*

Table 5 Primary Care Prognostic (PCP) Index

Primary Care Prognostic (PCP) Index			Circle scores accordingly		
Indicator		**Definition**	**No**	**Yes**	**Notes**
Low BMI		< 18. 5 kg/m^2 or weight loss[1]	0	1	
Weakness		Unable to rise from a chair (arms folded)	0	2	
Poor gait		POMA gait score ≤ 8	0	1	
Comorbidities[2]		≥ 3 medical conditions	0	1	
Polypharmacy[3]		≥ 6 drugs	0	1	
Disability[4]		Instrumental or basic activity of daily living	0	2	
Low albumin		Albumin < 40 g/L	0	1	
Low total cholesterol		Cholesterol < 4.14 mmol/L (< 160 mg/dL)	0	1	
Total Summed Score			0	10	___/10
Scoring	Mortality risk	Estimated probability of death within the next 10 years			
0–1	Low	5%			
2–3	Medium	15%			
4–5	High	32%			
≥ 6	Very High	55%			

[1]*At least 5% of body weight or 10 pounds (4.5 kg) in the last 6 months or 3 kg (6.6 pounds) in the last 3 months*
[2]*Hypertension, lipid abnormality, diabetes, stroke, myocardial infarction, atrial fibrillation, heart failure, major eye disorder, end-stage renal failure, asthma, chronic obstructive lung disease, arthritis, hip fracture, mental illness, dementia, neurodegenerative diseases, cancer, other chronic diseases*
[3]*Oral medications, not including vitamins or supplements*
[4]*Unable to perform any one or more IADL or BADL without assistance*

In addition, we developed and validated our measure in distinct patient populations. Third, our shorter prognostic indicator can be applied in the absence of having the serum markers available.

CONCLUSION

The Primary Care Prognostic Index using simple clinical assessments and point scoring is a prognostic tool for predicting long-term mortality risks that are well suited for risk stratification and shared clinical decision-making with older adults, as well as health policy formulation and research.

Acknowledgments: *We thank the following voluntary welfare organizations for their support: Geylang East Home for the Aged, Presbyterian Community Services, St Luke's Eldercare Services, Thye Hua Kwan Moral Society (Moral Neighbourhood Links), Yuhua Neighbourhood Link, Henderson Senior Citizens' Home, NTUC Eldercare Co-op Ltd, Thong Kheng Seniors Activity Centre (Queenstown Centre), and Redhill Moral Seniors Activity Centre.*

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Funding Information *The study was supported by research grants from the Agency for Science Technology and Research (A*STAR) Biomedical Research Council (BMRC) [Grant: 08/1/21/19/567] and from the National Medical Research Council [Grant: NMRC/1108/2007].*

Compliance with Ethical Standards:

Informed consent was obtained, and the study was approved by an institutional review board.

Conflict of Interest: *The authors declare that they do not have a conflict of interest.*

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