

APPENDIX A. SEARCH STRATEGY

MEDLINE (Ovid) through May 2016

- 1 (life adj expectancy).m_titl.
- 2 (survival or mortality or death).m_titl.
- 3 1 or 2
- 4 (calculat\$ or instrument\$ or index or indice\$ or model\$ or tool\$ or prognosis or risk or predict\$ or estimat\$).m_titl.
- 5 3 and 4
- 6 (valid\$ or calibrat\$ or compar\$).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
- 7 5 and 6
- 8 limit 5 to (english language and humans and yr="2011 -Current" and ("middle-aged (45 plus years)" or "all aged (65 and over)" or "aged (80 and over)"))
- 9 limit 7 to (english language and humans and yr="2011 -Current" and ("middle-aged (45 plus years)" or "all aged (65 and over)" or "aged (80 and over)"))
- 10 limit 8 to (clinical trial or comparative study or controlled clinical trial or evaluation studies or meta analysis or observational study or pragmatic clinical trial or randomized controlled trial or systematic reviews or validation studies)
- 11 limit 9 to (clinical trial or comparative study or controlled clinical trial or evaluation studies or meta analysis or observational study or pragmatic clinical trial or randomized controlled trial or systematic reviews or validation studies)
- 12 8 NOT 9

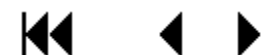
APPENDIX B. PEER REVIEW COMMENTS/AUTHOR RESPONSES

Question	Reviewer Comment	Author Response
Are the objectives, scope, and methods for this review clearly described?	Yes	Thank you
	Yes	
	Yes	
Is there any indication of bias in our synthesis of the evidence?	No	Thank you
	No	
	No	
Are there any <u>published</u> or <u>unpublished</u> studies that we may have overlooked?	No	No response needed
	Yes - 1. Cruz et al JAMA research letter 2012 Predicting 10 year mortality in older adults. Granted, a research letter not a full research publication, but a high impact journal and an important update to the prior 4 year mortality index. 2. Lee et al PLOS one 2014 Individualizing life expectancy estimates using Gompertz... The conclusion of the report discuss lack of prognostic models that estimate life expectancy (time to death) rather than mortality risk (risk of death over a given time frame). This study estimates life expectancy, using the Lee index mentioned in 1 above. 3. Schonberg M JAGS 2011 External Validation of an index to predict 9 year...Granted, included in our review by Yourman, published in 2011 so I believe should have been included.	We have reviewed the suggested studies. Although the Cruz and Schoenborn prognostic models are potentially useful, these reports were not included in this review because the mortality prediction models are based on self-reported national survey data and would require similar patient questionnaires be administered by primary care clinics. We have included the Lee et al 2014 reference so readers can see how one could model survival curves to estimate life expectancy.
	No	No response needed
Additional suggestions or comments can be provided below. If applicable, please	p. 5 line 5 - should be "insubstantial" rather than "unsubstantial" p. 5 line 10 - "quasi-validation" should probably be defined in the table	We have made the suggested change on pg 5, line 5. 'Quasi' simply means the studies were

<p>indicate the page and line numbers from the draft report.</p>	<p>on p 1 (or avoided altogether as an imprecise term).</p>	<p>not true external validation studies, however they were in a sense validation studies. We have pointed that none of the studies reviewed for KQ2 were true validation studies, and dropped 'quasi' from the Table title. We did not feel a need to define quasi in the table on page 1.</p>
	<p>Major points:</p> <ol style="list-style-type: none"> 1. As senior author of the Yourman systematic review of prognostic indices for older adults, I'm pleased that this report has been commissioned and well executed. Many of the conclusions remain the same - people just are not studying the use/usefulness of prognostic indices in clinical practice. As a key member of the eprognosis team, a free website dedicated to making prognostic models available to clinicians, I can testify that prognostic models are being used in everyday practice. Clinicians come up to me all the time, from all over the country, and say "I use eprognosis." It seems to be more the specialists that use the models rather than the primary care clinicians, as a recent study by Nancy Shoenborn in JAMA Internal Medicine 2016 suggests. 2. The conclusions are based on the time limited update between 2011 and 2016. Yet the underlying question "are there clinically useful prognostic models for VA primary care patients" need not be restricted to this time frame. Certainly, risk may change with time. But have things changed that much between, say 2000, and 2016? My guess is no, the same factors that put persons at risk in 2000 are likely to put persons at risk in 2016. Age, gender, functional limitations. We haven't cured cancer. To really address the underlying question, the VA will need to consider the accuracy and pragmatic usefulness of prior studies not included in this report. 3. Why no mention of the CAN score? This is the giant elephant in the room that VA researchers are talking about. Apparently it's calculated for veterans and hard but possible to access in the medical record. What's the evidence? How useful is it? Omission is a major limitation as it will be the first thing on many VA clinician/researcher's minds when they think VA data and prognostic index. 4. Minor points -Explain what a "quasi-validation" study means. 	<p>The Schoenborn article is now mentioned in the Introduction of the Evidence Report to support an important statement that providers often don't share long-term prognostic assessments with their patients in part due to their uncertainty.</p> <p>We agree. The VA can refer to these previous reviews, thus we focused on more recent studies.</p> <p>We had not pointed out that the 2 Wang articles cited for KQ1 and KQ2 represent the VA Care Assessment Needs (CAN) model. We have now repeatedly made this connection in the text and table footnotes.</p>



	<p>-The two studies by Austin seem to really be one study. This question comes up immediately as all data in the tables about them are essentially identical. One shouldn't have to wait for a footnote to discover one study is simply developing a point score system using the same model. Not clear if this requires a separate citation and line in the table, as it's the same index. Might be better organized if by index rather than by publication.</p>	<p>'Quasi' is used to indicate the studies were not true external validation studies, however they were in a sense validation studies. We have pointed that none of the studies reviewed for KQ2 were true validation studies, and dropped 'quasi' from the Table title. We did not feel a need to define quasi in the table on page 1.</p>
	<p>Thank you for the opportunity to review this excellent ESP.</p> <p>The authors sought to review recent life expectancy calculators for use in primary care practice. In particular, they looked for new calculators published since 2011, external validations of those new calculators, and clinical applications of the calculators.</p> <p>Their research questions were specific, their methods were clear, and the document is well written. Their primary findings are also clear. There have been multiple calculators created, including one in VA. These calculators have had quite good testing characteristics generally, but have not been validated in external samples and have not had any study in clinical practice.</p> <p>The tables and figures were clear and will be a valuable summary for anyone doing this type of work.</p> <p>Their findings drive home what I think will be a central issue in health services and implementation science for the next decade or more. This is that Big Data will make risk prediction reasonably easy and accurate, but having prediction tools does not tell us what predictions are useful, how do we use them, and how do we integrate tools into the system to be useful to patients, providers, and healthcare leaders. These questions will likely be very important, but they've shown few people seem to be asking them.</p> <p>At the broadest level, I feel like the questions were very well formulated, but the underlying problems the questions were trying to solve were somewhat less so. Exactly how is this information going to be used inside or outside VA? If this question were answered more explicitly, some of their other choices may have been slightly different.</p>	<p>Thank you.</p> <p>As pointed out in the text, the current VA model known as the CAN score doesn't predict all-cause model and wasn't developed to estimate life expectancy or evaluated as such, but could be adapted</p>



	<p>For example, they found a good study by Wang (the senior author of which is an operational partner on this project) that used VA data. If VA wants to implement a life expectancy calculator, shouldn't they just use this tool? Are there things other tools did that a modified VA-based tool would want to do?</p> <p>For KQ2 and KQ3, they were unlikely to find validation studies since the studies included were already recent. Here they could have also used any study in Yourman's 2011 JAMA paper, which was one of the inspirations for this study. The team that wrote the JAMA paper has a website, eprognosis.org, that does some of the things that KQ3 wanted to address, though I don't know if they have validated it in any way. While adding older studies may have been reasonably out of scope for this project, it could have found some interesting information.</p> <p>Their search strategy was reasonable. They only used Medline, which can miss citations. Because this is not a meta-analysis, missing citations is not a terribly big deal, so I find this reasonable.</p> <p>While I know this isn't the primary point of an ESP, I do wish the authors expanded their interpretive Research Gaps section a little. I was curious what they felt about each of the different scores, how they differ, and what future developers or users could learn from them.</p> <p>A few small typos P8 "appropriate to to" P12 Moons2014 should be inside the period.</p>	<p>to do so.</p> <p>If an effort to guide the VA, we tried to focus on what the good performing models had in common, and what further evaluation would be needed to support their use.</p> <p>The P8 typo has been corrected and all references have been converted to superscript format.</p>
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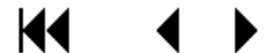
APPENDIX C. EVIDENCE TABLES

Table 1. Study Characteristics

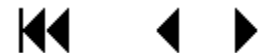
Author, Year Country, Region Study Dates	Source of Data ^a	Participants	Participant Description	Mortality Outcome	Risk of Bias
Aggregated Diagnosis Groups (not VHA)					
Austin, 2011¹⁵ (General Adult Population) Canada, Ontario 2007-2008	Administrative healthcare databases in Ontario, Canada -Registered Persons Database (RPDB) -Discharge Abstract Database -Ontario Health Insurance Plan physician billing database -Ontario Mental Health Reporting System	Inclusion criteria: all persons in RPDB alive on their birthday in 2007 Exclusion criteria: age <20, age >100 Recruitment method: N/A	N=10,498,413 Age (years): 46 (median) Gender (% male): 49 Race: NR Predictors: Aggregated Diagnosis Groups [ADGs] with largest adjusted odds ratios; all OR>1.5 a) Psychosocial: recurrent or persistent, unstable (23.4%) b) Malignancy (5.8%) c) Chronic medical: unstable (17.1%) d) Time limited: major – primary infections (7.4%) e) Time limited: major (4.5%) f) Likely to recur: progressive (2.4%)	Definition: mortality within 365 days of index date (birthday in 2007) Measurement method: from RPDB (linked by encrypted health number) Duration of follow-up: 365 days Number of deaths: 85,007 (0.8%)	Predictor definition/measurement same for deceased/survivors: Yes Outcome definition/measurement same for deceased/survivors: Yes Outcome assessed independent of predictors (eg, blinded): Yes Incomplete follow-up or missing predictor data (% , handling of): NR Method of validation: Assessed over fitting by bootstrap methods

Author, Year Country, Region Study Dates	Source of Data ^a	Participants	Participant Description	Mortality Outcome	Risk of Bias
<p>Austin, 2011¹⁴ (General Adult Population) Canada, Ontario 2007-2008</p>	<p>Administrative healthcare databases in Ontario, Canada -Registered Persons Database (RPDB) -Discharge Abstract Database -Ontario Health Insurance Plan physician billing database -Ontario Mental Health Reporting System</p>	<p>Inclusion criteria: all persons in RPDB alive on their birthday in 2007 Exclusion criteria: age <20, age >100 Recruitment method: N/A</p>	<p>N=10,498,413 Age (years): 46 (median) Gender (% male): 49 Race: NR Subgroup of 395,009 residing in rural areas Predictors: Aggregated Diagnosis Groups [ADGs] with largest adjusted odds ratios; all OR>1.5 a) Psychosocial: recurrent or persistent, unstable (23.4%) b) Malignancy (5.8%) c) Chronic medical: unstable (17.1%) d) Time limited: major – primary infections (7.4%) e) Time limited: major (4.5%) f) Likely to recur: progressive (2.4%)</p>	<p>Definition: mortality within 365 days of index date (birthday in 2007) Measurement method: from RPDB (linked by encrypted health number) Duration of follow-up: 365 days Number of deaths: 85,007 (0.8%) Rural subgroup: 4,464 (1.1%)</p>	<p>Predictor definition/measurement same for deceased/survivors: Yes Outcome definition/measurement same for deceased/survivors: Yes Outcome assessed independent of predictors (eg, blinded): Yes Incomplete follow-up or missing predictor data (% handling of): NR Method of validation: Assessed over fitting by bootstrap methods</p>

Author, Year Country, Region Study Dates	Source of Data ^a	Participants	Participant Description	Mortality Outcome	Risk of Bias
<p>Austin, 2012¹³ (Adult Population with Schizophrenia) Canada, Ontario 2007-2008</p>	<p>Administrative healthcare databases in Ontario, Canada -Registered Persons Database (RPDB) -Discharge Abstract Database -Ontario Health Insurance Plan physician billing database -Ontario Mental Health Reporting System</p>	<p>Inclusion criteria: all persons in RPDB alive on 1/1/ 2007 that had previous diagnosis of schizophrenia (295.x in ICD-9 or F20/F25 in ICD-10) Exclusion criteria: age <20, age >100 Recruitment method: N/A</p>	<p>N=94,466 Age (years): 47 (median) Gender (% male): 46 Race: NR Predictors: Aggregated Diagnosis Groups [ADGs] with largest adjusted odds ratios; all OR>1.5 a) Psychosocial: recurrent or persistent, unstable (71%) b) Time limited: major – primary infections (12%) c) Malignancy (4.9%) d) Likely to recur progressive (3.9%)</p>	<p>Definition: mortality within 365 days of index date (1/1/ 2007) Measurement method: from RPDB (linked by encrypted health number) Duration of follow-up: 365 days Number of deaths: 1915 (2.0%)</p>	<p>Predictor definition/measurement same for deceased/ survivors: Yes Outcome definition/measurement same for deceased/ survivors: Yes Outcome assessed independent of predictors (eg, blinded): Yes Incomplete follow-up or missing predictor data (% handling of): NR Method of validation: Application of previously developed model for general adult population</p>
<p>Charlson and/or Elixhauser Comorbidities</p>					



Author, Year Country, Region Study Dates	Source of Data ^a	Participants	Participant Description	Mortality Outcome	Risk of Bias
<p>Gagne, 2011⁷ (Medicare enrollees, age ≥ 65)</p> <p>Pennsylvania, New Jersey, United States</p> <p>2004-2005</p>	<p>Inpatient & outpatient Medicare claims data & pharmacy databases in Pennsylvania and New Jersey for low-income Medicare enrollees who don't qualify for Medicaid</p> <p>Development cohort: Pharmacy Assistance Contract for Elderly (PACE) Pennsylvania</p> <p>Validation cohort: Pharmacy Assistance for the Aged and Disabled) PAAD) New Jersey</p>	<p>Inclusion criteria: Medicare enrollees with continuous drug coverage through PACE (development cohort) or PAAD (validation cohort) and at least one pharmacy claim during the 4 months before baseline year and survived the baseline year</p>	<p>NPA=120,679 Age 80 Gender (% female): 83 Race: NR</p> <p>NNJ=123,855 Age 79 Gender (% female): 77 Race: NR</p> <p>Predictors: Weighted comorbidity score calculated for 37 Romano/Charlson or vanWalraven/Elixhauser ICD-9 comorbidity classifications, age and gender; key predictors</p> <p>Heart failure:23% Dementia: 9.0% Renal failure: 6.9% Metastatic cancer 1.8% Weight loss: 1.5%</p>	<p>Definition: 1 year mortality (also had 30,90,180 day mortality)</p> <p>Measurement method: NR</p> <p>Duration of follow-up: up to 1 year</p> <p>Number of deaths: Development cohort N=10,769 (8.9%)</p> <p>Validation cohort N=9,230 (7.5%)</p>	<p>Predictor definition/measurement same for deceased/survivors: Yes</p> <p>Outcome definition/measurement same for deceased/survivors: NR</p> <p>Outcome assessed independent of predictors (eg, blinded): NR</p> <p>Incomplete follow-up or missing predictor data (% handling of): NR</p> <p>Method of validation: External sample</p>



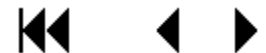
Author, Year Country, Region Study Dates	Source of Data^a	Participants	Participant Description	Mortality Outcome	Risk of Bias
Quail, 2011¹⁶ Canada, Saskatchewan (provincial health plan) Fiscal years 2001-2002	Provincial Discharge Abstract Database (ICD-9 & 10 codes), Medical Services Database (ICD-9 codes), Population Registry, & Vital Statistics Registry Income from residence in census region	Inclusion criteria: residents age 20 and older with uninterrupted coverage in year (comorbidities) were assessed (FY2001) Exclusion criteria: federal employees, inmates, & First Nation people	General Population/Age > 65 years N= 662,423/137,700 Age: 48/75 Female 51%/57% Race: NR Charlson score 0.3/0.7 Elixhauser Heart failure: 2.0/8.1 Metastatic cancer:0.8/2.4 Renal failure: 0.6/1.8 Weight loss: 0.1/0.2 Pulmonary disease: 8.4/12.7	1-year mortality General Population/Age > 65 years 1.3%/ 5.1%	Predictor definition/measurement same for deceased/survivors: Yes Outcome definition/measurement same for deceased/survivors: Yes Outcome assessed independent of predictors (eg, blinded): Yes Incomplete follow-up or missing predictor data (% handling of): missing income imputed Method of validation: external sample & time

Author, Year Country, Region Study Dates	Source of Data ^a	Participants	Participant Description	Mortality Outcome	Risk of Bias
<p>Tan 2013⁹ United States 1999-2009</p>	<p>5% random sample of Medicare enrollees in 2000</p> <p>Medicare enrollment files, carrier files, outpatient statistical analysis files (outpatient visits), Medicare provider analysis and review files (hospital stays)</p>	<p>Inclusion criteria: 66-90 years in 2000, full coverage in Medicare Parts A (hospital care) and B (physician and outpatient services) in 1999, and not in Medicare Advantage HMO coverage at any time in 1999</p>	<p>N=1,137,311 Medicare beneficiaries Women: 60% Age (SD) 76 (6.5) Men: 40% Age (SD) 75 (6.1)</p> <p>Prevalence of comorbidities with > 80% 10-year mortality rates in women/men (%) Heart failure: 8.2/8.8 Pulmonary circulation disease: 0.9/0.8 Metastatic cancer: 0.8/0.9 Renal failure: 1.3/2.0 Weight loss: 1.5/1.2 Neurological disorders: 2.9/3.3 Substance abuse: 0.2/0.5 Dementia: 2.6/1.7 Psychoses: 1.3/0.9</p>	<p>1-, 5-, 7-, 10-year mortality stratified by sex</p> <p>Measurement method: Medicare enrollment</p> <p>10-year mortality Women: 51% Men: 57%</p>	<p>Predictor definition/measurement same for deceased/survivors: Yes</p> <p>Outcome definition/measurement same for deceased/survivors: Yes</p> <p>Outcome assessed independent of predictors (eg, blinded): Yes</p> <p>Incomplete follow-up or missing predictor data (% handling of): NR</p> <p>Method of validation: random split sample</p>
<p>Electronic Medical Records</p>					

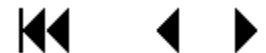
Author, Year Country, Region Study Dates	Source of Data ^a	Participants	Participant Description	Mortality Outcome	Risk of Bias
<p>Mathias, 2013¹⁰ US, Chicago 2003-2008</p>	<p>EHRs (EpicCare) from a large, academic, multispecialty group practice and affiliated hospitals</p> <p>National Center for Health Statistics National Death Index (NDI) for 2003-2008</p>	<p>Inclusion criteria: outpatients, age 50 and older, at least 1 visit to the group practice during 2003</p> <p>Exclusion criteria: none reported</p> <p>Recruitment method: N/A</p>	<p>N=7,463 Age (years): 62 (mean) Gender (% male): 40 Race: White 51%; Black 24%; Hispanic 5%; Asian 3%; Other/Unknown 8%</p> <p>-Predictors: Count (mean[SD]) 2.5 (2.0) Present in >10% a) Hypertension 52% b) Any vascular disease 17% c) Diabetes 17% d) Any cancer 15% e) Tobacco use 11%</p> <p>-Vital signs: BP 131/79</p> <p>-Lab results: Albumin (g/dl) 3.7 (0.4) Creatinine (mg/dl) 1.1 (0.8)</p> <p>-Outpatient medications Digoxin 3% Loop diuretic 8%</p> <p>-Utilization PCP visits 1.2 (1.8) Hospitalizations in past year 0.3 (1.6); 1-2 years prior 0.2 (0.7)</p>	<p>Definition: death within 5 years of last outpatient encounter in 2003</p> <p>Duration of follow-up: 5 years</p> <p>Number of deaths: 838 (11.2%)</p>	<p>Predictor definition/measurement same for deceased/survivors: Yes</p> <p>Outcome definition/measurement same for deceased/survivors: Yes</p> <p>Outcome assessed independent of predictors (eg, blinded): Yes</p> <p>Incomplete follow-up or missing predictor data (% handling of): NR</p> <p>Method of validation: 10 fold cross validation</p>
<p>Data from Other Studies</p>					



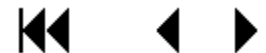
Author, Year Country, Region Study Dates	Source of Data ^a	Participants	Participant Description	Mortality Outcome	Risk of Bias
<p>Ogata, 2013¹⁷ Japan; Tanushimaru, Uka 1999-2009</p>	<p>Baseline data collected for other study (one site was part of Seven Countries Study in Japan); reportedly similar to general population of Japan</p> <p>Survival or death from review of obituaries, medical records, death certificates, hospital charts, and interviews with primary care physicians, families, and other witnesses</p>	<p>Inclusion criteria: residents age >40 years, gave informed consent</p> <p>Exclusion criteria: missing data or lost to follow-up</p> <p>Recruitment method: "invited"</p>	<p>N=2,021 Age (years): 63 (mean) Gender (% male): 41 Race: NR (Japanese study)</p> <p>Predictors: 6 established cardiovascular risk factors Age (see above) Sex (see above) Systolic blood pressure: 134 mmHg HbA1c: 5.6% Total cholesterol: 200 mg/dl Current smoker 16%</p>	<p>Definition: survival or death within 10 years of baseline testing</p> <p>Duration of follow-up: 10 years</p> <p>Number of deaths: -Training sample: 204/1486 (14%) -Test sample 1: 49/365 (13%) -Test sample 2: 48/170 (28%)</p>	<p>Predictor definition/measurement same for deceased/survivors: Yes</p> <p>Outcome definition/measurement same for deceased/survivors: Yes</p> <p>Outcome assessed independent of predictors (eg, blinded): Unclear</p> <p>Incomplete follow-up or missing predictor data: 3.6% missing data/lost at site 1; 80% excluded at site 2 due to missing data/lost or < 10 years follow-up</p> <p>Method of validation: a) split sample (random) from first site and b) second site only served as validation site</p>
<p>Veterans Health Administration</p>					



Author, Year Country, Region Study Dates	Source of Data ^a	Participants	Participant Description	Mortality Outcome	Risk of Bias
<p>Stefos, 2012⁸ US (VHA) Fiscal year 2007-2008</p>	<p>VA electronic administrative data files</p>	<p>Inclusion criteria: all patients who received care at a VA hospital in fiscal year 2008 that were assigned to a primary care provider</p> <p>Exclusion criteria: none reported</p> <p>Recruitment methods: N/A</p>	<p>N=4,774,000 Age: 62 Gender: 94% male Race: 55% white</p> <p>Key Predictors Categorizations of ICD-9 diagnosis codes from any type of encounter into Hierarchical Coexisting Conditions (HCC) using Diagnostic Cost Group (DCG) software (eg metastatic cancer, end-stage liver disease, respiratory arrest, coma of brain compression/anoxia) -Cancer: 17% -Chronic obstructive pulmonary disease: 10% -VA chronic disease registry: 4% -VA priority status (eg, catastrophically disabled (4%), low income or Medicaid (29%))</p>	<p>Definition: death from any cause within 12 months of last FY2008 VA clinical contact</p> <p>Measurement method: not clear</p> <p>Duration of follow-up: 1 year</p> <p>Number of deaths: 262,260 (5.5%)</p>	<p>Predictor definition/measurement same for deceased/survivors: Yes</p> <p>Outcome definition/measurement same for deceased/survivors: Yes</p> <p>Outcome assessed independent of predictors (eg, blinded): Yes (database)</p> <p>Incomplete follow-up or missing predictor data: NR</p> <p>Method of validation: Copas test for overfitting (repeated, split sample, cross validation design)</p>



Author, Year Country, Region Study Dates	Source of Data ^a	Participants	Participant Description	Mortality Outcome	Risk of Bias
<p>Wang, 2013¹² (VHA primary care population for FY 2011)</p>	<p>Predictors from VHA electronic National Patient Care Database & Corporate Data Warehouse including demographics, diagnoses from inpatient & outpatient records, medications, vital signs, laboratory tests & healthcare utilization</p> <p>VHA Databases Death: VHA's vital status file</p>	<p>Inclusion criteria: All patients enrolled and assigned to a primary care provider within VHA on October 1, 2010 (the index date)</p> <p>Exclusion criteria: Patients with no recorded use of any health service during the prior year (5%); patients who were hospitalized, admitted to a hospital, or died on October 1, 2010</p>	<p>N=4,598,408 Age: mean 64 years range 18-110 Gender (male): 94% Race: NR</p> <p>Predictors (select): Charlson comorbidities & hierarchial condition categories Heart failure: 5.1% Renal failure: 6.3% Chronic pulmonary disease: 11% Metastatic cancer: 1.3% Substance abuse: 6.1%</p> <p>Heart rate > 100: 2.9% Respiration rate > 20: 2.4% Albumin < 3.5: 4.1%</p>	<p>Definition: death without hospitalization within 90 days or 1 year</p> <p>Measurement method: VHA Vital Status File</p> <p>Duration of follow-up: 1 year</p> <p>Number of deaths: 32,147 (0.7%) in 90 days 120,192 (2.8%) in 1 year</p>	<p>Predictor definition/measurement same for deceased/survivors: Yes</p> <p>Outcome definition/measurement same for deceased/survivors: Yes</p> <p>Outcome assessed independent of predictors (eg, blinded): Yes</p> <p>Incomplete follow-up or missing predictor data (% handling of): Yes</p> <p>Method of validation: randomly split sample</p>



Author, Year Country, Region Study Dates	Source of Data ^a	Participants	Participant Description	Mortality Outcome	Risk of Bias
Wang, 2012¹¹ (VHA heart failure population from 2009)	-Predictors from VHA electronic National Patient Care Database & Corporate Data Warehouse including demographics, diagnoses from inpatient & outpatient records, medications, vital signs, laboratory tests & healthcare utilization VHA Databases -Death: VHA's vital status file	Inclusion criteria: Heart failure diagnosis within VHA in year prior to June 1, 2009, the index date Exclusion criteria: NR	N=198,640 Age: mean 73 years Gender (male): 98% Race: NR Predictors (select): Charlson comorbidities & hierarchial condition categories Heart failure: 100% Renal failure: 25% Chronic pulmonary disease: 31% Metastatic cancer: 2.7% Dementia: 8.3% Respiration rate > 20: 6.7% Albumin < 2.5: 1.3% Heart rate > 85: 16%	Definition: death without hospitalization within 30 days or 1 year Measurement method: VHA Vital Status File Duration of follow-up: 1 year Deaths: 1,788 (0.9%) in 30 days, 14,103 (7.1%) in 1 year	Predictor definition/measurement same for deceased/survivors: Yes Outcome definition/measurement same for deceased/survivors: Yes Outcome assessed independent of predictors (eg, blinded): Yes Incomplete follow-up or missing predictor data (% handling of): Yes Method of validation: randomly split sample

^a eg, cohort, clinical trial participants, registry

^b Lee SJ et al. Development and validation of a prognostic index for 4-year mortality in older adults. JAMA. 2006;295(7):801-808.

BP = blood pressure; EHR = electronic health record; N/A = not applicable; NR = not reported; PCP = primary care provider; VA = Veterans Affairs; VHA = Veterans Health Administration

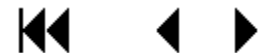


Table 2. Model Characteristics and Performance

Author, Year	Intended Use	Predictors ^a Timing of Predictor Assessment ^b	Modelling Method Method for Selection of Predictors for Inclusion	Mortality Risk Groups	Predictive Performance ^c
Aggregated Diagnosis Groups (not VHA)					
Austin 2011 ¹⁵ (General Adult Population)	Risk adjustment	<p><i>Demographic:</i> age, sex</p> <p><i>Patient History:</i> diagnoses associated with hospital admissions (ICD-10) and physician billing claims (ICD-9) from past 2 years matched with 32 Aggregated Diagnosis Groups (ADGs) (requires proprietary software license)</p> <p>Timing: Previous 2 years including index date</p>	<p>Logistic regression</p> <p>Backwards elimination- final model age, sex and 28 ADG's</p>	None pre-specified	<p>Predicted probabilities Range 0.00 to 0.90</p> <p>C-statistic <i>Validation cohort:</i> 0.92 Age ≥ 65: 0.81 Age < 65: 0.82</p> <p>Calibration Differences between observed and predicted mortality < 1% in all 100 centiles of predicted risk except top 3; biggest difference 3%</p> <p>Calibration plot Intercept 0.007 Slope 0.996</p>

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Austin 2011 ¹⁴ (General Adult Population)	Risk adjustment	<p><i>Demographic:</i> age, sex</p> <p><i>Patient History:</i> diagnoses associated with hospital admissions (ICD-10) and physician billing claims (ICD-9) from past 2 years matched with 32 ADGs (requires proprietary software license)</p> <p>Timing: Previous 2 years including index date</p>	<p>Mortality Risk Score (MRS) derived using regression coefficients of above final model including age and sex.</p> <p>Weighted ADG Score plus age and sex</p> <p>One- rather than 2-year look-back</p>	None pre-specified	<p>Predicted probabilities Range 0.00 to 0.90</p> <p>C-statistics <i>Validation cohort:</i> MRS: 0.92 for 1- and 2-year look-back period Rural subgroup: 0.90 ADG: 0.91 for 1- and 2-year look-back period</p> <p>Calibration Differences between observed and predicted mortality ~ 1% in 20 groups of predicted risk for both MRS and ADG</p> <p>Individual predicted probability of dying within 1 year increasingly under estimates observed mortality as predicted probabilities exceed ~0.2</p> <p>Calibration plots MRS: Intercept 0.007 Slope 0.996 Rural subgroup: Intercept 0.142 Slope 0.960 ADG: Intercept 0.006 Slope 0.996</p>



Author, Year	Intended Use	Predictors ^a Timing of Predictor Assessment ^b	Modelling Method Method for Selection of Predictors for Inclusion	Mortality Risk Groups	Predictive Performance ^c
<p>Austin, 2012¹³ (Adult population with schizophrenia) Canada, Ontario 2007-2008</p>	<p>Risk adjustment</p>	<p>Application of previously developed model for adult general population (See Austin 2011 a)</p>	<p>Application of previously developed model for adult general population (see Austin 2011 a) to subpopulation with schizophrenia</p>	<p>None pre-specified</p>	<p>Predicted probabilities NR for adult general population model C-statistic: 0.84 Calibration plot Intercept 0.356 Slope 0.0.805</p>
<p>Charlson and/or Elixhauser Comorbidities</p>					
<p>Gagne, 2011⁷ (Medicare enrollees, age ≥ 65) Pennsylvania, New Jersey, United States 2004-2005</p>	<p>Provide comorbidity score for risk adjustment</p>	<p><i>Demographic:</i> age, sex <i>Comorbidities:</i> ICD-9 diagnosis codes Recorded during a baseline year Jan 1, 2004 to Dec 31, 2004</p>	<p>Logistic regression to assign weights for 37 unique comorbidities; no variable selection Final weighted model 20 comorbidities with nonzero weights plus age, sex Comorbidity scores in validation cohort median: 1 interquartile range: 2 range: -2 to 18 zero: 27%</p>	<p>None pre-specified</p>	<p>Predicted probabilities; individual range NR; lower decile ~3% upper decile ~55% C-statistic <i>Validation cohort:</i> NJ 1 year 0.79 30 day 0.86 90 day 0.82 180 day 0.81 Calibration curve under predicted by ~ 3% in 5 % 6th deciles with 20 -25% mortality, over predicted by ~ 10% in 10th decile with ~ 45% mortality, otherwise observed and predicted mortality % within ~1%</p>



Author, Year	Intended Use	Predictors ^a Timing of Predictor Assessment ^b	Modelling Method Method for Selection of Predictors for Inclusion	Mortality Risk Groups	Predictive Performance ^c
<p>Quail, 2011¹⁶ Canada, Saskatchewan (provincial health plan) Fiscal years 2001-2002</p>	<p>Population risk-adjustment</p>	<p><i>Demographic:</i> patient: age, gender, income, & region <i>Comorbidities:</i> 17 in weighted Charlson score or 31 separate Elixhauser comorbidities based on diagnoses from baseline year (FY2001) from inpatient & outpatient records</p>	<p>Logistic regression model including age, sex, income, region plus Charlson comorbidity score or individual Elixhauser comorbidities fit to the data; no statistical variable selection</p>	<p>None pre-specified</p>	<p>Predicted probabilities: NR C-statistic general population/age > 65 years: Carlson model: 0.90/0.78 Elixhauser model: 0.91/0.80 Calibration: NR Prediction error (Brier score – mean squared difference between individual predicted probabilities and death =1 or survival=0) Carlson model: 0.01/0.04 Elixhauser model: 0.01/0.04</p>

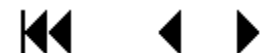
Author, Year	Intended Use	Predictors ^a Timing of Predictor Assessment ^b	Modelling Method Method for Selection of Predictors for Inclusion	Mortality Risk Groups	Predictive Performance ^c
<p>Tan 2013⁹ United States 1999-2009</p>	<p>Healthcare decision-making (expected to live long enough to benefit from a service such as cancer screening)</p>	<p><i>Demographic:</i> age, sex <i>Comorbidities:</i> 31 from Elixhauser, 17 from Charlson based on Quan coding algorithm of ICD-9 codes; appearing on 2 or more claims at least 30 days apart <i>Utilization:</i> number of hospital admissions, number of outpatient visits in previous 12 months (1999)</p>	<p>Variable selection: Series of logistic regression models with varying combinations of predictors; final model chosen based on best C-statistic, Akaike information criterion, and percent correctly classified Final model: Age + 31 individual Elixhauser comorbidities stratified by sex Sex-specific Cox proportional hazards models to generate K-M curves using median survival time as proxy of life expectancy</p>	<p>None prespecified; Predicted risk of death within 10 years categorized as <25%, 25-49%, 50-74%, and >75% by sex 5- and 10-year life expectancy often used for decisions about cancer screening</p>	<p>Predicted 10-year mortality: NR C-statistic Women/Men 10 years: 0.79/0.77 5 years: 0.78/0.76 1 year: 0.79/0.77 1-, 5-, and 10-year observed mortality fell within quartiles of predicted probabilities except 1-year observed mortality was less than predicted for 50% to 75% & ≥ 75% quartiles of risk for both women & men Positive predictive value (observed mortality by predicted life expectancy (LE using median survival time as proxy) was similar for women & men) LE < 10 years: 75% LE < 5 years: 69% LE < 1 year: 48%</p>
<p>Electronic Medical Records</p>					



Author, Year	Intended Use	Predictors ^a Timing of Predictor Assessment ^b	Modelling Method Method for Selection of Predictors for Inclusion	Mortality Risk Groups	Predictive Performance ^c
<p>Mathias, 2013¹⁰</p>	<p>Healthcare decision-making (eg, expected to live long enough to benefit from a service such as cancer screening)</p>	<p><i>Demographic:</i> 11 attributes; age, sex, marital status, race/ethnicity, socioeconomic status</p> <p><i>Comorbidities:</i> 117 attributes based on ICD-9 codes, current procedural terminology codes or substance use statuses; codes extracted from encounter diagnoses, past medical history, past surgical history, social history, and problem list; additional 26 attributes for counts of encounters related to frequent exacerbations of conditions or active diagnoses</p> <p><i>Vital signs:</i> 24 attributes of heart rate, SBP, DBP, pulse pressure</p> <p><i>Medications:</i> 664 medication attributes classified using VA codes; used medication list at index visit or medications ordered in year prior; added focus on some classes of medications</p> <p><i>Laboratory:</i> 120 laboratory attributes based on 24 tests</p> <p><i>Utilization:</i> 50 attributes; discharge status, hospital admissions, ED visits, home health referrals, provider visits</p> <p>Timing: year prior to index visit except home health referrals and provider visits included 1-2 years prior</p>	<p>Rotation forest ensembling technique with alternating decision tree</p> <p>Correlation Feature Selection (CFS) and manual review/reduction used to reduce number of attributes (eliminate low face validity, redundant, problematic reliability); information gain metric</p> <p>Final model: 24 predictors</p>	<p>Predicted risk of death within 5 years < 50% or ≥ 50%</p> <p>5-year life expectancy often used for decisions about cancer screening</p> <p>Predicted risk of 50% equivalent to median life expectancy of 5 years</p>	<p>Predicted Mortality Lowest risk decile 3.6% Highest risk decile 92.5%</p> <p>C-statistic 0.86 (0.85, 0.87)</p> <p>Sensitivity: 31% Specificity: 98% Positive predictive value: 63% Negative predictive value: 92% Correct predictions: 90%</p> <p>Calibration Difference between observed and predicted mortality <3% across all deciles of predicted risk</p>
<p>Data from Other Studies</p>					



Author, Year	Intended Use	Predictors ^a Timing of Predictor Assessment ^b	Modelling Method Method for Selection of Predictors for Inclusion	Mortality Risk Groups	Predictive Performance ^c																						
<p>Ogata, 2013¹⁷ Japan; Tanushimaru, Uka 1999-2009</p>	<p>Predict if individual will live or die within 10 years using only cardiovascular risk factors</p>	<p><i>Demographic:</i> Age, gender, smoking status <i>Vital signs:</i> SBP <i>Laboratory:</i> HbA1c, total cholesterol</p>	<p>Supervised statistical pattern recognition with a minimum distance classifier to derive regression coefficients for 6 predictors preselected by authors Coefficient for total cholesterol is negative; opposite of Western cohorts</p>	<p>Live or die within 10 years</p>	<p>Predicted to die in 10 years in validation samples Site 1: 36/365 (9.9%) Site 2: 35/170 (20.6%) C-statistic for predicting survival and death Site 1: 0.83 Site 2: 0.85 Calibration: difference (in % dead) between observed and expected Site 1: 3.5% Site 2: 7.6%</p>																						
Veterans Health Administration																											
<p>Stefos, 2012⁸ US (VHA) Fiscal year 2007-2008</p>	<p>Estimate adjusted mortality statistics for VA hospital-based patient populations</p>	<p>Age, gender, VA priority status, marital status, race, insurance (<i>ie</i>, not insured by public or private insurance plan) Average driving time to 3 VA institutions (closest providing primary care, closest providing secondary/intermediate care, closest providing tertiary/specialty care) 139 Hierarchical Coexisting Conditions (HCCs) Membership in a VA Registry Program (special emphasis programs for specific chronic conditions) Timing of Assessment: VA administrative data from FY 2008</p>	<p>Hierarchical generalized linear mixed model with random effect for hospital population 2-stage estimation with insignificant ($P > .10$) covariates eliminated after first stage; final model included 14 demographic and 139 morbidity HCC measures</p>	<p>None pre-specified</p>	<p>Range of predictive probabilities 2.5% in lowest decile to 94% in highest decile C-statistic: 0.86 Calibration: Observed:Predicted (O/P) - number of deaths by risk decile</p> <table border="1" data-bbox="1638 1120 1953 1461"> <thead> <tr> <th>Predicted</th> <th>O/P ratio</th> </tr> </thead> <tbody> <tr><td>2.5%</td><td>0.94</td></tr> <tr><td>13%</td><td>1.12</td></tr> <tr><td>24%</td><td>1.12</td></tr> <tr><td>34%</td><td>1.06</td></tr> <tr><td>45%</td><td>0.98</td></tr> <tr><td>55%</td><td>0.95</td></tr> <tr><td>65%</td><td>0.91</td></tr> <tr><td>75%</td><td>0.87</td></tr> <tr><td>85%</td><td>0.87</td></tr> <tr><td>94%</td><td>0.86</td></tr> </tbody> </table>	Predicted	O/P ratio	2.5%	0.94	13%	1.12	24%	1.12	34%	1.06	45%	0.98	55%	0.95	65%	0.91	75%	0.87	85%	0.87	94%	0.86
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Author, Year	Intended Use	Predictors ^a Timing of Predictor Assessment ^b	Modelling Method Method for Selection of Predictors for Inclusion	Mortality Risk Groups	Predictive Performance ^c
<p>Wang, 2013¹² (VHA primary care population from FY 2011)</p>	<p>Identify high-risk (of hospitalization or death without hospitalization) primary care patients who might benefit from care coordination and special management programs such as intensive case management, telehealth, home care, specialized clinics, and palliative care</p>	<p><i>Demographic:</i> age, sex, marital status, VHA enrollment priority</p> <p><i>Medical conditions:</i> Deyo-Charlson index (ICD-9) & hierarchical condition classification of diagnoses</p> <p><i>Vital signs:</i> blood pressure, heart rate, respiratory rate, BMI</p> <p><i>Prior year use of VHA health services:</i> indicators for categories of numbers & types of outpatient visits, ER visits, and hospitalizations over the past year and past month</p> <p><i>Medications dispensed:</i> number of refills, 31 types of medications</p> <p><i>Laboratory results:</i> Albumin, blood urea nitrogen, creatinine, potassium, white blood cell count</p>	<p>Multinomial logistic regression with 3 mutually exclusive categories: hospitalization, death without hospitalization, and neither event. Separate models for 90-day and 1-year endpoints.</p> <p>Backwards elimination followed by forward selection including select 2-way interactions.</p> <p>Final models contained up to 190 coefficients (numerous categorical variables had multiple coefficients)</p>	<p>None pre-specified</p>	<p>Predicted probabilities 90-day: lower decile <0.1% to upper decile ~4% 1-year: lower decile <0.1% to upper decile ~14% 1-year: age > 65 years: lower 5% <0.1%, upper 5% ~27%</p> <p><i>C-statistic</i> 90-day death: 0.86 1 year death: 0.85 1 year death >65 years: 0.80</p> <p><i>Calibration plots (Cox)</i> 90-day death: Intercept: -0.016 Slope: 0.999 1 year death: Intercept: 0.001 Slope: 1.002</p> <p>Small differences between observed and predicted in each decile of predicted probabilities; same if age > 65 years</p> <p>Observed deaths if in upper 5% of predicted probabilities of death without hospitalization 90-day: 6.2% 1-year: 19.4% 1-year age >65 years: 24.6%</p>



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<p>Wang, 2012¹¹ (VHA heart failure population from 2009)</p>	<p>Identify high-risk (of hospitalization or death without hospitalization) patients with heart failure who might benefit from care coordination and special management programs such as intensive case management, telehealth, home care, specialized clinics, and palliative care</p>	<p><i>Demographics:</i> age, sex, marital status, VHA enrollment priority</p> <p><i>Medical conditions:</i> Deyo-Charlson index (ICD-9) & hierarchical condition classification of diagnoses</p> <p><i>Vital signs:</i> blood pressure, heart rate, respiratory rate, BMI</p> <p><i>Prior year use of VHA health services:</i> indicators for categories of numbers & types of outpatient visits, ER visits, and hospitalizations over the past year and past month</p> <p><i>Medications dispensed:</i> number of refills, 31 types of medications</p> <p><i>Laboratory results:</i> Albumin, blood urea nitrogen, creatinine, potassium, white blood cell count</p>	<p>Multinomial logistic regression with 3 mutually exclusive categories: hospitalization, death without hospitalization, and neither event. Separate models for 30-day and 1-year endpoints.</p> <p>Backwards elimination followed by forward selection including select 2-way interactions such as age > 65 with medical conditions, medications & hospitalizations.</p> <p>Final models contained up to 190 coefficients (numerous categorical variables had multiple coefficients); same variables as other Wang report but regression coefficients and variable selection specific to this sample</p>	<p>None pre-specified</p>	<p>Predicted probabilities 30-day: lower decile <0.1% to upper decile ~4% 1-year: lower decile <0.8% to upper decile ~23%</p> <p><i>C-statistic</i> 30-day death: 0.80 1 year death: 0.76</p> <p><i>Calibration plots (Cox)</i> 30-day death: Intercept: -0.44% Slope: 1.000 1 year death: Intercept: -0.094 Slope: 0.96</p> <p>Differences between observed and predicted mortality % in each decile of predicted probabilities were not substantial</p> <p>Observed mortality rates if in upper 5% of predicted probabilities of death without hospitalization 30-day: 0.9 1-year: 0.34</p>

^a Definition and method of measurement

^b eg, at patient presentation, at event (retrospective)

^c Distribution of predicted probabilities, C-statistic, sensitivity/specificity for select cutpoints/risk groups, predicted/observed mortality in different risk groups, calibration slope, positive and negative predictive values

ADG = Aggregated Diagnosis Groups (Johns Hopkins); DBP = diastolic blood pressure; SBP = systolic blood pressure

