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Review Article

Morbidity Measures Predicting Mortality in Inpatients: A Systematic Review

Cheng Hwee Soh BBmed [a], Syed Wajih Ul Hassan BBmed [a], Julian Sacre PhD [a], Andrea B. Maier MD, PhD [a,b,*]

[a] Department of Medicine and Aged Care, @AgeMelbourne, The Royal Melbourne Hospital, The University of Melbourne, Melbourne, VIC, Australia
[b] Department of Human Movement Sciences, @AgeAmsterdam, Vrije Universiteit Amsterdam, Amsterdam Movement Sciences, Amsterdam, the Netherlands

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A B S T R A C T

Objectives: Morbidity is an important risk factor for mortality and a variety of morbidity measures have been developed to predict patients' health outcomes. The objective of this systematic review was to compare the capacity of morbidity measures in predicting mortality among inpatients admitted to internal medicine, geriatric, or all hospital wards.
Design: A systematic literature search was conducted from inception to March 6, 2019 using 4 databases: Medline, Embase, Cochrane, and CINAHL. Articles were included if morbidity measures were used to predict mortality (registration CRD42019126674).
Setting and Participants: Inpatients with a mean or median age ≥65 years.
Measurements: Morbidity measures predicting mortality.
Results: Of the 12,800 articles retrieved from the databases, a total of 34 articles were included reporting on inpatients admitted to internal medicine, geriatric, or all hospital wards. The Charlson Comorbidity Index (CCI) was reported most frequently and a higher CCI score was associated with greater mortality risk, primarily at longer follow-up periods. Articles comparing morbidity measures revealed that the Geriatric Index of Comorbidity was better predicting mortality risk than the CCI, Cumulative Illness Rating Scale, Index of Coexistent Disease, and disease count.
Conclusions and Implications: Higher morbidity measure scores are better in predicting mortality at longer follow-up period. The Geriatric Index of Comorbidity was best in predicting mortality and should be used more often in clinical practice to assist clinical decision making.

Chronologic age is a major risk factor for the development and accumulation of age-related diseases.[1] Multimorbidity, defined as the concurrent presence of 2 or more diseases, is prevalent in 62% of adults aged 65 to 74 years and 81.5% of those aged 85 years or older living in major western countries.[2] The clinical relevance of multimorbidity and comorbidities, defined as conditions that coexist with a disease of interest,[3] is the synergistic effect of co-occurring diseases in prediction of poor health outcomes.[4–7] These poor health outcomes include hospitalization, readmission, functional decline, and mortality.[6]

A number of measures have been developed to characterize the quantity and severity of individuals' disease burden and associated prognostic implications. The Charlson Comorbidity Index (CCI), Elixhauser Comorbidity Index, and Cumulative Illness Rating Scale (CIRS) are examples that are being frequently used in clinical settings[8–10] to predict both short- and long-term mortality.[11] These measures differ in the number and type of included diseases and their assigned weightings.[6,12,13] Consequently, the appropriateness and predictive capacity of specific measures varies according to the clinical profile of the patient cohorts.

The aim of this systematic review is to compare the capacity of morbidity measures for the prediction of mortality among inpatients.

Methods

Search Strategy

A systematic literature search was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines and registered on PROSPERO (registration number CRD42019126674). The search was conducted from inception to

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* Address correspondence to Andrea B. Maier, MD, PhD, Department of Medicine and Aged Care, @AgeMelbourne, The Royal Melbourne Hospital, The University of Melbourne, Melbourne, Victoria, Australia.
E-mail address: andrea.maier@mh.org.au (A.B. Maier).

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March 6, 2019, using 4 electronic databases: (1) MEDLINE(R), (2) Embase Classic + Embase, (3) Cochrane Central Register of Controlled Trials via the Ovid platform, and (4) CINAHL complete. To avoid selection bias of comorbidity scores, our search terms included the keywords "comorbidity" or "multimorbidity" adjacent to "index," "indices," "measure," "rating," or "scoring." Known comorbidity scores or their abbreviation were also included in our search strategy to reduce the possibility of missing articles. Therefore, both widely used and new (unknown) comorbidities scores were included (Supplementary Material 1). Titles and abstracts of articles were screened independently by 2 authors (C.S. and S.H.). Conflicts were resolved by a third reviewer (J.S. or A.M.).

Study Selection

Longitudinal studies that reported the association between morbidity measures and mortality in inpatients were included. Exclusion criteria were (1) mean or median age of the cohort below 65 years, (2) cross-sectional data analyses, (3) language other than English, and (4) American Society of Anesthesiologist (ASA) physical status classification status being the only measure used. The ASA classification was excluded because of its subjective assessment of patients' overall health without objective consideration of diseases.[14]

Articles were divided into 7 subgroups of inpatients: (1) cancer; (2) musculoskeletal conditions; (3) respiratory diseases; (4) cardiovascular and metabolic diseases; (5) other diseases; (6) surgical interventions; and (7) inpatient groups being admitted to internal medicine wards, geriatric wards, or all hospital wards without focus on a specific diseases. This review solely describes articles describing the results of the last group (7).

Data Extraction and Quality Assessment

For each included article, information relating to study design, population demographics, morbidity measures, baseline score, follow-up duration, and mortality were extracted in a standardized way by 2 independent authors (C.S. and S.H.). The quality assessment was performed using an adapted Newcastle-Ottawa Scale (NOS) (Supplementary Material 2). Disagreement in data extraction was resolved by a third reviewer (J.S. and A.M.).

Data Analysis

The predictive ability of each morbidity measure was reported as the area under the curve (AUC) in a receiver operating characteristic

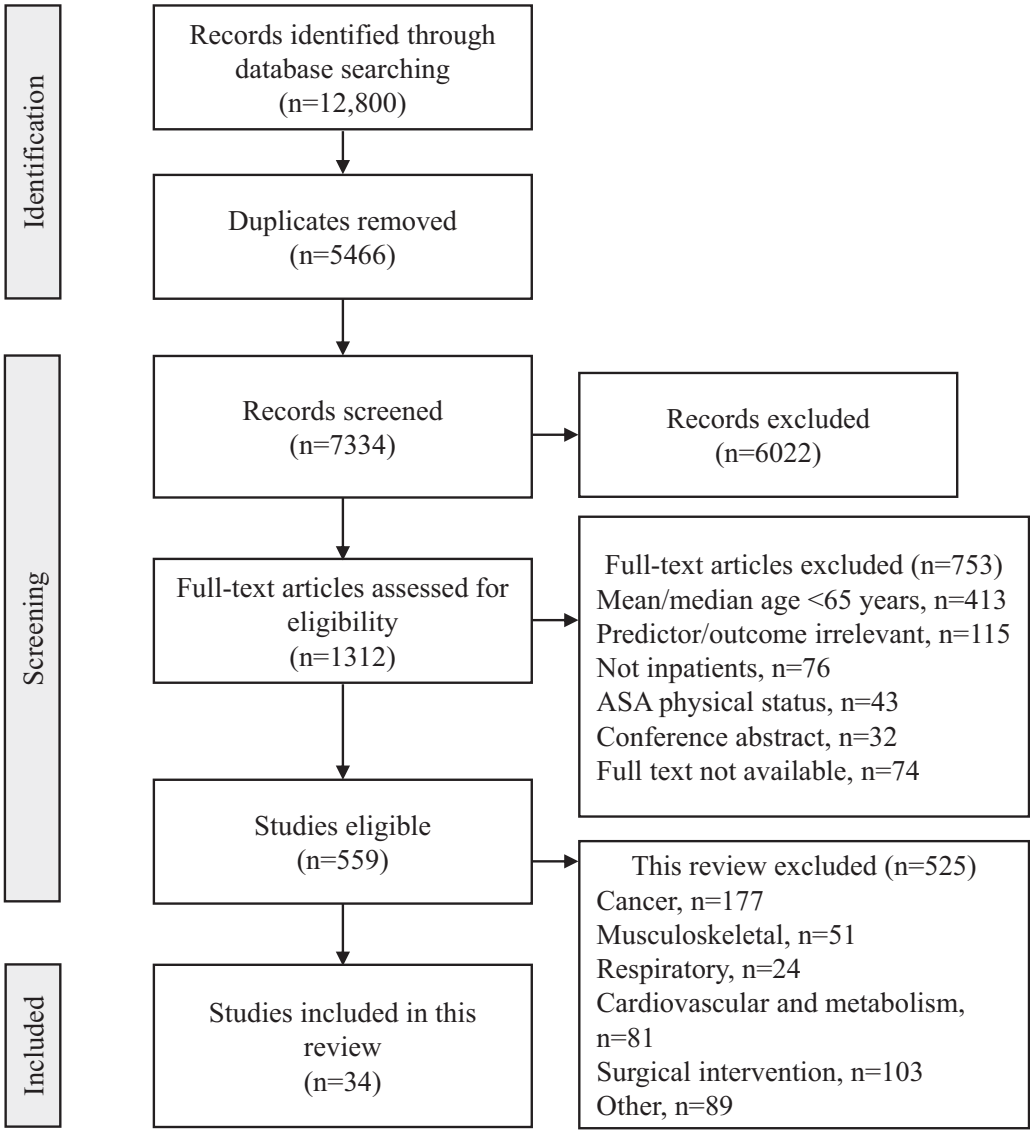

Fig. 1. PRISMA flowchart for the selection of articles.

Table 1
Characteristics of Included Studies

Author (Year)	Ctry	Design	Age (Y)		Sample size, n	Female, %
			Criteria	Cohort		
Internal Medicine Wards						
Arminanzas (2013)[16]	ES	P	≥18	78.0 ± 14.0	539	48.8
Barba (2011)[17]	ES	R*	≥65	NG	1,135,423	50.1
Beglinger (2015)[18]	CH	P	≥18	Median: 81	1278	61.2
Buurman (2011)[19]	NL	P	≥65	78.2 ± 7.8	639	53.8
Conde-Martel (2012)[20]	ES	P	≥90	92.8 ± 2.6	124	63.7
Dias (2015)[21]	PT	P	≥65	80.6 ± 7.8	100	42
Duque (2011)[22]	PT	P	No	67.1 ± 19.3	288	NG
Fabbian (2017)[23]	IT	R*	No	72.7 ± 16.3	75,586	53.4
Frenkel (2014)[24]	NL	P	≥65	77.8 ± 7.9	1313	54.2
Helvik (2013)[25]	NO	P	≥65	80.7 ± 7.4	484	50.2
Hernandez-Luis (2018)[26]	ES	P	≥60	76.6	298	50
Incalzi (1997)[27]	IT	P	NG	78.7 ± 5.9	370	55.1
Iwata (2006)[28]	JP	P	≥85	88.7 ± 2.4	403	63.8
Olsson (2005)[29]	SE	P	No	68.8 ± 7.1	865	50.9
Salvi (2008)[30]	IT	P	≥65	76.7 ± 7.0	387	39.8
Tal (2011)[31]	IL	R*	≥65	81.5	1509	62
Acute Geriatric Wards						
Beloosesky (2011)[32]	IL	P	≥65	81.0 ± 7.3	212	61.8
Bien (2015)[33]	PL	R	NG	77.9 ± 6.8	478	71.5
Martinez-Velilla (2014)[34]	ES	P	≥75	85.4 ± 5.4	122	56.6
Martinez-Velilla (2013)[35]	ES	P	≥75	85.4 ± 5.4	122	56.6
Ritt (2017)[36]	DE	P	≥65	82.9 ± 6.4	307	67.4
Zekry (2009)[37]	CH	P	≥75	85.3 ± 6.7	444	74.1
Zekry (2010)[38]	CH	P	≥75	85.3 ± 6.7	444	74.1
Zekry (2010)[39]	CH	P	≥75	85.3 ± 6.7	444	74.1
Zekry (2011)[40]	CH	P	≥75	85.3 ± 6.7	444	74.1
Zekry (2012)[41]	CH	P	≥75	85.3 ± 6.7	444	74.1
Zekry (2012)[42]	CH	P	≥75	85.3 ± 6.7	444	74.1
Subacute Geriatric Wards						
Bellelli (2008)[43]	IT	P	≥65	76.6 ± 10.5	1323	71.8
Bernard (2016)[44]	AU	P	≥65	81.9 ± 8.0	306	58.2
Rozzini (2002)[45]	IT	P	NG	78.9 ± 7.4	493	70.8
Rozzini (2005)[46]	IT	P	≥60	78.3 ± 8.5	950	69.3
All admitted inpatients						
D'Hoore (1993)[47]	CA	R*	No	Median: 66	62,456	40.6
Moore (2017)[48]	US	R*	≥18	NG	21,911,643	53.3
Quan (2011)[49]	CA	R*	≥18	NG	55,929	64.6

AU, Australia; CA, Canada; CH, Switzerland; Ctry, country; DE, Germany; ES, Spain; IL, Israel; IT, Italy; JP, Japan; NG, not given; NL, the Netherlands NO, Norway; P, prospective; R, retrospective; PL, Poland. PT, Portugal; R, retrospective; SE, Sweden; US, United States of America.
Age was stated in mean ± SD year unless stated otherwise.
*Administrative data used.

curve, relative risk (RR), odds ratio (OR), or hazard ratio (HR) depending on the statistical analysis used in each article. Comprehensive Meta-Analysis (CMA) was used to visualize the association of morbidity measure and mortality (v 3.3; Biostat Inc, Englewood, NK). Publication bias was assessed via a funnel plot using CMA and tested by the Egger regression.[15]

Results

The literature search revealed a total of 12,800 articles. After removing 5466 duplicates, 7334 articles were screened based on titles and abstracts. Of these, 6022 articles were excluded, leaving 1312 articles for full-text screening. A total of 525 articles focused on disease-specific patient populations, leaving 34 articles reporting on patients admitted to internal medicine wards, geriatric wards, or the entire hospital to be included (Figure 1). Risk of bias for every included article were assessed and reported in Supplementary Table 1.

Table 1 summarizes the characteristics of each study. A total of 23,256,611 inpatients (mean age 73.82 years, 53.1% female) were included in 27 prospective and 7 retrospective cohort studies. Among the 7 retrospective studies, 6 studies used administrative data (n = 23,242,546 inpatients). Sixteen articles described the association between morbidity measures and mortality in patients admitted to internal medicine wards, 11 articles in patients admitted to acute geriatric wards, 4 articles in patients admitted to subacute geriatric wards, and 3 articles included entire hospital inpatients. The Charlson Comorbidity Index (CCI) was used most frequently (26/34 articles) in predicting mortality, followed by Cumulative Illness Rating Scale (CIRS) (8/34 articles) and Geriatric Index of Comorbidity (GIC) (8/34 articles). Other morbidity measures including Chronic Disease Score (CDS) and Index of Coexistent Disease (ICED) were reported in 3 and 6 articles respectively. The median follow-up period was 12 months.

Table 2 shows the association of morbidity measures and mortality according to follow-up period. Overall, higher CCI, CIRS, GIC, and ICED scores predicted at a longer follow-up period, which is summarized in Supplementary Table 2.

Four out of 7 articles reported that CCI score, per 1-point increase, was significantly associated with in-hospital mortality.[17,22,31,37,38,44,49] For postdischarge mortality, higher CCI scores were associated with greater mortality.[16,18–20,24–26,28,29,32,34,35,37,39,43,43,46,47,49,33] Figure 2 visualizes the association of a higher CCI scores with increased mortality risk at a longer follow-up period.

CIRS was not predictive for in-hospital mortality,[38] but a CIRS score of 15 points and higher was predictive for post-discharge mortality.[34,35,39,43] All 3 articles reported that CIRS, as per 1 point increase, is significantly associated with postdischarge mortality.[30,32,36] Of the study that reported GIC and its association with in-hospital mortality,

Table 2
Morbidity Measures and its Association With Mortality According to Morbidity Measure and Follow-Up Period

Author (Y)	FU	Result		P
CCI				
Barba (2011)[17]	IH	OR	1.21 (1.16–1.26)	Sig.
Bernard (2016)[44]	IH	Higher CCI score groups did not have a significantly greater proportion of deaths†		
Duque (2011)[22]	IH	OR	1.16 (1.01–1.31)	Sig.
		AUC	0.59 (0.49–0.69)	NS
Quan (2011)[49]	IH	AUC	0.88	Sig.
Tal (2011)[31]	IH	OR	1.18 (0.98–1.41)	NS
Zekry (2009)[37]	IH	OR	3.93 (1.86–8.29)	Sig.
Zekry (2010)[38]	IH	OR	0–6: Ref	-
			7–14: 1.15 (0.96–1.37)	NS
Olsson (2005)[29]	3 d	HR	0.87 (0.74–1.03)	.11
	7 d	HR	0.91 (0.79–1.05)	.19
	30 d	HR	1.02 (0.92–1.13)	.71
Arminanzas (2013)[16]	1 mo	AUC	0.65	Sig.
		Sens.	0.60 (0.48–0.72)	
		Spec.	0.68 (0.63–0.72)	
		OR	0–1: Ref	-
			2: 1.92 (0.80–4.61)	NS
			>2: 3.54 (1.70–7.36)	Sig.
Beglinger (2015)[18]	1 mo	OR*	1.26 (1.15–1.37)	Sig.
		AUC	0.67 (0.61–0.74)	Sig.
Quan (2011)[49]	1 mo	AUC	0.88	Sig.
Olsson (2005)[29]	90 d	HR	1.07 (0.98–1.17)	.1
Beloosesky (2011)[32]	3 mo	OR	2.06 (1.40–3.02)	Sig.
Frenkel (2014)[24]	3 mo	AUC	0.66	Sig.
		OR	0: Ref	-
			1–2: 0.7 (0.3–1.3)	.24
			3–4: 1.1 (0.6–2.2)	.69
			≥5: 3.3 (2.0–7.2)	Sig.
Rozzini (2005)[46]	6 mo	RR*	2.5 (1.3–4.8)	Sig.
Bellelli (2008)[43]	12 mo	OR*	0–2: Ref	-
			3–4: 2.4 (1.2–12.0)	Sig.
			≥5: 6.0 (3.0–11.8)	Sig.
Buurman (2011)[19]	12 mo	HR	1.19 (1.13–1.26)	Sig.
D'Hoore (1993)[47]	12 mo	OR	0: Ref	-
			1–2: 0.67 (0.64–0.71)	NS
			3–4: 1.17 (1.13–1.21)	Sig.
			5–6: 1.68 (1.62–1.73)	Sig.
			≥7: 2.15 (2.07–2.22)	Sig.
Dias (2015)[21]	12 mo	Actual mortality is 3 times lower than the predicted mortality (in %)†		
Iwata (2006)[28]	12 mo	HR	0: Ref	-
			1: 3.79 (0.85–16.99)	NS
			>2: 4.71 (1.09–20.42)	.04
Frenkel (2014)[24]	12 mo	AUC	0.7	Sig.
		OR	0: Ref	-
			1–2: 1.2 (0.6–2.2)	.63
			3–4: 2.2 (1.2–4.1)	Sig.
			≥5: 8.1 (4.5–14.6)	Sig.
Martinez-Velilla (2013)[35]	12 mo	AUC	0.62 (0.52–0.72)	Sig.
		OR	1: Ref	-
			2: 2.86 (1.05–7.81)	Sig.
			3: 2.73 (0.91–8.13)	NS
			4: 2.82 (1.01–7.90)	Sig.
Olsson (2005)[29]	12 mo	HR	1.16 (1.09–1.23)	Sig.
Quan (2011)[49]	12 mo	AUC	0.9	Sig.
Zekry (2012)[41]	12 mo	OR*	0–3: Ref	-
			4: 1.68 (0.88–3.21)	Sig.
			5–6: 1.74 (0.92–3.28)	NS
			7–14: 2.49 (1.34–4.60)	Sig.
Hernandez-Luiz (2018)[26]	24 mo	HR	0–2: Ref	-
			≤3: 1.68 (1.15–2.45)	Sig.
Helvik (2013)[25]	36 mo	HR	1.73 (1.09–2.74)	Sig.
Olsson (2005)[29]	36 mo	HR	1.18 (1.13–1.24)	Sig.
	56 mo	HR	1.20 (1.15–1.25)	Sig.
Frenkel (2014)[24]	60 mo	AUC	0.73	Sig.
		OR	0: Ref	-
			1–2: 4.4 (1.4–14.4)	.01
			3–4: 6.3 (1.9–21.2)	Sig.
			≥5: 39.9 (9.3–170.9)	Sig.

(continued)

Table 2 (*continued*)

Author (Y)	FU	Result		P
Martinez-Velilla (2014)[34]	60 mo	AUC	0.64 (0.53–0.75)	Sig.
		OR	1: Ref	-
			2: 1.92 (0.66–5.61)	NS
			3: 2.30 (0.67–7.90)	NS
			4: 4.03 (1.06–15.31)	Sig.
Zekry (2010)[39]	60 mo	HR*	0–3: Ref	-
			4: 1.14 (0.81–1.62)	NS
			5–6: 1.46 (1.05–2.04)	Sig.
			7–14: 2.49 (1.23–2.32)	Sig.
Bien (2015)[33]	65 mo	HR	1.25 (1.17–1.33)	Sig.
CIRS				
Zekry (2010)[38]	IH	OR	0–18: Ref	-
			19–30: 1.21 (0.20–7.14)	NS
Beloosesky (2011)[32]	3 mo	OR	1.50 (1.22–1.84)	Sig.
Martinez-Velilla (2013)[35]	12 mo	AUC	0.54 (0.44–0.65)	NS
		OR	1: Ref	-
			2: 1.26 (0.44–3.60)	NS
			3: 0.77 (0.27–2.20)	NS
			4: 1.85 (0.62–5.50)	NS
Ritt (2017)[36]	12 mo	AUC	0.77 (0.71–0.91)	Sig.
		HR	1.76 (1.49–2.09)	Sig.
Zekry (2012)[42]	12 mo	OR*	0–11: Ref	-
			12–14: 1.61 (0.71–3.62)	.25
			15–18: 3.70 (1.82–7.53)	Sig.
			19–30: 6.33 (3.17–12.65)	Sig.
Salvi (2008)[30]	18 mo	HR	1.08 (1.03–1.14)	.01
Martinez-Velilla (2014)[34]	60 mo	AUC	0.54 (0.42–0.66)	NS
		OR	1: Ref	-
			2: 1.23 (0.40–3.78)	NS
			3: 0.97 (0.34–2.80)	NS
			4: 2.25 (0.60–8.46)	NS
Zekry (2010)[39]	60 mo	HR*	0–11: Ref	-
			12–14: 1.15 (0.79–1.69)	NS
			15–18: 2.01 (1.42–2.84)	Sig.
			19–30: 3.17 (2.24–4.48)	Sig.
GIC				
Zekry (2010)[38]	IH	OR	1–2: Ref	-
			3: 3.68 (3.01–6.26)	Sig.
			4: 4.34 (3.92–9.52)	Sig.
Martinez-Velilla (2013)[35]	12 mo	AUC	0.69 (0.59–0.79)	Sig.
		OR	1: Ref	-
			2: 0.90 (0.23–3.51)	NS
			3: 1.85 (0.47–7.32)	NS
			4: 5.03 (1.40–18.1)	Sig.
Rozzini (2002)[45]	12 mo	RR	2.3 (1.7–3.1)	Sig.
Zekry (2012)[41]	12 mo	OR*	1–2: Ref	-
			3: 8.15 (1.13–58.91)	Sig.
			4: 27.6 (3.80–200.51)	Sig.
Martinez-Velilla (2014)[34]	60 mo	AUC	0.66 (0.56–0.76)	Sig.
		OR	1: Ref	-
			2: 0.50 (0.15–1.67)	NS
			3: 1.04 (0.27–4.01)	NS
			4: 4.62 (0.96–22.09)	NS
Zekry (2010)[39]	60 mo	HR*	1–2: Ref	-
			3: 1.63 (1.00–2.66)	Sig.
			4: 3.85 (2.29–6.47)	Sig.
Zekry (2011)[40]	60 mo	HR	1–2: Ref	-
			3: 1.43 (0.86–2.39)	NS
			4: 2.74 (1.58–4.89)	Sig.
Zekry (2012)[41]	60 mo	HR	1–2: Ref	-
			3: 1.24 (0.75–2.06)	NS
			4: 2.45 (1.40–4.28)	Sig.
ICED				
Zekry (2010)[38]	IH	OR	1–3: Ref	-
			4: 1.36 (1.01–1.83)	Sig.
Martinez-Velilla (2013)[35]	12 mo	AUC	0.58 (0.47–0.68)	NS
		OR	1: Ref	-
			2: 0.98 (0.29–3.32)	NS
			3: 1.41 (0.51–3.84)	NS
			4: 2.28 (0.79–6.61)	NS
Rozzini (2002)[45]	12 mo	RR	1.0 (0.9–1.2)	NS
Zekry (2012)[42]	12 mo	OR*	1–3: Ref	-
			4: 2.58 (1.34–4.96)	Sig.

(continued on next page)

Table 2 (*continued*)

Author (Y)	FU	Result		*P*
Martinez-Velilla (2014)[34]	60 mo	AUC	0.56 (0.45–0.67)	NS
		OR	1: Ref	-
			2: 0.70 (0.21–2.34)	NS
			3: 0.75 (0.26–2.12)	NS
			4: 2.17 (0.58–8.20)	NS
Zekry (2010)[39]	60 mo	HR*	1–3: Ref	-
			4: 1.71 (1.23–2.37)	Sig.
CDS				
Zekry (2010)[38]	IH	OR*	0–3: Ref	-
			4–6: 0.62 (0.14–2.64)	NS
			7-8: 1.60 (0.49–5.21)	NS
			9–15: 2.13 (0.67–6.70)	NS
Zekry (2012)[42]	12 mo	OR*	0–3: Ref	-
			4–6: 1.04 (0.59–1.82)	.89
			7–8: 1.20 (0.68–2.16)	.44
			9–15: 1.24 (0.71–2.13)	.55
Zekry (2010)[39]	60 mo	HR*	0–3: Ref	-
			4–6: 1.12 (0.80–1.57)	NS
			7–8: 1.16 (0.83–1.64)	NS
			9–15: 1.38 (0.98–1.94)	NS
DC				
Moore (2017)[48]	IH	AUC	0.73 (0.73–0.73)	Sig.
Martinez-Velilla (2013)[35]	12 mo	AUC	0.61 (0.50–0.71)	Sig.
		OR	1: Ref	-
			2: 0.81 (0.24–2.72)	NS
			3: 2.01 (0.77–5.26)	NS
			4: 1.81 (0.66–4.96)	NS
Rozzini (2002)[45]	12 mo	RR	0.8 (0.8–1.1)	NS
Martinez-Velilla (2014)[34]	60 mo	AUC	0.58 (0.45–0.70)	NS
		OR	1: Ref	-
			2: 5.76 (1.17–28.24)	Sig.
			3: 2.38 (0.84–6.75)	NS
			4: 1.92 (0.66–5.56)	NS
KFI				
Zekry (2010)[38]	IH	OR	0–2: Ref	-
			6–16: 1.71 (0.28–10.50)	NS
Zekry (2012)[42]	12 mo	OR*	0–2: Ref	-
			3–4: 1.54 (0.84–2.84)	.17
			5: 2.47 (1.22–4.99)	Sig.
			6–16: 3.45 (1.92–6.19)	Sig.
Zekry (2010)[39]	60 mo	HR*	0–2: Ref	-
			3–4: 1.36 (0.98–1.89)	NS
			5: 2.04 (1.36–3.05)	Sig.
			6–16: 2.46 (1.75–3.45)	Sig.
EI				
Fabbian (2017)[23]	IH	AUC‡	0.72 (0.71–0.73)	Sig.
	IH	AUC	0.66 (0.65–0.66)	Sig.
Moore (2017)[48]	IH	AUC	0.80 (0.80–0.80)	Sig.
ICI				
Incalzi (1997)[27]	IH	AUC‡	0.57	Sig.
		Sens.‡	0.71	
		Spec.‡	0.69	
		OR‡	1.77 (1.15–2.72)	Sig.
	IH	AUC	0.46	NS
		Sens.	0.64	
		Spec.	0.64	
		OR	1.58 (1.03–2.43)	Sig.

AUC, area under the receiver operating characteristic curve; CDS, chronic disease score; d, days in follow-up period; DC, diagnosis count; EI, Elixhauser Comorbidity Index; FU, follow-up; KFI, Kaplan-Feinstein Index; HR, hazard ratio; ICI, Incalzi Comorbidity Index; IH, in-hospital; MM, morbidity measure; mo, months in follow-up period; NG, not given; NS, not significant; OR, odds ratio; Ref, reference; RR, relative risk; Sens, sensitivity; Sig., significant; Spec, specificity.

Statistical results were stated as morbidity score: statistical result (95% confidence interval) or statistical result per 1-point increase and adjusted for at least age and sex unless stated otherwise.

*Univariate analysis.

†Statistical report and result were not given.

‡Age modified morbidity measure.

a GIC score of 3 or higher was reported significant.[38] For postdischarge mortality, a greater proportion of articles reported that a higher GIC score and longer follow-up period is significantly predictive.[34,35,39,42,43,45]

Among the 6 articles reporting ICED, 1 article reported an insignificant association with in-hospital mortality. Two out of the 5 articles reporting postdischarge mortality showed that only ICED score of 4 was significantly associated with mortality.[34,35,38,39,43,45] All 3 studies that reported CDS showed that all CDS score did not associate with in-hospital, 12-month, or 60-month mortality risk.[38,39,43]

Two studies compared the capacity of morbidity measures predicting mortality and GIC was shown to have the highest AUC among CCI, ICED, CIRS, and disease count (Table 2).[34,35] By including age in the scoring system, 2 studies showed that a modified morbidity measure had a higher AUC predicting mortality than the original morbidity measure itself (Table 2).[23,27]

The visual inspection of the funnel plot and the Egger regression test indicated insignificant publication bias (*P* value = .134) (Supplementary Figure 1).

Discussion

Higher CCI, CIRS, and GIC morbidity scores predict greater postdischarge mortality risk in patients admitted to internal medicine wards, geriatric wards, and the overall hospital wards. The predictive capacity of morbidity scores is higher at longer follow-up periods. Among the studies comparing the capacity of morbidity measure, GIC was shown to be better in predicting mortality than CCI, CIRS, ICED, and disease count among inpatients.

As the most frequently used morbidity measure, the CCI significantly predicted postdischarge mortality among patients with a higher predictive capacity at longer follow-up periods. CCI is not predictive for in-hospital mortality, and this may be due to the fact that morbidities and their corresponding weight listed in CCI was initially assigned and validated in predicting 10-years mortality.[8]

CIRS is a comprehensive measure that comprised all physiological systems with clear ranking severity, and it was shown to be predictive for postdischarge mortality. However, CIRS was shown to be unable to predict in-hospital mortality,[38] and this is possibly because of the inclusion of specific diseases such as psychiatric morbidities. They are highly prevalent in older inpatients[50,51] but generally have insignificant association with in-hospital mortality,[52] which in turn results in the inability of CIRS in predicting in-hospital mortality.

Among all morbidity measures, GIC was shown to have the greatest predictive capacity with mortality in comparative studies. Although most morbidity measures focus on weighing the severity of each morbidity, GIC is different as it incorporates both the number and severity of diseases, hence, the ability to capture the co-occurrence of diseases and corresponding severity.

Among all morbidity measures, ICED is the only one incorporating patients' physical impairment as one of the components.[53] ICED was developed in patients undergoing total hip replacement to predict patients' recovery and postoperative complications.[54] Hence, by considering physical impairment as a morbidity, it was mainly used to predict patients' physical function and disability.[38,55] However, it was not developed nor validated for the purpose of predicting mortality, resulting in its inability to reflect those who are at higher risk.

CDS was shown to be unable to predict in-hospital, 12-month, or 60-month mortality. CDS is a morbidity measure that incorporates drugs dispensed as surrogate markers for morbidity instead of clinical diagnoses.[56,57] The poor performance of CDS in predicting mortality may not only be because it was designed initially to predict hospitalizaion, but may also be due to the addition of new drug classes since the development of the CDS in 1992, and the possibility of morbidity that is not treated with medication.

Morbidity measures taking the age of the patients into account were shown to be better in predicting mortality.[23,27] Most of the chronic morbidities were age-related, caused by the progressive deterioration in the function of organs.[58] Chronologic age was also

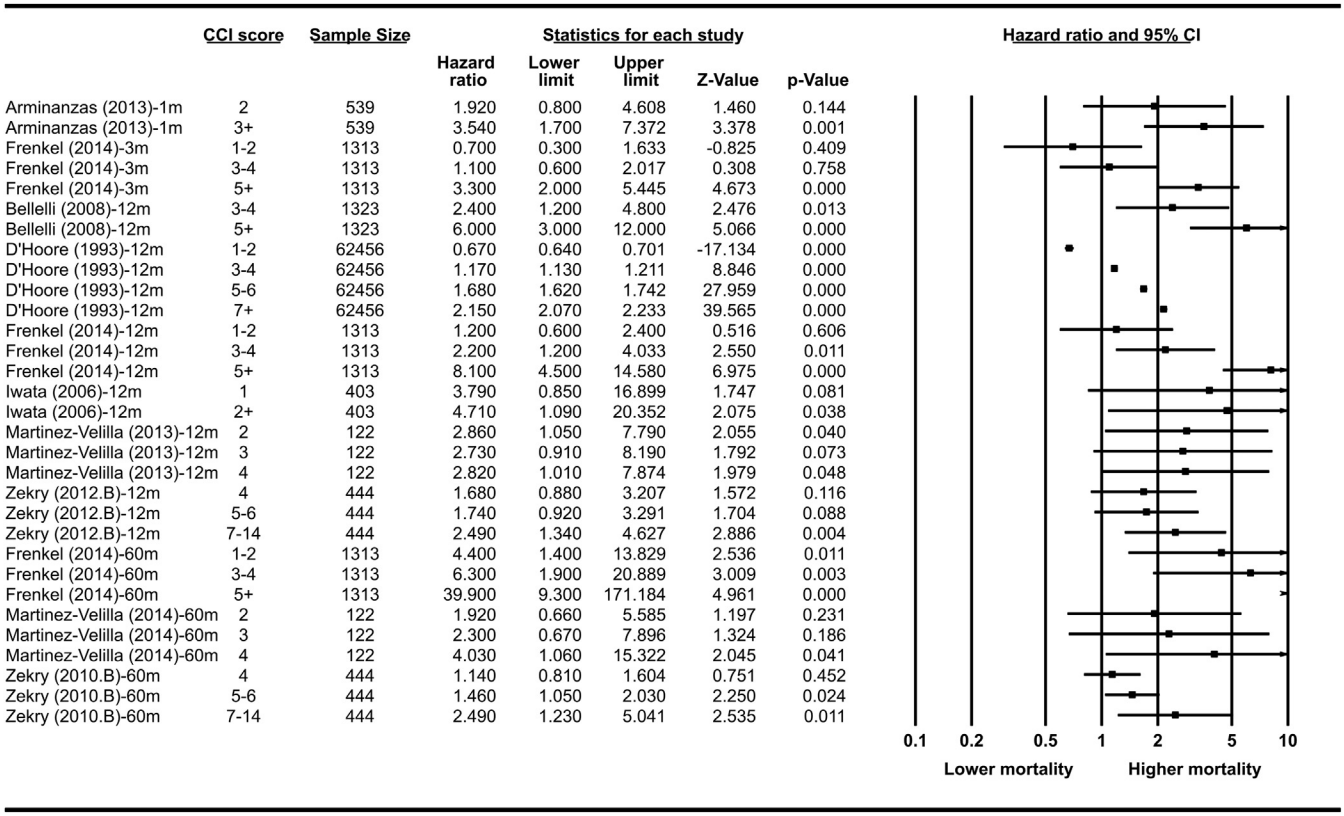

Fig. 2. Predictive capacity of CCI scores on mortality stratified by morbidity score and follow-up period.

shown to be a significant predictor of mortality, hence, including age in the model is conceivable.[59]

To the best of our knowledge, this is the first systematic review that compares all morbidity measures that were used in a general medical hospital setting regardless of administrative or clinical data. Administrative data provide a large sample size, however, incomplete or incorrect coding in addition to temporal changes in coding practices may impact the sensitivity and specificity of the risk models. On the other hand, clinical data are more likely to detect historical or asymptomatic morbidities, such as prior myocardial infarction and hyperlipidemia.[60,61] A meta-analysis was not performed due to the differences in statistical analysis, follow-up period, and cut-off value chosen for each morbidity measure. Further research is required to determine the predictive capacity of each morbidity measure within specific disease population as it is important to determine if the finding from this review is valid and consistent throughout the study population with different index diseases.

Conclusions and Implications

The CCI is the most frequently used morbidity measure, and it is better predicting mortality at higher scores and longer follow-up period. The GIC has better predictive capacity than CCI, CIRS, ICED, and disease count in clinical settings. Overall, a weighted comorbidity index is useful in reflecting inpatients' health status and GIC should be used more often as a prognostic tool to reflect high-risk patients.

Acknowledgments

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Supplementary Data

Supplementary data related to this article can be found online at https://doi.org/10.1016/j.jamda.2019.12.001.

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Supplementary Material 1. Search Strategy

(1) Medline

1	((comorbid* or "co morbid*" or multimorbid* or "multi morbid*") adj3 (index* or indice* or measure* or rating* or scale* or score or scoring)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	9988
2	("Cumulative Illness Rating Scale" or (CIRS and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	433
3	("Kaplan Feinstein index" or (KFI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	26
4	("charlson comorbidity index" or "Charlson index" or (CCI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	4902
5	("Deyo Charlson comorbidity index" or "Deyo charlson index" or (DCI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*")) or (DCCI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	115
6	("Charlson deyo comorbidity index" or "Charlson deyo index" or (CDI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*")) or (CDCI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	364
7	("aggregated diagnosis group" or (ADG and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	13
8	("adjusted clinical group" or (ACG and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	123
9	("chronic disease score" or (CDS and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	206
10	("index of coexistent disease" or (ICED and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	55
11	("satariano index" or (SI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	258
12	("total illness burden index" or (TIBI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	12
13	("Elixhauser comorbidity index" or "Elixhauser index" or (EI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*")) or (ECI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	167
14	("comprehensive prognostic index" or (CPI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	25
15	("american society of anesthesiologists physical status" or (ASA and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	2653
16	("adult comorbidity evaluation 27" or (ACE-27 and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	143
17	("simplified comorbidity index" or (SCI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	391
18	("multipurpose australian comorbidity scoring system" or (MACSS and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	2
19	("national cancer institute comorbidity index" or (NCI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	99
20	("functional comorbidity index" or (FCI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	69
21	("geriatric index of comorbidity" or (GIC and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	16
22	(mortality or death).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	1513826

23	("Activit* of Daily Living" or "Activit* of Daily Life" or "ADL" or "iADL" or "functional decline" or (disabil* adj3 function)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	77492
24	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21	14564
25	22 OR 23	1584691
26	24 AND 25	6475
27	Limit 26 to ("all aged (65 and over)" or "aged (80 and over)")	4597
28	(elderly or ((old or older or aged) adj (person* or patient* or people or male or female or males or females or men or women or individual* or population)) or elder or geriatric*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	550569
29	26 NOT 27	1878
30	28 AND 29	276
31	27 OR 30	4873
32	Limit 31 to English language	4652

(2) Embase

1	((comorbid* or "co morbid*" or multimorbid* or "multi morbid*") adj3 (index* or indice* or measure* or rating* or scale* or score or scoring)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	26712
2	("Cumulative Illness Rating Scale" or (CIRS and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	1065
3	("Kaplan Feinstein index" or (KFI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	63
4	("charlson comorbidity index" or "Charlson index" or (CCI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	16150
5	("Deyo Charlson comorbidity index" or "Deyo charlson index" or (DCI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*")) or (DCCI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	288
6	("Charlson deyo comorbidity index" or "Charlson deyo index" or (CDI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*")) or (CDCI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	880
7	("aggregated diagnosis group" or (ADG and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	20
8	("adjusted clinical group" or (ACG and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	207
9	("chronic disease score" or (CDS and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	349
10	("index of coexistent disease" or (ICED and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	78
11	("satariano index" and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*")).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	4
12	("total illness burden index" or (TIBI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	24
13	("Elixhauser comorbidity index" or "Elixhauser index" or (EI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*")) or (ECI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	966
14	("comprehensive prognostic index" or (CPI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	67
15	("american society of anesthesiologists physical status" or (ASA and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	4985
16	("adult comorbidity evaluation 27" or (ACE-27 and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	318
17	("simplified comorbidity index" or (SCI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	566
18	("multipurpose australian comorbidity scoring system" or (MACSS and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	3

19	("national cancer institute comorbidity index" or (NCI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	358
20	("functional comorbidity index" or (FCI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	146
21	("geriatric index of comorbidity" or (GIC and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	33
22	(mortality or death).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	2166576
23	("Activit* of Daily Living" or "Activit* of Daily Life" or "ADL" or "iADL" or "functional decline" or (disabil* adj3 function)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	51124
24	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21	34500
25	22 OR 23	2211660
26	24 AND 25	15140
27	Limit 26 to aged <65+ years>	7231
28	(elderly or ((old or older or aged) adj (person* or patient* or people or male or female or males or females or men or women or individual* or population)) or elder or geriatric*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	924670
29	26 AND 28	4494
30	27 OR 29	8024
31	Limit 30 to conference abstract status	2348
32	30 NOT 31	5677
33	Limit 32 to English language	5467

(3) Cochrane

1	((comorbid* or "co morbid*" or multimorbid* or "multi morbid*") adj3 (index* or indice* or measure* or rating* or scale* or score or scoring)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	1289
2	("Cumulative Illness Rating Scale" or (CIRS and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	68
3	("Kaplan Feinstein index" or (KFI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	0
4	("charlson comorbidity index" or "Charlson index" or (CCI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	544
5	("Deyo Charlson comorbidity index" or "Deyo charlson index" or (DCI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*")) or (DCCI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	8
6	("Charlson deyo comorbidity index" or "Charlson deyo index" or (CDI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*")) or (CDCI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	31
7	("aggregated diagnosis group" or (ADG and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	0
8	("adjusted clinical group" or (ACG and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	3
9	("chronic disease score" or (CDS and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	15
10	("index of coexistent disease" or (ICED and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	5
11	("satariano index" or (SI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	773
12	("total illness burden index" or (TIBI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	0
13	("Elixhauser comorbidity index" or "Elixhauser index" or (EI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*")) or (ECI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	35
14	("comprehensive prognostic index" or (CPI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	0

15	("american society of anesthesiologists physical status" or (ASA and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	776
16	("adult comorbidity evaluation 27" or (ACE-27 and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	19
17	("simplified comorbidity index" or (SCI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	28
18	("multipurpose australian comorbidity scoring system" or (MACSS and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	0
19	("national cancer institute comorbidity index" or (NCI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	25
20	("functional comorbidity index" or (FCI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	10
21	("geriatric index of comorbidity" or (GIC and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	2
22	(mortality or death).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	77551
23	("Activit* of Daily Living" or "Activit* of Daily Life" or "ADL" or "iADL" or "functional decline" or (disabil* adj3 function)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	9161
24	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21	2886
25	22 OR 23	86054
26	24 AND 25	697
27	Limit 26 to English language	668

(4) Cinahl

S1	(comorbid* or "co morbid*" or multimorbid* or "multi morbid*") W3 (index* or indice* or measure* or rating* or scale* or score* or scoring*)	3401
S2	"Cumulative Illness Rating Scale" or (CIRS and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))	184
S3	"kaplan feinstein index" or (KFI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))	6
S4	"charlson comorbidity index" or "Charlson Index" or (CCI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))	1710
S5	"Deyo Charlson Comorbidity Index" or "Deyo charlson index" or (DCI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*")) or (DCCI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))	63
S6	"Charlson deyo comorbidity index" or "Charlson deyo index" or (CDI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*")) or (CDCI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))	145
S7	"aggregated diagnosis group" or (ADG and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))	6
S8	"adjusted clinical groups" or (ACG and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))	55
S9	"chronic disease score" or (CDS and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))	79
S10	"index of coexistent disease" or (ICED and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))	9
S11	"satariano index"	0
S12	"total illness burden index" or (TIBI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))	5
S13	"Elixhauser comorbidity index" or "Elixhauser index"	52
S14	"comprehensive prognostic index" or (CPI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))	12
S15	"american society of anesthesiologists physical status" or (ASA and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))	761
S16	“adult comorbidity evaluation 27" or (ACE-27 and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))	31
S17	"simplified comorbidity index" or (SCI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))	240
S18	"multipurpose australian comorbidity scoring system"	69
S19	"national cancer institute comorbidity index" or (NCI and (comorbid* or "co morbid*" or multimorbid* or "multi morbid*"))	41
S20	mortality or death	328565
S21	"activit* of daily living" or "activit* of daily life" or "ADL" or "iADL" or "functional decline" or (disabil* W3 function)	35185
S22	S20 OR S21	361153
S23	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19	4916
S24	S22 and S23 (Limiters – Language: English)	2013

Supplementary Material 2. Risk of Bias Assessment Tool: Newcastle-Ottawa Quality Assessment Scale for Cohort Study

Selection (S)

(1) Representativeness of the study cohort
- a) recruiting participants consecutively *
- b) recruiting participants by selection
- c) no description

(2) Selection of the exclusion cohort
- a) report key criteria for patients that are excluded from the study *
- b) no description

(3) Ascertainment of scoring system (how is the index scored)
- a) scored by physician *
- b) medical record
- c) no description

Comparability (C)

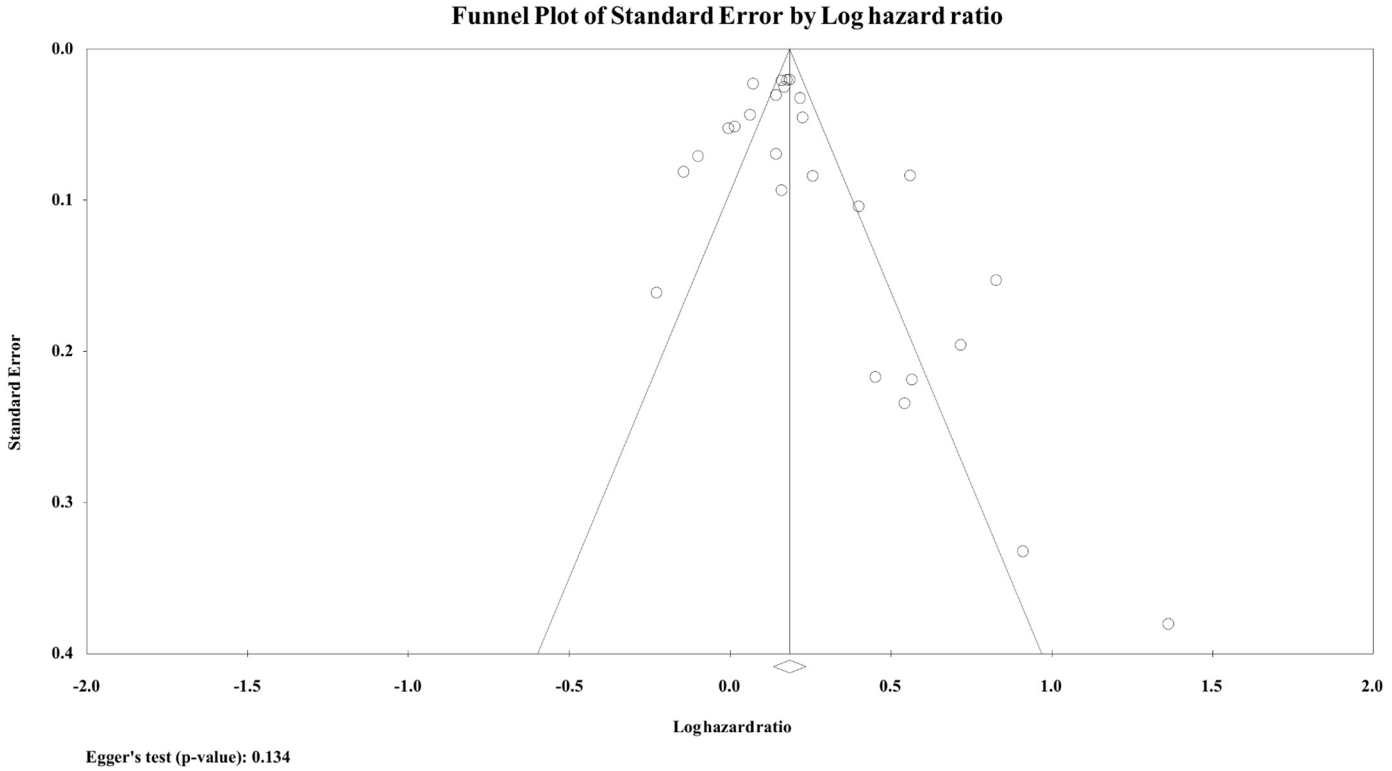
(4) Comparability of cohorts on the basis of the design or analysis
- a) index adjusts for age/sex *
- b) index adjust for any additional factor (ie, disease severity) *
- c) index do not adjust for anything
- d) index do not report for adjustment

Outcome (O)

(5) Assessment of outcome (mortality or ADL dependency)
- a) independent blind assessment (reporting type of mortality in the context of blind assessment) *
- b) record linkage (ie, all-cause mortality) *
- c) self-report (ie, follow-up interview for ADL dependency)
- d) no description

(6) Was follow-up long enough for outcomes to occur
- a) yes (select an adequate follow up period for outcome of interest) *
- b) no

(7) Adequacy of follow-up of cohorts
- a) complete follow-up: all subjects accounted for *
- b) small number lost - >20 % *
- c) follow-up rate <20% or no description of those lost
- d) no statement



Supplementary Fig. 1. Publication Bias.

Supplementary Table 1
Risk of Bias for Individual Articles

Author (year)	S			C	O			Total Stars
	1	2	3	4	5	6	7	
Arminanzas (2013)[16]	*	*			*	*		4/8
Barba (2011)[17]	*	*	*		*	*	*	6/8
Beglinger (2015)[18]		*		*	*	*	*	5/8
Bellelli (2008)[43]	*	*	*		*	*	*	6/8
Beloosesky (2011)[32]	*		*	**	*			5/8
Bernard (2016)[44]	*	*		*	*	*	*	6/8
Bien (2015)[33]	*	*		**	*	*	*	7/8
Buurman (2011)[19]	*	*		**	*	*	*	7/8
Conde-Martel (2012)[20]	*	*		**	*	*	*	7/8
D'Hoore (1993)[47]	*	*		*	*	*	*	6/8
Dias (2015)[21]	*	*	*		*	*	*	6/8
Duque (2011)[22]	*	*		*	*	*	*	6/8
Fabbian (2017)[23]	*	*			*	*	*	5/8
Frenkel (2014)[24]	*	*		**	*	*	*	7/8
Helvik (2013)[25]		*	*	*	*	*	*	6/8
Hernandez-Luiz (2018)[26]	*	*		**	*	*	*	7/8
Incalzi (1997)[27]	*	*	*	*	*	*	*	7/8
Iwata (2006)[28]		*	*	**	*	*	*	7/8
Martinez-Velilla (2014)[34]	*			*	*			3/8
Martinez-Velilla (2013)[35]	*			*				2/8
Moore (2017)[48]	*	*		*	*	*	*	6/8
Olsson (2005)[29]	*			*	*	*		4/8
Quan (2011)[49]	*	*		*	*	*	*	6/8
Ritt (2017)[36]	*	*	*	**	*	*	*	8/8
Rozzini (2002)[45]	*	*	*	**	*	*	*	8/8
Rozzini (2005)[46]		*	*	**	*	*	*	7/8
Salvi (2008)[30]	*	*			*	*	*	5/8
Tal (2011)[31]	*	*			*	*	*	5/8
Zekry (2009)[37]		*			*	*	*	4/8
Zekry (2010)[38]		*		*	*	*	*	5/8
Zekry (2010)[39]		*		*	*	*	*	5/8
Zekry (2011)[40]		*		*	*	*	*	5/8
Zekry (2012)[41]		*		*	*	*	*	5/8
Zekry (2012)[42]		*			*	*	*	4/8

C, comparability; O, outcome; S, selection.

Supplementary Table 2
Proportion of Articles Reporting a Significant Association of Morbidity Measures and Mortality According to Morbidity Scores and Follow-Up Period

FU	Score																													
	CCI											CIRS					GIC					ICED					CDS			
	0	1	2	3	4	5	6	7	8	9+	C	0-11	12-14	15-18	19-30	C	1	2	3	4	C	1	2	3	4	C	0-3	4-6	7-8	9-15
IH	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	4/6	0/1	0/1	0/1	0/1		0/1	0/1	1/1	1/1		0/1	0/1	0/1	1/1		0/1	0/1	0/1	0/1
3 d											0/1																			
7 d											0/1																			
1 mo	0/1	0/1	0/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	2/3																			
3 mo	0/1	0/1	0/1	0/1	0/1	1/1	1/1	1/1	1/1	1/1	1/2					1/1														
6 mo											1/1																			
12 mo	0/6	0/6	2/6	5/6	5/6	5/6	5/6	6/6	6/6	6/6	3/4	0/2	0/2	1/2	1/2	1/1	0/2	0/2	1/2	2/2	1/1	0/2	0/2	0/2	1/2	0/1	0/1	0/1	0/1	0/1
18 mo																1/1														
24 mo	0/1	0/1	0/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1																				
36 mo											1/1																			
56 mo											2/2																			
60 mo	0/3	1/3	1/3	1/3	2/3	3/3	3/3	3/3	3/3	3/3	1/1	0/2	0/2	1/2	1/2		0/4	2/4	3/4	4/4		0/2	0/2	0/2	1/2		0/1	0/1	0/1	0/1
65 mo											1/1																			

C, continuous; CDS, chronic disease score; FU, follow-up period; IH, inhospital. Portions indicate the number of articles reporting significant results out of the total number of articles.