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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Aged
comorbidity
multimorbidity
mortality
prognosis

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. 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. The clinical relevance of multimorbidity and comorbidities, defined as conditions that coexist with a disease of interest, is the synergistic effect of co-occurring diseases in prediction of poor health outcomes. These poor health outcomes include hospitalization, readmission, functional decline, and mortality. 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 to predict both short- and long-term mortality. These measures differ in the number and type of included diseases and their assigned weightings. 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
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. 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.](image-url)
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 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. Postdischarge mortality, higher CCI scores were associated with greater mortality. CIRS was not predictive for in-hospital mortality, but a CIRS score of 15 points and higher was predictive for post-discharge mortality. All 3 articles reported that CCI score, per 1-point increase, was significantly associated with postdischarge mortality. Of the study that reported GIC and its association with in-hospital mortality, 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 with the Egger regression.

### 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 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.

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

<table>
<thead>
<tr>
<th>Author (Y)</th>
<th>FU</th>
<th>Result</th>
<th>P</th>
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<tbody>
<tr>
<td><strong>CCI</strong></td>
<td></td>
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<tr>
<td>Olsson (2005)</td>
<td>3 mo</td>
<td>OR</td>
<td>2.06 (1.40—2.90)</td>
</tr>
<tr>
<td>Olsson (2005)</td>
<td>60 mo</td>
<td>AUC</td>
<td>0.64 (0.53—0.75)</td>
</tr>
<tr>
<td>Zekry (2010)</td>
<td>60 mo</td>
<td>HR</td>
<td>1:19 (1:1—1:2)</td>
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<tr>
<td><strong>Beloosesky (2011)</strong></td>
<td>3 mo</td>
<td>OR</td>
<td>0: Ref -</td>
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<tr>
<td>Beloosesky (2011)</td>
<td>12 mo</td>
<td>AUC</td>
<td>0.54 (0.44—0.65)</td>
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<tr>
<td>Zekry (2012)</td>
<td>12 mo</td>
<td>OR</td>
<td>1: Ref -</td>
</tr>
<tr>
<td><strong>Biel (2015)</strong></td>
<td>60 mo</td>
<td>AUC</td>
<td>0.54 (0.42—0.66)</td>
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<tr>
<td><strong>Bien (2015)</strong></td>
<td>65 mo</td>
<td>HR</td>
<td>1:22 (1:1—1:4)</td>
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<tr>
<td><strong>CIRS</strong></td>
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<tr>
<td>Zekry (2010)</td>
<td>18 mo</td>
<td>OR</td>
<td>0: Ref -</td>
</tr>
<tr>
<td><strong>Frenkel (2014)</strong></td>
<td>3 mo</td>
<td>OR</td>
<td>0.66</td>
</tr>
<tr>
<td><strong>Rozzini (2005)</strong></td>
<td>6 mo</td>
<td>RR</td>
<td>2.5 (1.3—4.8)</td>
</tr>
<tr>
<td><strong>Biel (2015)</strong></td>
<td>60 mo</td>
<td>AUC</td>
<td>0.64 (0.53—0.75)</td>
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<tr>
<td><strong>Dias (2015)</strong></td>
<td>12 mo</td>
<td>Actual mortality is 3 times lower than the predicted mortality (in %)</td>
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<tr>
<td><strong>Iwata (2006)</strong></td>
<td>12 mo</td>
<td>HR</td>
<td>1: Ref -</td>
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<tr>
<td><strong>Frenkel (2014)</strong></td>
<td>12 mo</td>
<td>HR</td>
<td>1: Ref -</td>
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<tr>
<td><strong>Martinez-Velilla (2013)</strong></td>
<td>12 mo</td>
<td>OR</td>
<td>1: Ref -</td>
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<tr>
<td><strong>Olsson (2005)</strong></td>
<td>12 mo</td>
<td>HR</td>
<td>1: Ref -</td>
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<tr>
<td><strong>Zekry (2012)</strong></td>
<td>12 mo</td>
<td>OR</td>
<td>1: Ref -</td>
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<tr>
<td><strong>Hernandez-Luis (2018)</strong></td>
<td>24 mo</td>
<td>HR</td>
<td>2.39 (1:1—1:6)</td>
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<tr>
<td><strong>Helvik (2013)</strong></td>
<td>36 mo</td>
<td>HR</td>
<td>1.33 (0.83—2.11)</td>
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<tr>
<td><strong>Olsson (2005)</strong></td>
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<tr>
<td><strong>Frenkel (2014)</strong></td>
<td>60 mo</td>
<td>AUC</td>
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(continued on next page)
Sex unless stated otherwise.

Table 2 (continued)

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<th>Author (Y)</th>
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<tr>
<td>Martinez-Velilla (2014)</td>
<td>60 mo</td>
<td>AUC</td>
<td>0.56 (0.45–0.67) NS</td>
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<tr>
<td></td>
<td>OR</td>
<td>1: Ref</td>
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<td></td>
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<td>2: 0.70 (0.21–2.34) NS</td>
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<td>3: 0.75 (0.26–2.12) NS</td>
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<td>4: 2.17 (0.85–8.20) NS</td>
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<tr>
<td>Zekry (2010)</td>
<td>60 mo</td>
<td>HR</td>
<td>1–3: Ref - 4: 1.71 (1.23–2.37) Sig.</td>
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<td>CDS</td>
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<tr>
<td>Zekry (2010)</td>
<td>IH</td>
<td>OR</td>
<td>0–3: Ref - 4–6: 0.62 (0.14–2.64) NS</td>
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<td></td>
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<td>7–8: 1.60 (0.49–5.21) NS</td>
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<td>9–15: 2.13 (0.67–6.70) NS</td>
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<tr>
<td>Zekry (2012)</td>
<td>12 mo</td>
<td>OR</td>
<td>0–3: Ref - 4–6: 1.04 (0.59–1.82) .89</td>
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<td>7–8: 1.20 (0.68–2.16) .44</td>
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<td>9–15: 1.24 (0.71–2.34) .55</td>
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<tr>
<td>Zekry (2010)</td>
<td>60 mo</td>
<td>HR</td>
<td>0–3: Ref - 4–6: 1.12 (0.80–1.57) NS</td>
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<td>7–8: 1.16 (0.83–1.64) NS</td>
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<td>9–15: 1.38 (0.98–1.94) NS</td>
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<td>DC</td>
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<tr>
<td>Moore (2017)</td>
<td>IH</td>
<td>AUC</td>
<td>0.73 (0.73–0.73) Sig.</td>
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<tr>
<td>Martinez-Velilla (2013)</td>
<td>12 mo</td>
<td>AUC</td>
<td>0.61 (0.50–0.71) Sig.</td>
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<tr>
<td></td>
<td>OR</td>
<td>1: Ref</td>
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<td></td>
<td></td>
<td>2: 0.81 (0.24–2.72) NS</td>
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<td>3: 2.01 (0.77–5.26) NS</td>
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<td></td>
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<td>4: 1.81 (0.66–4.96) NS</td>
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<tr>
<td>Rozzini (2002)</td>
<td>12 mo</td>
<td>RR</td>
<td>0.8 (0.8–1.1) - 3: Ref - 2: 3.84 (0.84–6.75) NS</td>
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<tr>
<td>Martinez-Velilla (2014)</td>
<td>60 mo</td>
<td>OR</td>
<td>0.58 (0.45–0.70) - 4: 1.92 (0.66–5.56) NS</td>
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<td></td>
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<td>1: Ref</td>
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<tr>
<td></td>
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<td>2: 5.76 (1.17–28.24) Sig.</td>
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<td></td>
<td></td>
<td>3: 2.38 (0.84–6.75) NS</td>
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<td>4: 1.92 (0.66–5.56) NS</td>
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<td>KFI</td>
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<tr>
<td>Zekry (2010)</td>
<td>IH</td>
<td>OR</td>
<td>0–2: Ref - 6–16: 1.71 (0.28–10.50) NS</td>
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<td></td>
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<td>3–4: 1.54 (0.84–2.84) .17</td>
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<td></td>
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<td>5: 2.47 (1.22–4.99) Sig.</td>
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<td>6–16: 3.45 (1.92–6.19) Sig.</td>
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<td>Zekry (2010)</td>
<td>60 mo</td>
<td>HR</td>
<td>0–2: Ref - 3–4: 4.16 (0.98–1.89) NS</td>
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<td></td>
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<td>5: 2.04 (1.36–3.05) Sig.</td>
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<td>6–16: 2.46 (1.75–3.45) Sig.</td>
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<td>EI</td>
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<tr>
<td>Fabbian (2017)</td>
<td>IH</td>
<td>AUC</td>
<td>0.72 (0.71–0.73) Sig.</td>
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<tr>
<td></td>
<td>OR</td>
<td>0.66 (0.65–0.66) Sig.</td>
<td></td>
</tr>
<tr>
<td>Moore (2017)</td>
<td>IH</td>
<td>AUC</td>
<td>0.80 (0.80–0.80) Sig.</td>
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<tr>
<td></td>
<td>OR</td>
<td>0.80 (0.80–0.80) Sig.</td>
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<td>ICI</td>
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<tr>
<td>Incalzi (1997)</td>
<td>IH</td>
<td>AUC</td>
<td>0.57 Sig.</td>
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<td></td>
<td>Sens.</td>
<td>0.71</td>
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<td>Spec.</td>
<td>0.69</td>
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<tr>
<td></td>
<td>OR</td>
<td>1.77 (1.15–2.72) Sig.</td>
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<tr>
<td></td>
<td>IH</td>
<td>AUC</td>
<td>0.46 NS</td>
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<tr>
<td></td>
<td>Sens.</td>
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<tr>
<td></td>
<td>Spec.</td>
<td>0.64</td>
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<tr>
<td></td>
<td>OR</td>
<td>1.58 (1.03–2.43) Sig.</td>
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</table>

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; IC, 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.

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.34,35,39,42,43 All 3 studies that reported CDS showed that all CDS score did not associate with in-hospital, 12-month, or 60-month mortality risk.30,39,41

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).42,43 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).12,27

The visual inspection of the funnel plot and the Egger regression test indicated insignificant publication bias (P value = 1.34) (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.

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,48 and this is possibly because of the inclusion of specific diseases such as psychiatric morbidities. They are highly prevalent in older inpatients,40,51 but generally have insignificant association with in-hospital mortality,42 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 disease count among inpatients.34,35 By including age in the scoring system, GIC is shown to be better in predicting mortality than CCI, ICED, and disease count among inpatients.34,35,39,42

Among all morbidity measures, ICED is the only one incorporating patients’ physical impairment as one of the components.33 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 hospitalization, 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.23,24 Most of the chronic morbidities were age-related, caused by the progressive deterioration in the function of organs.58 Chronicologic age was also
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

The authors thank Mr. Patrick Condron (senior liaison librarian, Brownless Biomedical Library, Faculty of Medicine, Dentistry and Health Sciences, the University of Melbourne), who greatly assisted with the construction of the search strategy.

Supplementary Data

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

References


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


34. Martínez-Velilla N, Cambra-Contín K, Ibáñez-Berioz B. Comorbidity and prognostic indices do not improve the 5-year mortality prediction of components of comprehensive geriatric assessment in hospitalized older patients. BMC Geriatr 2014;14:64.


57. C.H. Soh et al. / JAMDA 21 (2020) 462–468
Supplementary Material 1. Search Strategy

(1) Medline

1. 
• 
•

2. 
• Cumulative Illness Rating Scale or (CIRS and (comorbidity or "co morbid" or multimorbidity or "multi morbid"))
• mp.

3. 
• Kaplan Feinstein index or (KFI and (comorbidity or "co morbid" or multimorbidity or "multi morbid"))
• mp.

4. 
• Charlson comorbidity index or "Charlson index" or (CCI and (comorbidity or "co morbid" or multimorbidity or "multi morbid"))
• mp.

5. 
• "Deyo Charlson comorbidity index" or "Deyo charlson index" or (DCI and (comorbidity or "co morbid" or multimorbidity or "multi morbid")) or (DCID and (comorbidity or "co morbid" or multimorbidity or "multi morbid"))
• mp.

6. 
• Charlson dyeo comorbidity index or "Charlson dyeo index" or (CDI and (comorbidity or "co morbid" or multimorbidity or "multi morbid")) or (CDICI and (comorbidity or "co morbid" or multimorbidity or "multi morbid"))
• mp.

7. 
• "aggregated diagnosis group" or (ADG and (comorbidity or "co morbid" or multimorbidity or "multi morbid"))
• mp.

8. 
• "adjusted clinical group" or (ACG and (comorbidity or "co morbid" or multimorbidity or "multi morbid"))
• mp.

9. 
• "chronic disease score" or (CDS and (comorbidity or "co morbid" or multimorbidity or "multi morbid"))
• mp.

10. 
• "index of coexistent disease" or (ICED and (comorbidity or "co morbid" or multimorbidity or "multi morbid"))
• mp.

11. 
• "Satariano index" or (SI and (comorbidity or "co morbid" or multimorbidity or "multi morbid"))
• mp.

12. 
• "Elixhauser comorbidity index" or "Elixhauser index" or (EI and (comorbidity or "co morbid" or multimorbidity or "multi morbid")) or (ECI and (comorbidity or "co morbid" or multimorbidity or "multi morbid"))
• mp.

13. 
• "comprehensive prognostic index" or (CPI and (comorbidity or "co morbid" or multimorbidity or "multi morbid"))
• mp.

14. 
• "total illness burden index" or (TIBI and (comorbidity or "co morbid" or multimorbidity or "multi morbid"))
• mp.

15. 
• "american society of anesthesiologists physical status" or (ASA and (comorbidity or "co morbid" or multimorbidity or "multi morbid"))
• mp.

16. 
• "adult comorbidity evaluation 27" or (ACE-27 and (comorbidity or "co morbid" or multimorbidity or "multi morbid"))
• mp.

17. 
• "simplified comorbidity index" or (SCI and (comorbidity or "co morbid" or multimorbidity or "multi morbid"))
• mp.

18. 
• "multipurpose australian comorbidity scoring system" or (MACSS and (comorbidity or "co morbid" or multimorbidity or "multi morbid"))
• mp.

19. 
• "national cancer institute comorbidity index" or (NCI and (comorbidity or "co morbid" or multimorbidity or "multi morbid"))
• mp.

20. 
• "functional comorbidity index" or (FCI and (comorbidity or "co morbid" or multimorbidity or "multi morbid"))
• mp.

21. 
• "geriatric index of comorbidity" or (GIC and (comorbidity or "co morbid" or multimorbidity or "multi morbid"))
• mp.

22. 
• "mortality or death"
• mp.
23 "(Activit of Daily Living" or "Activit of Daily Life" or "ADL" or "tADL" 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 (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 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 (DCI and (comorbid or "co morbid" or multimorbid or "multi morbid")) or (DCI 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 (CDI 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 (Elbhauser comorbidity index or Elbhauser index or (El 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 morb" or "co morbidity" or "mult morb" or "multi morb"))).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 ("functional comorbidity index" or (FCI and (comorbid* or "co morb" or "co morbidity" or "mult morb"))).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)

21 ("geriatric index of comorbidity" or (GIC and (comorbid* or "co morb" or "mult morb"))).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)

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)

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)

24 (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)

25 (geriatric index of comorbidity or (GIC and (comorbid* or "co morb" or "co morbidity" or "mult morb"))).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 ("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)

27 Limit 26 to aged <65– years>

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)

29 26 AND 28

30 27 OR 29

31 Limit 30 to conference abstract status

32 NOT 31

33 Limit 30 to English language

(3) Cochrane

1 ((comorbid* or "co morb" or "mult morb" or "multi morb") 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)

2 (Cumulative Illness Rating Scale" or "CIRS and (comorbid* or "co morb" or "co morbidity" or "mult morb" or "multi morb"))).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 (Kaplan Feinstein index" or (KFI and (comorbid* or "co morb" or "mult morb" or "multi morb"))).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 (charlson comorbidity index or "Charlson index or (CCI and (comorbid* or "co morb" or "mult morb" or "multi morb"))).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 (Deyo charlson comorbidity index or "Deyo charlson index or (DCI and (comorbid* or "co morb" or "mult morb" or "multi morb"))).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)

6 (charlson deyo comorbidity index or "Charlson deyo index or (CDI and (comorbid* or "co morb" or "mult morb" or "multi morb"))).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)

7 (aggregated diagnosis group or (ADG and (comorbid* or "co morb" or "mult morb" or "multi morb"))).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 (adjusted clinical group or (ACG and (comorbid* or "co morb" or "mult morb" or "multi morb"))).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)

9 (chronic disease score" or (CDS and (comorbid* or "co morb" or "mult morb" or "multi morb"))).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 (index of coexistent disease" or (ICED and (comorbid* or "co morb" or "mult morb" or "multi morb"))).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)

11 (satariano index or (SI and (comorbid* or "co morb" or "mult morb" or "multi morb"))).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 (total illness burden index or (TIBI and (comorbid* or "co morb" or "mult morb" or "multi morb"))).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 (Elixhauser comorbidity index or "Elixhauser index or (EI and (comorbid" or "co morb" or "mult morb" or "multi morb"))).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)

14 (comprehensive prognostic index or (CPI and (comorbid" or "co morb" or "mult morb" or "multi morb"))).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)
("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

("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

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[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

("multipurpose australian comorbidity scoring system" or (MACSS and (comorbid* or "co morbid"* or multimorbid* or "multi morbid"*)).mp.
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("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

("functional comorbidity index" or (FCI and (comorbid* or "co morbid"* or multimorbid* or "multi morbid"*)).mp.
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("geriatric index of comorbidity" or (GC 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

(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

(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

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

22 AND 23 86054

24 AND 25 697

Limit 25 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"*)) 63
S6 (DCI and (comorbid* or "co morbid"* or multimorbid* or "multi morbid"*))
S7 "Charlson Deyo comorbidity index" or "Charlson deyo index" or (CDI and (comorbid* or "co morbid"* or multimorbid* or "multi morbid"*)) 145
S8 (CDI and (comorbid* or "co morbid"* or multimorbid* or "multi morbid"*))
S9 "aggregated diagnosis group" or (ADG and (comorbid* or "co morbid"* or multimorbid* or "multi morbid"*)) 6
S10 "adjusted clinical groups" or (ACG and (comorbid* or "co morbid"* or multimorbid* or "multi morbid"*)) 55
S11 "chronic disease score" or (CDS and (comorbid* or "co morbid"* or multimorbid* or "multi morbid"*)) 79
S12 "index of coexistent disease" or (ICED and (comorbid* or "co morbid"* or multimorbid* or "multi morbid"*)) 9
S13 "satariano index" 0
S14 "total illness burden index" or (TIBI and (comorbid* or "co morbid"* or multimorbid* or "multi morbid"*)) 5
S15 "Elxhauser comorbidity index" or "Elxhauser index" 52
S16 "comprehensive prognostic index" or (CPI and (comorbid* or "co morbid"* or multimorbid* or "multi morbid"*)) 12
S17 "adult comorbidity evaluation 27" or (ACE-27 and (comorbid* or "co morbid"* or multimorbid* or "multi morbid"*)) 31
S18 "simplified comorbidity index" or (SCI and (comorbid* or "co morbid"* or multimorbid* or "multi morbid"*)) 240
S19 "multipurpose australian comorbidity scoring system" 69
S20 "national cancer institute comorbidity index" or (NCI and (comorbid* or "co morbid"* or multimorbid* or "multi morbid"*)) 41
S21 mortality or death 328565
S22 "activit* of daily living" or "activit* of daily life" or "ADL" or "iADL" or "functional decline" or (disabil* W3 function) 35185
S23 31 361153
S24 S22 and S23 (Limiters 4916
S25 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 Table 1**

Risk of Bias for Individual Articles

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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

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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.