INTRODUCTION

Life expectancy has increased significantly, but the healthspan, the time spent living without disease, is not increasing proportionally.1-3

The co-existence of two or more chronic diseases is termed multimorbidity4,5 and its effect on patients’ functioning is of increasing interest.6,7 Amongst major western countries, 62% of adults aged 65-74 years and 81.5% of adults aged 85 years and over suffer from multimorbidity.8

To quantify morbidity, morbidity measures such as the Charlson Comorbidity Index (CCI) have been developed to predict clinical outcomes, including readmission to hospital, functional decline, and mortality.8-12 Activities of daily living (ADL) and Instrumental (I) ADL are often used to assess functional performance13,14 and it has been associated with poor quality of life, hospital admission and mortality.15,16 Older patients suffering from functional decline utilise more healthcare resources and are at risk of rehospitalisation and mortality,17 hence the importance of predicting functional decline

Abstract

Objectives: Older adults often suffer from multimorbidity, which results in hospitalisations. These are often associated with poor health outcomes such as functional dependence and mortality. The aim of this review was to summarise the current literature on the capacities of morbidity measures in predicting activities of daily living (ADL) and instrumental activities of daily living (IADL) amongst inpatients.

Methods: A systematic literature search was performed using four databases: Medline, Cochrane, Embase, and Cinahl Central from inception to 6th March 2019.

Keywords included comorbidity, multimorbidity, ADL, and IADL, along with specific morbidity measures. Articles reporting on morbidity measures predicting ADL and IADL decline amongst inpatients aged 65 years or above were included.

Results: Out of 7334 unique articles, 12 articles were included reporting on 7826 inpatients (mean age 77.6 years, 52.7% females). Out of five morbidity measures, the Charlson Comorbidity Index was most often reported. Overall, morbidity measures were poorly associated with ADL and IADL decline amongst inpatients aged 65 years or above were included.

Conclusion: Morbidity measures are poor predictors for ADL or IADL decline amongst older inpatients and follow-up duration does not alter the performance of morbidity measures.

1 | INTRODUCTION

Life expectancy has increased significantly, but the healthspan, the time spent living without disease, is not increasing proportionally.1-3 The co-existence of two or more chronic diseases is termed multimorbidity4,5 and its effect on patients’ functioning is of increasing interest.6,7 Amongst major western countries, 62% of adults aged 65-74 years and 81.5% of adults aged 85 years and over suffer from multimorbidity.8

To quantify morbidity, morbidity measures such as the Charlson Comorbidity Index (CCI) have been developed to predict clinical outcomes, including readmission to hospital, functional decline, and mortality.8-12 Activities of daily living (ADL) and Instrumental (I) ADL are often used to assess functional performance13,14 and it has been associated with poor quality of life, hospital admission and mortality.15,16 Older patients suffering from functional decline utilise more healthcare resources and are at risk of rehospitalisation and mortality,17 hence the importance of predicting functional decline
amongst inpatients.\textsuperscript{16} Morbidity measures are often applied in clinical settings to reflect the severity of patients’ condition. However, the capacity of morbidity measures in predicting ADL and IADL decline remains contentious.\textsuperscript{9,10}

The objective of this systematic review is to summarise the current literature on the capacities of morbidity measures to predict ADL and IADL decline amongst older inpatients.

2 | METHODS

2.1 | Search strategy

A systematic search was performed from inception to 6th March 2019 in four databases: MEDLINE(R), Embase Classic and Embase, Cochrane Central Register of Controlled Trials via the Ovid platform, and CINAHL complete. Keywords included “comorbidity,” “multimorbidity,” “activities of daily living,” and a list of morbidity measures (Table S1). After removing duplicates, articles were screened by two independent reviewers (CHS and SWH). Any conflicts were resolved by a third reviewer (JS or ABM).

2.2 | Eligibility criteria

Longitudinal studies reporting morbidity measures and their association with ADL and IADL amongst inpatients were included. Exclusion criteria were articles in a language other than English, cross-sectional study design, case reports and reviews, mean or median age of the cohort being less than 65 years, and American Society of Anaesthesiologists (ASA) physical status score. ASA score is being excluded because of its subjective assessment of patients’ overall health without objective scoring of diseases.\textsuperscript{18}

2.3 | Quality assessment

The quality of the included articles was assessed by two independent reviewers (SWH and CHS) by an adjusted Newcastle-Ottawa Quality Assessment scale (NOS) (Table S2).\textsuperscript{19} A maximum of eight stars could be awarded to an article for its quality. Articles with six stars or above were deemed to be high quality, three to five stars being fair quality, and two stars or below being poor quality.\textsuperscript{20} A high-quality study indicates a low risk of bias, a fair quality study indicates a medium risk of bias and a poor quality study indicates a high risk of bias.\textsuperscript{21}

2.4 | Data extraction

Data extracted from the included articles included sample size, mean or median age, sex, index disease, morbidity measure, follow-up duration, outcome measure, and association between the morbidity measure used and ADL and/or IADL.

2.5 | Statistical interpretation

A $P$ value of .05 or below was considered significant. If the results were expressed as area under the curve, values between 0.5 and 0.7 were considered as a weak association, 0.7-0.8 as a moderate association, and 0.8-1.0 as a strong association.\textsuperscript{19} Spearman correlation values of .4 or below, .4-.6, and above .6 were considered weak, moderate and strong, respectively.\textsuperscript{22}

3 | RESULTS

A total of 12 800 articles were identified by the search. After duplicate removal, 7334 articles were included for the title and abstract screening and 1312 articles were selected for full-text screening. Twelve articles met the eligibility criteria (Figure 1) including a total of 7826 inpatient (mean age 77.6 years, 52.7% females). Articles reported patient populations admitted to internal medicine wards ($n = 5$),\textsuperscript{23-27} cancer patients ($n = 2$),\textsuperscript{28,29} acute stroke patients ($n = 2$),\textsuperscript{30,31} infectious diseases patients ($n = 1$),\textsuperscript{32} and geriatric rehabilitation patients ($n = 1$)\textsuperscript{33} (Table 1). The follow-up duration ranged from the length of hospital stay to two years post-discharge.

Reported morbidity measures included the CCI ($n = 8$),\textsuperscript{23,24,28,32,34} Cumulative Illness Rating Scale-Geriatrics (CIRS-G) ($n = 2$),\textsuperscript{27,28} Geriatric Index of Comorbidity (GIC) ($n = 3$),\textsuperscript{25,26,33} Functional Comorbidity Index (FCI) ($n = 1$),\textsuperscript{20} and Kaplan Feinstein Index (KFI) ($n = 1$).\textsuperscript{29} Instruments used to measure ADLs included Katz index of Activities of Daily Living (KADL) ($n = 6$),\textsuperscript{23,26,28,29,52,33} Barthel Index of Activities of Daily Living (BADL) ($n = 3$),\textsuperscript{24,25,27} and Instrumental Activities of Daily Living ($n = 3$).\textsuperscript{28-30}
Table 2 shows the reported associations of morbidity measures and ADL/IADL. Two articles reported weak associations (AUC of 0.59 and $R^2$ of .12)\textsuperscript{24,29} between CCI and ADL dependency at discharge, while another article showed a significant association (OR = 4.6, 95% CI: 2.7-7.8).\textsuperscript{31} One article reported the performance of CCI conducted in three different ways: self-report CCI, administrative
data-derived CCI, and combined CCI, and all of them were shown to be weak predictors (AUC = 0.51, 0.54 and 0.52, respectively) for ADL decline 4 months postdischarge. One article showed a moderate association between CCI and IADL decline (AUC = 0.72), while another article showed a signification association (OR = 4.2, 95% CI: 1.2-14.7) between CCI score of three or above and KADL decline at 6 months postdischarge. CCI was insignificantly associated with KADL and IADL decline one- and two-years post-discharge.

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### TABLE 2  
The association between morbidity measures and ADL and IADL decline amongst older inpatients

| Author (year) | Morbidity measures | ADL/IADL | FU | Results | Sig | Assoc |
|---------------|--------------------|----------|----|---------|-----|-------|
| **Follow-up <3 mo** | | | | | | |
| Dent 2015[^24] | CCI | BADL | dcg | AUC | 0.59 (0.52-0.67) | — | Weak |
| | | | | Sens. | 47.7 | — | |
| | | | | Spec. | 61.2 | — | |
| Marengoni 2004[^26] | GIC (65-75 y.o.) | KADL | dcg | OR | 1.1 (0.8-1.6)^[^b] | NS | — |
| | | | | | 1.1 (0.8-1.6)^[^b] | — | — |
| | GIC (75 y.o.+ | | | OR | 1.5 (1.2-2.0)^[^b] | S | — |
| | | | | | 1.5 (1.2-2.0)^[^c] | — | — |
| Maestu 2007[^29] | CCI scores | KADL | dcg | R² | 0.034 | NS | Weak |
| | | IADL | dcg | | 0.122 | NS | Weak |
| | KFI | KADL | dcg | | -0.116 | NS | Weak |
| | IADL | dcg | | | -0.385 | S | Weak |
| Rozzini 2002[^33] | GIC | KADL | dcg | R² | 0.32 | — | Weak |
| Tuttolomondo 2008[^31] | CCI | ADL | dcg | OR | 0:1:1 | S | — |
| | | KADL | dcg | R² | ≥2: 4.6 (2.7-7.8) | — | — |
| Fimognari 2017[^25] | GIC | BADL | dcg | OR | 1:3:1 | NS | — |
| | | KADL | dcg | 3:4:1 | (0.6-2) | — | — |
| Valpato 2007[^27] | CIRS | BADL | dcg | OR | 0:6:1 | S | — |
| | | KADL | dcg | 7:9:2 | (1.1-3.5) | — | — |
| | | KADL | dcg | ≥10:2 | (1.2-3.9) | — | — |
| **3 mo < Follow-up ≤ 6 mo** | | | | | | |
| Susser 2008[^34] | sr-CCI | ADL | 4 mo | AUC | 0.51 (0.44-0.62) | — | Weak |
| | ad-CCI | | | | 0.54 (0.47-0.60) | — | Weak |
| | c-CCI | | | | 0.52 (0.46-0.58) | — | Weak |
| Goto 2018[^32] | CCI | KADL | 6 mo | OR | <3:1 | S | — |
| | | | | | ≥3:4.2 (1.2-14.0) | — | — |
| Tessier 2008[^30] | CCI | IADL | 6 mo | AUC | 0.71 | — | Mod. |
| | FCI | IADL | 6 mo | AUC | 0.71 | — | Mod. |
| **Follow-up >6 mo** | | | | | | |
| Buurman 2011[^23] | CCI | KADL | 1 y | OR[^a] | 1.04 (0.93-1.2) | NS | — |
| Extermann 1998[^28] | CCI | KADL | 2 y | R² | 0.2 | — | Weak |
| | IADL | 2 y | | 0.18 | — | Weak |
| | CIRS-G | KADL | 2 y | | 0.18 | — | Weak |
| | IADL | 2 y | | 0.23 | — | Weak |

Abbreviations: ad-CCI, administrative data-derived CCI; ADL, Activities of Daily Living; Assoc., Association; AUC, Area Under the Curve; BADL, Barthel Index of Activities of Daily Living; c-CCI, combined CCI; CCI, Charlson Comorbidity Index; CIRS-G, Cumulative Illness Rating Score-Geriatric; dcg, discharge; FCI, Functional Comorbidity Index; FU, follow-up; GIC, Geriatric Index of Comorbidity; IADL, Instrumental Activities of Daily Living; KADL, Katz Index of Activities of Daily Living; KFI, Kaplan Feinstein Index; Mod., moderate; NS, Not significant; OR, Odds ratio; R², Coefficient of determination; S, Significant; sens., sensitivity; Sig., Significance; spec., specificity; sr-CCI, self-report CCI; y.o., years old.

[^a]Univariate analysis.

[^b]Model 1 = All patients included;

[^c]Model 2 = Patients with MMSE > 16 included. Results were stated as morbidity score: statistical result (95% confidence interval) or statistical result per one-point increase.
Of the two articles reporting CIRS, a score of 7 or above was shown to be significantly associated with BADL decline at discharge (OR = 2.0, 95% CI: 1.1-3.5),\textsuperscript{27} while another article showed an insignificant association with IADL and KADL 2 years post-discharge ($R^2 = .23$ and $R^2 = .18$, respectively).\textsuperscript{28} Amongst the two articles reporting GIC and KADL decline at discharge, one article reported a moderate association ($R^2 = .32$),\textsuperscript{33} while another article indicated a significant association but only amongst inpatients aged 75 years or above (OR = 1.5, 95% CI: 1.2-2.0).\textsuperscript{26} One article showed an insignificant association between GIC and BADL decline at discharge (OR = 1.1, 95% CI: 0.6-2.0).\textsuperscript{25}

One article reported KFI and its association with ADLs decline at discharge. KFI was shown to be unable to predict KADL ($R^2 = .12$) but predicted IADL moderately ($R^2 = .39$).\textsuperscript{29} For IADL decline 6 months postdischarge, FCI was shown to be a moderate predictor (AUC = 0.72).\textsuperscript{30}

A complete breakdown of the quality assessment of all included studies is shown in Table 3. Overall, the included studies had a fair quality with a mean score of 5.5 out of 8.

### 4 | DISCUSSION

Morbidity measures inconsistently predict ADL and IADL decline amongst older inpatients independent of the follow-up period.

The poor performance of morbidity measures predicting ADL and IADL in older inpatients might be because of the heterogeneity of older adults presenting to the hospital with a wide range of acute diseases. The development of morbidity measures was based on homogenous populations\textsuperscript{35-40} and hence applying these morbidity measures to heterogeneous populations might reduce its performance as a prognostic tool. The wide range of acute diseases resulting in hospitalisation has a huge impact on patients’ physiological reserve that even if patients suffer from the same comorbidities, their functional decline because of the impact of the index disease might be different.\textsuperscript{41} Previous studies including older inpatients have shown that not only typically disabling conditions, such as a stroke or hip fracture, but also exacerbations of cardiorespiratory chronic conditions can lead to functional deterioration.\textsuperscript{42,43} Moreover, the severity of acute diseases is strongly associated with a functional decline.\textsuperscript{25} Hence, including index diseases in morbidity measures could possibly improve the performance as prognostic tools for clinical outcomes.

Despite being the most reported morbidity measure and a predictor for long-term mortality amongst older inpatients,\textsuperscript{44} the CCI predicted functional decline poorly. The CCI includes 22 chronic diseases\textsuperscript{35} and has been validated in predicting mortality amongst older breast cancer patients in 1987. The pre-defined weighted diseases included in the CCI might, therefore, limit the capacity to predict other clinical outcomes. Furthermore, diseases such as sarcopenia\textsuperscript{45} and arthritis\textsuperscript{46} are not part of the CCI and might be better in predicting functional decline.

While the majority of morbidity measures were developed to predict mortality, FCI was developed to predict physical function,\textsuperscript{37} measured by the physical functioning subscale of the Short Form Health Survey (SF-36). The SF-36 is a precursory measure of ADL and IADL decline\textsuperscript{47} and this could, therefore, explain the moderate association shown between FCI and IADL. However, the FCI still requires further validation as it was only reported in one article.

The inter-rater reliability of morbidity measures has been reported to be poor and it could potentially dampen the performance as a prognostic tool.\textsuperscript{48-51} Despite the availability of guidelines to score morbidity measures such as KFI and CIRS, the scoring of the diseases and the disease severity is still prone to subjectivity and

### TABLE 3  Risk of Bias Assessment

| Author (Year) | Sel/3 | Comp/2 | Out/3 | Total |
|---------------|-------|--------|-------|-------|
| Buurman 2011\textsuperscript{23} | * | * | * | 5/8 |
| Dent 2015\textsuperscript{24} | * | * | * | 5/8 |
| Extermann 1998\textsuperscript{28} | * | * | ** | 5/8 |
| Goto 2018\textsuperscript{32} | * | * | * | 3/8 |
| Marengoni 2004\textsuperscript{26} | * | * | * | 8/8 |
| Maestu 2007\textsuperscript{29} | * | * | * | 3/8 |
| Rozzini 2002\textsuperscript{33} | * | * | * | 6/8 |
| Susser 2008\textsuperscript{34} | * | * | * | 5/8 |
| Tessier 2008\textsuperscript{30} | * | * | * | 5/8 |
| Tuttolomondo 2008\textsuperscript{21} | * | * | * | 8/8 |
| Fimognari 2017\textsuperscript{25} | * | * | * | 7/8 |
| Valpato 2007\textsuperscript{27} | * | * | * | 6/8 |

Note: Refer to the adapted NOS (Table S2) in Appendices for the criteria to score Risk of Bias for the studies.

Abbreviations: Comp: Comparability; Out: Outcome; Sel: Selection.
this could be because of varying quality in reporting the medical history.\textsuperscript{52,53} The medical history is crucial in assessing the severity of diseases. A systematic review has shown that medical history information is frequently missing in the electronic medical record, which is a major concern in clinical practice.\textsuperscript{54} Poor organisation of contents, missing or conflicting information in medical history could lead to the misinterpretation of the severity of diseases and disagreement between clinicians.\textsuperscript{55} Moreover, the inter-rater reliability was shown to not improve, despite clinicians using the morbidity measure over time.\textsuperscript{51}

While morbidity measures are poor predictors for ADL and IADL decline, other health domains such as physical performance and cognitive function are strongly associated with functional decline.\textsuperscript{56,56} The Short Physical Performance Battery (including gait speed, chair stand, and balance test) is an assessment tool used to evaluate physical performance of the lower extremity\textsuperscript{57} and it strongly predicts functional decline amongst older inpatients.\textsuperscript{58,59} Global cognitive function, measured with tools such as the Mini-Mental State Examination and Montreal Cognitive Assessment, is also a strong predictor for a functional decline.\textsuperscript{60-62} Incorporation of physical performance and cognitive function into morbidity measures might improve the predictive capacity of morbidity measures in predicting a functional decline.

To the best of our knowledge, this is the first systematic review summarising the association of morbidity measures with ADL and IADL decline amongst inpatients. The search strategy for this review was comprehensive to include a wide variety of morbidity measures used in older hospitalised patients.\textsuperscript{63} Only a limited number of articles addressed the use of morbidity measures predicting ADL and IADL decline. Because of the differences in statistical analysis and cut-off values chosen for each morbidity measure, a meta-analysis could not be performed.

5 | CONCLUSION

Overall, morbidity measures are poor predictors for ADL and IADL decline amongst older inpatients. A prognostic tool for inpatients' functional decline is crucial as identifying those who are at higher risk of functional decline could guide tailored interventions to improve functional outcomes.

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DISCLOSURES

The authors report no conflict of interest.

AUTHOR CONTRIBUTIONS

Cheng Hwee Soh: Concept/design, Screening for the eligible article, Data extraction, Data analyses/interpretation, Drafting article.

Syed Wajih Ul Hassan: Concept/design, Screening for the eligible article, Data extraction. Julian Sacre: Concept/design, Resolving conflicts, Critical revision of the article. Wen Kwang Lim: Critical revision of the article, Approval of article. Andrea B Maier: Concept/design, Resolving conflicts, Critical revision of article, Approval of article.

DATA AVAILABILITY STATEMENT

All data generated or analysed in this study are extracted from the published articles included in this systematic review.

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**SUPPORTING INFORMATION**

Additional supporting information may be found online in the Supporting Information section.

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