Supplementary File 1. Database Search Terms

Subject headings	Chronic Kidney Failure Kidney Failure Chronic Renal Insufficiency Renal Insufficiency Kidney Disease Kidney Dysfunction Mild renal impairment Moderate renal impairment Severe renal impairment Subclinical renal impairment Renal replacement therapy Hemodialysis Peritoneal Dialysis Continuous Ambulatory Peritoneal DIalysis Kidney transplantation Kidney graft	Multimorbidity Multiple Chronic Conditions	Humans Adult
Textwords	Chronic kidney or chronic renal CKF, CKD, CRF or CRD Predialysis or pre-dialysis Renal failure or kidney failure Kidney disease Renal insufficienc* Hemodialysis or Haemodialysis Hemodiafiltration or haemodiafiltration Dialysis Endstage renal or endstage kidney Peritoneal dialysis CAPD or APD or CCPD or PD Kidney Transplant	Multimorbid* or multi morbid Condition count Multiple condition or multicondition or multi condition Multiple disease or multidisease or multi disease Multiple disorder or multidisorder or multi disorder Multiple comorbidities or multiple co morbidities Discordant comorbidities or concordant comorbidities	Adult* or aged* or elderly

Supplementary File 2. NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability

Selection

1) Representativeness of the exposed cohort ie chronic kidney disease (CKD) with multimorbidity (MM)
   a) truly representative of the average CKD/MM population in the community *
   b) somewhat representative of the average CKD/MM population in the community *
   c) selected group of users eg only one disease group
   d) no description of the derivation of the cohort

2) Selection of the unexposed cohort ie CKD without MM
   a) drawn from the same community as the exposed cohort *
   b) drawn from a different source
   c) no description of the derivation of the non exposed cohort
   d) no control group

3) Ascertainment of CKD/MM status
   a) secure record (eg medical records) *
   b) structured interview *
   c) written self report
   d) no description

4) Demonstration that outcomes were not present at start of study
   a) yes *
   b) no

Comparability

1) Comparability of cohorts on the basis of the design ie are exposed/non-exposed individuals matched or do the authors actively control for confounding factors?
   a) study controls for ischaemic heart disease *
   b) study controls for additional factor(s) *
   Statements of no differences between groups or that differences were not statistically significant are not sufficient for establishing comparability.

Outcomes

1) Assessment of outcome(s)
   a) independent blind assessment *
   b) record linkage *
   c) self report
   d) no description

2) Was follow-up long enough ie > 1 year
   a) yes *
   b) no

3) Adequacy of follow up of cohorts
   a) complete follow up - all subjects accounted for *
   b) subjects lost to follow up unlikely to introduce bias - small number lost to follow up, or description provided of those lost) *
   c) high lost to follow up rate and no description of those lost
   d) no statement

Total stars /8

Supplementary File 3. Results from included studies

Reference	Effect size	CCI groups	Effect size (95% Confidence Interval)
CATEGORICAL PRESENTATION OF EFFECT SIZE			
Chae 2010	HRs	**A. Standard CCI variables**	
		Quartile 1 (CCI 2)	Ref
		Quartile 2 (CCI 4-5)	9.22 (3.29-25.84)
		Quartile 3 (CCI 6)	16.77 (5.97-47.11)
		Quartile 4 (CCI 7-11)	22.37 (8.08-61.93)
		B. CCI excluding age and diabetes	
		Tertile 1 (CCI 2)	Ref
		Tertile 2 (CCI 3)	1.39 (1.01-2.05)
		Tertile 3 (CCI 4-8)	1.98 (1.25-3.14)
Wu 2005	HRs	**CCI excluding age**	
		CCI < 5	Ref
		CCI ≥ 5	2.88 (1.90-4.37)
Grosso 2012	HRs	**Modified CCI** 1 point: myocardial infarction, heart failure, peripheral vascular disease, COPD, connective tissue disease or mild liver disease 2 points: diabetes mellitus, cerebrovascular accident, solid tumour or leukaemia	
		CCI ≤ 1	Ref
		CCI > 1	3.87 (1.06-14.06)
Rattanasompattikul 2012	HRs	**CCI excluding age and renal disease**	
		Quartile 1 (CCI 0)	Ref
		Quartile 2 (CCI 1-2)	1.72 (1.26-2.36)
		Quartile 3 (CCI 3)	2.60 (1.13-3.26)
		Quartile 4 (CCI 4-9)	3.40 (2.41-4.79)
Wu 2013	HRs	**CCI excluding age**	
		CCI ≤ 3	Ref
		CCI 4-6	2.49 (2.35-2.63)
		CCI 7-9	3.53 (3.34-3.73)
		CCI 10-12	3.66 (3.45-3.88)
		CCI 13-15	4.12 (3.84-4.42)
		CCI > 15	4.42 (4.02-4.86)

CONTINUOUS PRESENTATION OF EFFECT SIZES			
Beddhu 2000	HRs	**Modified CCI** 1 point: coronary artery disease, heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, connective tissue disorder, peptic ulcer disease, mild liver disease, diabetes 2 points: hemiplegia, moderate or severe renal disease, diabetes with end-organ damage, any tumour, leukaemia, lymphoma 3 points: moderate or severe liver disease 6 points: metastatic solid tumour, AIDS	
		Each increase in CCI	1.24 (1.11-1.39)
Fried 2001	Relative risk	**Standard CCI variables**	
		Each increase in CCI	1.54 (1.36-1.74)
Park 2015	HRs	**A. Standard CCI variables**	
		Each increase in CCI	1.42 (1.39-1.45)
		B. Modified CCI in incident haemodialysis patients Details not provided	
		Each increase in CCI	1.72 (1.66-1.78)
Shum 2013	HRs	**ESRD Modified CCI**	
		Each increase in CCI (PD group only)	1.36 (1.18-1.56)
CONTINUOUS AND CATEGORICAL PRESENTATION OF EFFECT SIZES			
Fernandez 2019	HRs	**ESRD Modified CCI**	
		Each increase in CCI	1.08 (1.03-1.13)
		Low comorbidity burden CCI 0-1	Ref
		High comorbidity burden CCI ≥ 2	1.38 (1.01-1.89)

Results from studies using Charlson Comorbidity Index (CCI) as Multimorbidity Measure. HR; hazard ratio. COPD; Chronic Obstructive Pulmonary Disease. AIDS; Acquired Immune Deficiency Syndrome. PD; peritoneal dialysis.

Reference	Effect size	Conditions and groups	Effect size (95% Confidence Interval)
CATEGORICAL PRESENTATION OF EFFECT SIZE			
Bowling 2016	HRs	22 conditions: hypertension, hyperlipidemia, coronary heart disease, atrial fibrillation, heart failure, peripheral arterial disease, arthritis, osteoporosis, gout, diabetes, hypothyroidism, cancer, prostate cancer, anaemia, cerebrovascular disease, depression, dementia, epilepsy, Parkinson's disease, gastroesophageal reflux disease/peptic ulcer disease, benign prostatic hypertrophy and COPD/asthma	
		1	Ref
		2	0.95 (0.93-0.97)
		3	1.03 (1.01-1.05)
		4	1.24 (1.21-1.26)
		5	1.43 (1.39-1.47)
		≥ 6	1.72 (1.64-1.80)

Fraser 2015	HRs	11 conditions: hypertension, diabetes, ischaemic heart disease, heart failure, peripheral vascular disease, cerebrovascular disease, chronic respiratory disorder, depression, chronic painful condition, thyroid disorder and anaemia	
		0-1	Ref
		2	2.31 (1.36-3.94)
		≥ 3	4.58 (2.85-7.38)
Lee 2018	10-year survival rates	12 conditions: diabetes, hypertension, gout, heart failure, ischemic heart disease, cerebrovascular disease, liver disease, malignancy, tuberculosis, hyperlipidaemia, anaemia and connective tissue disease	
		0	93.7%
		1	94.3%
		2	92.9%
		≥ 3	92.7%
Tonelli 2015	HRs	29 conditions: alcohol misuse, asthma, atrial fibrillation, lymphoma, non-metastatic cancer, metastatic cancer, heart failure, chronic pain, COPD, chronic hepatitis B, cirrhosis, severe constipation, dementia, depression, diabetes, epilepsy, hypertension, hypothyroidism, inflammatory bowel disease, irritable bowel syndrome, multiple sclerosis, myocardial infarction, Parkinson's disease, peptic ulcer disease, peripheral vascular disease, psoriasis, rheumatoid arthritis, schizophrenia, and stroke or transient ischemic attack	
		0	Ref
		1	1.57 (1.50-1.63)
		2	2.34 (2.24-2.44)
		3	3.43 (3.29-3.58)
		4	4.81 (4.60-5.02)
		≥ 5	7.74 (7.43-8.07)
CONTINUOUS PRESENTATION OF EFFECT SIZES			
Davies 1995	HRs	**Development of the Stoke Comorbidity Grade** 11 conditions: ischaemic heart disease, peripheral vascular disease, cerebrovascular disease, left ventricular dysfunction, diabetes mellitus, systemic collagen vascular disease, COPD, pulmonary fibrosis, pulmonary tuberculosis, asthma and cirrhosis Low grade: 0 conditions Intermediate grade: 1-2 conditions High grade: ≥ 3 conditions	
		Each increase in grade	2.66 (1.55-4.55)
Davies 2002	Relative risk	**Stoke Comorbidity Grade**	
		Each increase in grade	2.4 (1.4-4.1)
Ellam 2008	Narrative	**Stoke Comorbidity Grade**	"No statistically significant effect on survival"
Wong 2007	HRs	**Stoke Comorbidity Grade**	
		Each increase in grade	2.53 (1.32-4.83)
Lhotta 2003	HRs	Five conditions: diabetes, heart failure, coronary artery disease, cerebrovascular disease and peripheral vascular disease	
		Each increase in comorbidity score	1.78 (1.32-2.40)

Results from studies using Condition Count as Multimorbidity Measure. COPD; chronic obstructive pulmonary disease. HR; hazard ratio.

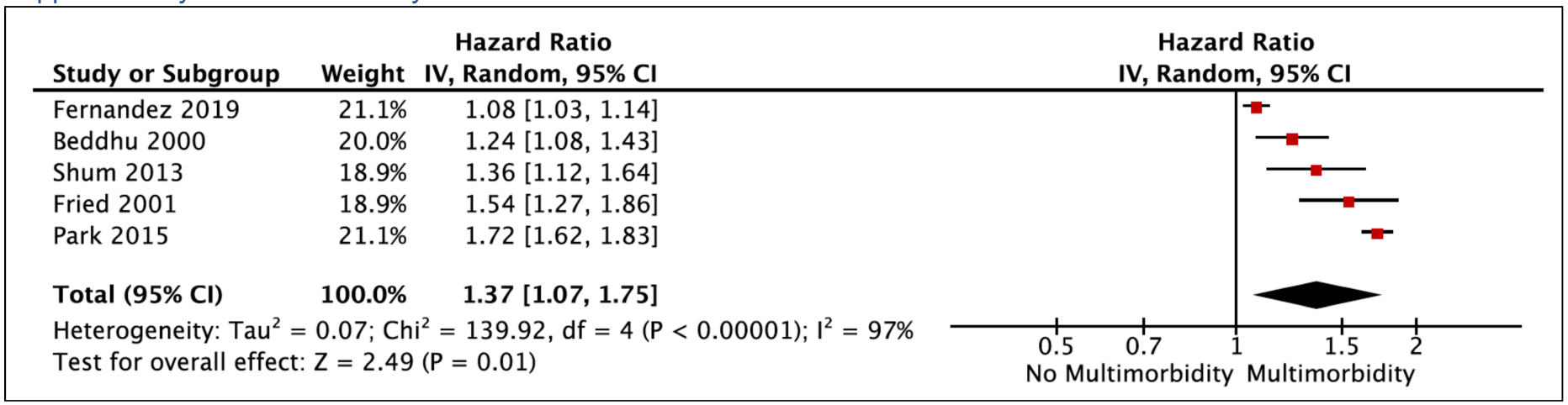
Reference	Effect size measure	Multimorbidity measure and groups	Effect size (95% Confidence Interval)
Chandna 1999	HRs	**Comorbidity severity score (CSS)** Cardiac score, according to New York Heart Association, respiratory disease score (1-4), cerebrovascular disease score (1-4), peripheral vascular disease score (1-4), cirrhosis (4), and malignancy score (1-4)	
		Each increase in CSS	1.238 (1.145-1.338)
Chandna 2010	HRs	**Comorbidity severity score**	
		Low comorbidity (CSS ≤ 4)	Ref
		High comorbidity (CSS > 4)	1.823 (1.255-2.650)
Pieloch 2015	HRs	**Kidney Transplant Morbidity Index**	
		0	Ref
		1	1.85 (1.45-2.36)
		2	3.11 (2.46-3.94)
		3	5.00 (3.96-6.31)
		4	7.37 (5.83-9.32)
		5	9.41 (7.41-11.94)
		6	12.15 (9.45-15.63)
		≥ 7	13.03 (9.68-17.54)
Ritchie 2009	HRs	**Heart failure, CKD and diabetes**	
		Heart failure and CKD	Ref
		Heart failure, CKD and diabetes	1.25 (1.07-1.46)

Results from studies using other Multimorbidity Measures. HR; hazard ratio. CKD; chronic kidney disease.

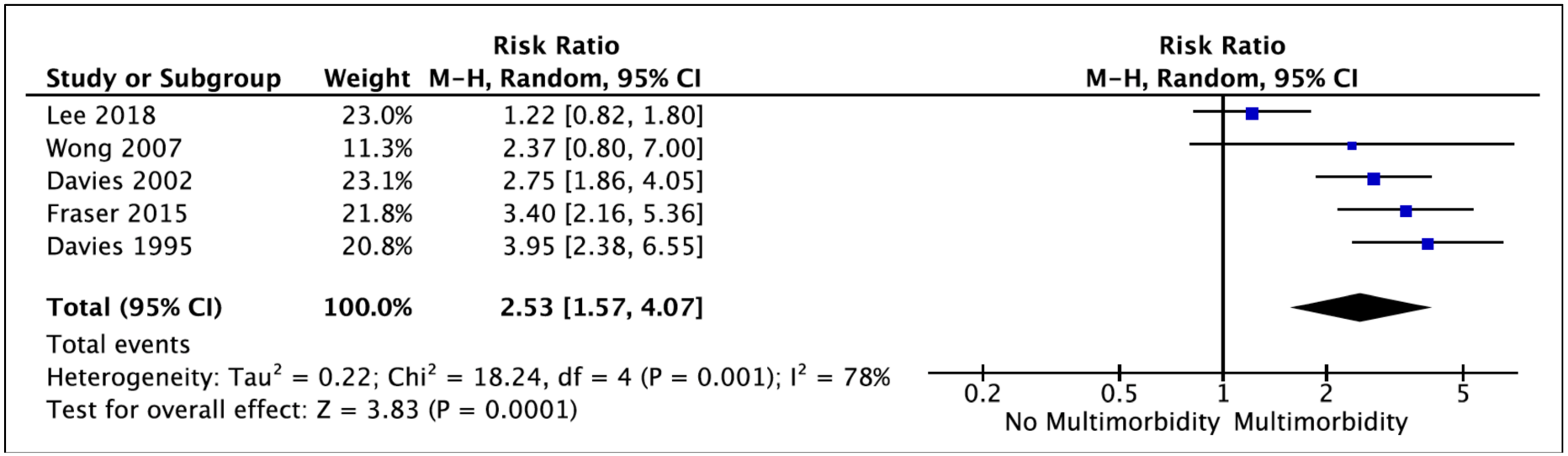
Reference	Scores studied	Presentation of effect size
Hemmelgarn 2003	CCI Development of ESRD modified CCI	Kaplan-Meier curves
Di Iorio 2004	CCI Development of CCI modified for haemodialysis patients	Relative risk, 5.5 for CCI
van Manen 2002	CCI Khan index Davies index Development of a new index	Kaplan-Meier curves

Studies that analyse different Multimorbidity Measures. CCI; Charlson Comorbidity Index

Supplementary File 4. Meta-analysis with random effects models



Mortality risk for Charlson Comorbidity Index as a continuous variable (Random Effects Model)



Mortality risk for patients with multimorbidity (Random Effects Model)

Supplementary File 5. Risk of bias: Results from Newcastle Ottawa Scale

Reference	Selection				Comparability	Outcome assessment			Quality score
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	
Beddhu 2000		✸	✸	✸	✸	✸	✸		6
Bowling 2016	✸	✸	✸	✸	✸	✸	✸		7
Chae 2010		✸	✸	✸	✸	✸	✸		6
Chandna 1999		✸	✸	✸	✸	✸	✸		6
Chandna 2010		✸	✸	✸		✸	✸		5
Davies 1995		✸	✸	✸	✸	✸	✸		6
Davies 2002		✸	✸	✸	✸	✸	✸		6
Di Iorio 2004		✸	✸	✸	✸	✸	✸		6
Ellam 2008		✸	✸	✸		✸	✸		5
Fernandez 2019		✸	✸	✸	✸	✸	✸		6
Fraser 2015		✸	✸	✸	✸	✸	✸		6
Fried 2001		✸	✸	✸	✸	✸	✸		6
Grosso 2012		✸	✸	✸	✸	✸	✸		6
Hemmelgarn 2003		✸	✸	✸	✸	✸	✸	✸	7
Lee 2018	✸	✸	✸	✸	✸	✸	✸		7
Lhotta 2003		✸	✸	✸	✸	✸	✸		6
Park 2015		✸	✸	✸	✸	✸	✸		6
Pieloch 2015		✸	✸	✸	✸	✸	✸		6
Rattanasompattikul 2012		✸	✸	✸	✸	✸	✸		6
Ritchie 2009		✸	✸	✸	✸	✸	✸		6
Shum 2013		✸	✸	✸	✸	✸	✸		6
Tonelli 2015	✸	✸	✸	✸	✸	✸	✸		7
van Manen 2002		✸	✸	✸	✸	✸	✸		6
Wong 2007		✸	✸	✸	✸	✸	✸		6
Wu 2005		✸	✸	✸	✸	✸	✸		6
Wu 2013		✸	✸	✸	✸	✸	✸		6

Table 3. Newcastle Ottawa Scale. 1. Representativeness of the exposed cohort. 2. Selection of the non-exposed cohort. 3. Ascertainment of chronic kidney disease/multimorbidity status. 4. Demonstration that outcomes were not present at start of study. 5. Comparability of cohorts on the basis of the design. 6. Assessment of outcome(s). 7. Was follow-up long enough. 8. Adequacy of follow up of cohort.