Supplementary file to *Multimorbidity in South Africa: A systematic review of prevalence studies*

Appendix 1: PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix 2
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6

Roomaney RA, *et al. BMJ Open* 2021; 11:e048676. doi: 10.1136/bmjopen-2021-048676

Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	NA
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	NA
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	NA
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	8
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	9
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	9
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	14
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	NA
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	NA
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	NA

DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	16
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	17
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	18
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	19

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

Appendix 2: Search Strategy

Study search output for multimorbidity study- December 2020

Search number	Query	Results
5	#4 NOT (animals[mh] NOT humans[mh])	1,106
4	(#4) AND (prevalence OR "prevalence"[mh] OR epidemiology OR endemic OR "epidemic outbreaks")	1,145
3	#1 and #2	1506
2	South Africa[mh] OR South Africa*[tiab] OR RSA [tiab] OR Africa, Southern[mh:noexp] OR Southern Africa[tiab]	68485
1	Multimorbidity OR multi-morbidity OR multimorbidity[tiab] OR multi morbidities OR multi morbidities OR multimorbidity[mh] OR multimorbidit* OR multimorbid OR multi-morbidit* OR "multiple morbidities" OR "multiple-morbidit*" OR co-morbid[tiab] OR co-morbid* OR comorbidity OR co-occur OR coexist OR co-exist OR multi-disease* OR multi-disease*	394636

Scopus database search output: 91 document reports

(TITLE-ABS-KEY (multistability OR multi-morbidity OR comorbidities OR multi-morbidities OR multimorbidit* OR multi-morbidit*) AND TITLE-ABS-KEY ("South Africa*" OR rsa OR "Southern Africa") AND TITLE-ABS-KEY (prevalence OR epidemiology OR endemic OR "epidemic outbreaks")) AND DOCTYPE (ar)

Web of science search output: 31 document reports

TOPIC: (multimorbidity OR multi-morbidity OR multimorbidities OR multi-morbidities OR multimorbidit* OR multi-morbidit*) AND TOPIC: ("South Africa" OR rsa OR "Southern Africa") AND TOPIC: (prevalence OR epidemiology OR endemic OR "epidemic outbreaks"). Indexes: SCI-EXPANDED.

Appendix 3: Additional information on each study

Study	Study population and size	Year	Location	Study type	Conditions included	Definition of MM used	Why were conditions included?	Factors associated with multimorbidity (MM)
Afshar, Roderick, Kowal et al. (2015). *Multimorbidity and the inequalities of global ageing: a cross-sectional study of 28 countries using the World Health Surveys*	N= 2629. Adults 18 years and older in the 2003 World Health Survey.	2003	South Africa. (56.3% urban)	Population-based survey. WHS 2003.	• Angina / Angina Pectoris (Heart Disease) • Arthritis • Asthma • Depression • Diabetes • Schizophrenia or Psychosis	The presence of two or more **chronic** diseases.	Chronic conditions were chosen in this survey to reflect health system coverage and corresponded to conditions known to affect older people.	- Increasing country GDP - Increasing age - Lower education
Garin, Koyanagi, Chatterji et al (2016). *Global Multimorbidity Patterns: A Cross-Sectional, Population-Based, Multi-Country Study*.	N = 3836. Adults older than 50 years in the WHO Study on global AGEing and adult health (SAGE) 2007.	2007-2008	South Africa. Not stated if urban or rural.	Population based survey. SAGE 2007.	• Angina` • Arthritis • Asthma • Cataract • Cognitive impairment' • COPD • Depression` • Diabetes • Edentulism • Hypertension* • Obesity* • Stroke	Having at least 2 of 12 **chronic** conditions included in the study.	Selected 12 chronic conditions with high prevalence in most settings that significantly affect health	- Generally increased with age but decreased in people over 60 years - Being female - Lower education - Being separated/ divorced/widowed - Living in a rural area
Weimann, Dai, Oni (2016). *A cross-sectional and spatial analysis of the prevalence of multimorbidity and its association with socioeconomic disadvantage in South Africa: A comparison*	N=18526 (2008) & N=20015 (2012) Adults (age 15+ years) sub-sample from National Income Dynamic Survey Wave 1	2008, 2012	South Africa. Urban and rural areas included.	Population based survey. NIDS 2008 & 2012.	• Diabetes • HIV • Hypertension (self-reported or measured) • TB	The presence of two or more **chronic** health conditions existing simultaneously in an individual.	Hypertension and diabetes were included due to being the most prevalent non-communicable diseases. HIV and TB were included to monitor trends over time.	- Increasing age - Being female - Socioeconomic deprivation - Obesity - Living in urban areas - Living in Kwa-Zulu Natal or Eastern Cape provinces (Province) - Being Indian/Asian (Race)

between 2008 and 2012.	(2008) and 3 (2012).							
Ghose, Razak (2017). *Memory and Learning Complaints in Relation to Depression among Elderly People with Multimorbidity*.	N=422. Adults aged 50+ infected and / or affected by HIV in the SAGE WOPS 2010.	2010	Hlabisa subdistrict, Kwa-Zulu Natal. Not stated if urban or rural.	Population based survey. SAGE WOPS 2010.	• Arthritis • Asthma • Cancer • Chronic lung disease • Diabetes • Heart Disease • Hypertension • Stroke	>1 condition	Not clearly stated.	- Memory complaints in women - Being diagnosed with depression
van Heerden, Barnabas, Norris et al (2017). *High prevalence of HIV and non-communicable disease risk factors in rural KwaZulu-Natal, South Africa*.	N=570. Participants in a cohort study of a package of HIV testing, referral to care and follow-up visits to increase engagement in HIV care	Nov 2011 - Jun 2012	KwaZulu-Natal. Rural.	Cross-sectional study. Community based.	• Depression • HIV*[1] • Hyperglycaemia* • Hyperlipidaemia* • Hypertension* • Obesity*	Not reported.	Links to study objectives to investigate HIV and NCD risk factors.	Not reported
Chang, Gómez-Olivé, Payne et al. (2019). *Chronic multimorbidity among older adults in rural South Africa*	N = 3889. Adults enrolled in the Health and Ageing in Africa: A longitudinal study of an INDEPTH Community in South Africa (HAALSI) Programme.	2014-2015	Agincourt Health and Demographic Surveillance System, Bushbuckridge subdistrict, Mpumalanga. Rural.	Cross sectional study. Community based.	• Alcohol Dependence` • Anaemia* • Angina` • Chronic Bronchitis • Depression` • Diabetes* • Dyslipidaemia* • HIV* • Hypertension* • Post-Traumatic Stress Disorder`	Two definitions of multimorbidity were applied: the presence of more than one condition and the presence of more than one category of conditions (cardiometabolic conditions, mental disorders, HIV and anaemia).	Based on selection of conditions in sister studies, known health conditions in area and based on consultation with community.	- Increased with age until 69 years and then decreased - Being separated/divorced or widowed - HIV associated with higher levels of MM using the second definition - Physical functioning and well-being and self-rated health were worse with increasing numbers of conditions and categories ---------- - Living with more people (household size) decreased odds of multimorbidity

[1] HIV is measured but data on HIV is presented as a sub-group and thus excluded in this analysis

								- No relationship between wealth and multimorbidity - Females has higher levels of multimorbidity but it was not significantly different
Sharman, Bachmann (2019). *Prevalence and health effects of communicable and non- communicable disease comorbidity in rural KwaZulu-Natal, South Africa.*	N= 47 334. Participants 15 years and older enrolled in the population-based HIV and health surveillance study, conducted by the Africa Health Research Institute.	2009-2015	Umkhanyakude district of rural KwaZulu-Natal. Rural.		• Hypertension (self-reported or on treatment) • Diabetes • TB within past 12 months • HIV (measured or on treatment)*	Proportion of participants with two or more conditions *(termed as co-morbidity)*	Based on research gap where few studies examine the prevalence of communicable and non-communicable diseases.	- Increasing age were associated with MM - Self-reported health poorer with multimorbidity
Lalkhen, Mash (2015). *Multimorbidity in non-communicable diseases in South African primary healthcare.*		2010	Primary healthcare facilities in the Western Cape, North West, Northern Cape and Limpopo. Rural and urban.	Cross sectional study. Facility based.	• Asthma* • COPD* • Diabetes* • Epilepsy* • Hypertension* • Osteoarthritis* • And other diseases	The presence of two or more diseases.	Study aimed to examine non-communicable diseases. All conditions recorded.	Not reported
Roche, de Vries (2017). *Multimorbidity in a large district hospital: A descriptive cross-sectional study.*	N= 491. Consecutive admissions to an internal medicine department of a large district hospital.	2015	District hospital, Cape Town. Urban.	Cross sectional study. Facility based-Internal medicine department	• Anaemia* • Asthma* • Bronchiectasis* • Cancer* • Cardiac failure* • Cerebrovascular accident* • COPD* • Cor pulmonale* • Current TB* • Deep vein thrombosis* • Delirium*	More than one disease concurrently.	Not clearly stated but appears to include all conditions that were seen in the district hospital.	- Length of stay not related to multimorbidity. - Lifestyle risk factors were not associated with multimorbidity.

					• Diabetes* • Dilated cardiomyopathy* • Dyslipidaemia* • Epilepsy* • Gastroenteritis* • HIV* • Hypertension* • Ischaemic heart disease* • Lower respiratory tract infection* • Pneumonia* • Renal failure* • Sepsis* • Urinary tract infection*			
Oni, Youngblood, Boulle et al. (2015). *Patterns of HIV, TB, and non-communicable disease multi-morbidity in peri-urban South Africa- a cross sectional study*.	N=14364. Chronic disease patients (adults) with at least one disease (HIV, TB, diabetes, and hypertension) identified on electronic databases.	Sep 2012 - May 2013	Michael Mapongwana clinic, Khayelitsha, Cape Town. Peri-urban area.	Facility based RHIS. Western Cape Department of Health Data Repository, electronic prescription system.	• Diabetes* • HIV* • Hypertension* • TB*	Coexistence of more than one **chronic** condition in one person.	Informed by the research gap between NCDs and communicable diseases.	- Increasing age associated with MM. --- - No significant differences between males and females.

Appendix 4: Common disease conditions / disease clusters

Study	Year	Conditions included	Common disease clusters identified in South Africa
Garin, et al (2016)	2007-2008	• Angina` • Arthritis • Asthma • Cataract • Cognitive impairment' • COPD • Depression` • Diabetes • Edentulism • Hypertension* • Obesity* • Stroke	**Disease Combinations** - Hypertension was commonly present with diabetes, stroke, angina, cataract and all other conditions. - Obesity and diabetes commonly co-occurred.
Weimann et al (2016)	2008, 2012	• Diabetes • HIV • Hypertension **(self-reported or measured)** • TB	Of the extrapolated 8,6 million people included, 89.2% had a single condition, 10.5% had two conditions, and 0.2% had three conditions. **Disease Combinations (2008):** **Two disease conditions:** 1) Diabetes and Hypertension (70.8%) 2) TB and Hypertension (13.2%) 3) HIV and Hypertension (10.8%) 4) HIV and TB (3.9%) 5) TB and Diabetes (0.8%) 6) HIV and Diabetes (0.3%) **Three disease conditions:** 1) TB, Diabetes and Hypertension (63.9%) 2) Hypertension, HIV and TB (36.0%)
Chang et al (2019)	2014-2015	• Alcohol Dependence` • Anaemia* • Angina` • Chronic Bronchitis • Depression` • Diabetes* • Dyslipidaemia* • HIV* • Hypertension* • Post-Traumatic Stress Disorder`	Disease clusters limited to more than 1.5% of study population. **Disease profile and clusters** - Hypertension only (11.7%) - Hypertension and Dyslipidaemia (9.4%) - None (6.9%) - Hypertension and Anaemia (6.4%) - Hypertension and Dyslipidaemia and Anaemia (4.7%) - Dyslipidaemia (3.9%) - Anaemia (3.8%) - Anaemia and HIV (2.6%) - Hypertension and Anaemia and HIV (2.6%) - HIV (2.4%) - Dyslipidaemia and Anaemia (2.1%) - Dyslipidaemia and Anaemia and HIV (2.0%) - Hypertension and HIV (1.9%) - Hypertension and Dyslipidaemia and Diabetes (1.8%) - Hypertension and Depression (1.7%) - Dyslipidaemia and HIV (1.6%) - Hypertension and Dyslipidaemia and HIV (1.6%)

Study	Year	Conditions included	Common disease clusters identified in South Africa
Sharman, Bachmann (2019).	2009 - 2015	• Hypertension (self-reported or on treatment) • Diabetes • TB within past 12 months • HIV (measured or on treatment)*	Overlapping NCD and infectious disease co-morbidity was seen most frequently in adults older than 40 years where chronic NCDs increase alongside HIV. **Disease Clusters in 2015** (only percentages >2% shown. Percentages may overlap and thus not add up to 100%) - **In participants with hypertension** • Hypertension only (61.3%) • Diabetes (16.8%) • HIV (15.2%) • TB (1.6%) • HIV, diabetes and TB (2.5%) - In participants with diabetes: • Diabetes only (9.7%) • Hypertension (70.5%) • Hypertension and HIV (10.6%) • HIV (3.9%) • TB, HIV and hypertension (2.7%) - In participants with HIV • HIV only (75.9%) • Hypertension (12.1%) • TB (7.6%) • Hypertension, diabetes and TB (2.0%) - In participants with TB • TB only (25.6%) • HIV (61.0%) • hypertension (8.4%) • HIV and hypertension (8.3%) - In all participants over age 40 years • 34% had none of the four diseases examined. • Diabetes and hypertension (9.8%) • Hypertension, HIV and diabetes (6.5%)
Lalkhen et al (2015).	2010	• Asthma* • COPD* • Diabetes* • Epilepsy* • Hypertension* • Osteoarthritis*	- Hypertension and diabetes were the most common combination. - Hypertension was commonly comorbid with diabetes, epilepsy, asthma and COPD. **Disease combinations (only clusters larger than 2% listed)** - Of those that hypertension (n=3219), people also had: • Diabetes (18.2%) • Osteoarthritis (8.0%) • Asthma (3.6%) • COPD (2.1%) • Ischaemic heart disease (2.1%) - Of those that had diabetes (n=946), people also had: • Hypertension (63.1%) • Osteoarthritis (4.3%) - Of those that had epilepsy (n=375), people also had: • Hypertension (14.4%) • Osteoarthritis (2.4%) - Of those that had ashtma (n=485), people also had: • Hypertension (28.7%) • Osteoarthritis (5.8%)

Study	Year	Conditions included	Common disease clusters identified in South Africa
			• Diabetes (5.4%) • Acute bronchitis (4.7%) • Allergic rhinitis (3.1%) • TB (2.2%) - Of those that had COPD (n=140), people also had: • Hypertension (47.9%) • Osteoarthritis (12.1%) • Diabetes (9.3%) • TB (6.4%) • Epilepsy (3.6%) • Ischaemic heart disease with angina (3.6%) • TB (2.1%) • Lipid dysfunction (2.1%) • Tobacco abuse (2.1%) • Ischaemic heart disease with angina (2.1%) - Of those that had Osteoarthritis (n=530), people also had: • Ischaemic heart disease (2.3%)
Oni et al (2015).	Sep 2012 - May 2013	• Diabetes* • HIV* • Hypertension* • TB*	Of the 14364 participants, 21.3% had two diseases, 1.2% had three diseases and 0.1% had four diseases. **Of those that had two diseases (n=3058)** 1. Hypertension and diabetes (69.1%) 2. Hypertension and HIV (21.4%) 3. HIV and TB (6.2%) 4. HIV and diabetes (1.6%) 5. Hypertension and TB (1.5%) 6. TB and diabetes (0.2%) **Of those that had three diseases (n=173)** 1. Hypertension, diabetes and HIV (63%) 2. Hypertension, HIV and TB (26.6%)

Appendix 5: Multimorbidity prevalence by sex and age group

Study	Year	Age band (years)	Prevalence of multimorbidity					
			Persons		Males		Females	
			n/N	% (95% CI)	n/N	%	n/N	%
Population-based surveys								
Afshar, Roderick, Kowal et al. (2015)[‘]	2003	18 - 49	-	5.0 (3.9 – 6.0)	-	-	-	-
		50 - 64	-	21.6 (16.6 – 26.0)	-	-	-	-
		65+	-	30.1 (20.6- 39.7)	-	-	-	-
		Overall (18+)	**-**	**11.2 (9.8 - 12.5)**	-	-	-	-
Garin, Koyanagi, Chatterji et al (2016).	2007/8	50 - 59	-	60.1	-	*50.5*	-	*68.4*
		60 - 69	-	69.1	-	*63.3*	-	*73.2*
		70 - 79	-	65.9	-	*63.6*	-	*67.1*
		80+	-	55.9	-	*61.0*	-	*51.3*
		Overall (50+)	**2376 / 3747***	**63.4**	-	-	-	-
Weimann, Dai, Oni (2016).	2008	15 - 24	-	*0.0*	-	-	-	-
		25 - 34	-	*1.3*	-	-	-	-
		35 - 44	-	*2.1*	-	-	-	-
		45 - 54	-	*5.5*	-	-	-	-
		55 - 64	-	*9.9*	-	-	-	-
		65+	-	*9.0*	-	-	-	-
		Overall (15+)	-	**2.7 (2.5 – 3.0)**	-	-	-	-
	2012	15 - 24	-	*0.0*	-	-	-	-
		25 - 34	-	*0.8*	-	-	-	-
		35 - 44	-	*3.1*	-	-	-	-
		45 - 54	-	*3.1*	-	-	-	-
		55 - 64	-	*9.0*	-	-	-	-
		65+	-	*10.5*	-	-	-	-
		Overall (15+)	-	**2.8 (2.6 – 3.1)**	-	-	-	-
Ghose, Razak (2017).	2010	**Overall (50+)**	**130 / 422**	**30.8**	-	**16.0**	-	**35.8**
Community-based studies (cross-sectional study)								
	2011/12	18 - 25		*10.0*	-	-	-	-

Study	Year	Age band (years)	Prevalence of multimorbidity					
			Persons		Males		Females	
			n/N	% (95% CI)	n/N	%	n/N	%
van Heerden, Barnabas, Norris et al (2017).		26 - 35		*24.3*	-	-	-	-
		36 - 45		*53.2*	-	-	-	-
		46 - 65		*60.9*	-	-	-	-
		66+		*68.9*	-	-	-	-
Chang, Gómez-Olivé, Payne et al. (2019).	2014/15	40 - 49	430 / 685	62.8	-	*61.0*	-	*64.3*
		50 - 59	750 / 1069	70.2	-	*66.2*	-	*72.8*
		60 - 69	754 / 1056	71.4	-	*69.9*	-	*73.0*
		70 - 79	471 / 685	68.7	-	*65.8*	-	*71.7*
		80+	295 / 393	75.1	-	*76.0*	-	*74.3*
		Overall (40+)	**2700 / 3889**	**69.4**	**1182 / 1758**	**67.2**	**1518 / 2130**	**71.2**
Sharman, Bachmann (2019).	2009	**Overall (18+)**		**8.4**				
	2015	**40+**		**18.4**				
	2015	**Overall (18+)**		**13.2**				
Health facility-based studies (cross-sectional surveys and routine health information systems)								
Lalkhen, Mash (2015).	2010	**Overall (Mean ages±)**	**-**	**48.4**	-	-	-	-
Roche, de Vries (2017).	2015	**Overall (Mean age 49 years)**	**371 / 427**	**87.0**	-	-	-	-
Oni, Youngblood, Boulle et al. (2015).	2012/13	**Overall (18+)**	**3246 / 14364**	**22.6**	-	-	-	-

Italicised data extracted from graphs using Webplot digitizer
*estimated from available information
ˈstandardised multimorbidity prevalence
NR indicates Not Reported.
±Mean age of patients with: osteoarthritis (56.9 years), COPD (56.8 years), diabetes (56.6 years), hypertension (56.4 years), asthma (45.5 years), epilepsy (37.9 years).