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## Multimorbidity in South Africa: A systematic review of prevalence studies

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## Multimorbidity in South Africa: A systematic review of prevalence studies

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1  
2  
3 28 **ABSTRACT**  
4

5 29 **Objectives:**  
6

7 30 To review prevalence studies of multimorbidity in South Africa to identify prevalence estimates,  
8 31 common disease clusters and factors associated with multimorbidity.  
9

10 32  
11 33 **Design:**

12 34 Systematic review.  
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15 35

16 36 **Setting:**

17 37 South Africa (general community and healthcare facilities).  
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20 38

21 39 **Data sources:**

22 40 Articles were retrieved from electronic databases (PubMed, Web of Science, Scopus, CINAHL,  
23 41 Science Direct and JSTOR).  
24  
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26 42

27 43 **Eligibility criteria:**

28 44 Studies addressing the prevalence of multimorbidity in South Africa were eligible for inclusion. A  
29 45 systematic search was done in various databases up to December 2020. A risk of bias assessment  
30 46 was conducted for each article using a modified checklist.  
31  
32  
33 47

34 48 **Study selection:**

35 49 Two researchers independently screened titles and abstracts; assessed the risk of bias of each study  
36 50 and extracted data. Included studies were described using a narrative synthesis.  
37  
38  
39 51

40 52 **Results:**

41 53 In total, 1,407 titles were retrieved; of which and ten articles were included in the narrative  
42 54 synthesis. Six studies had a low risk of bias, three had a moderate risk of bias and one based on a  
43 55 routine health information system was not assessed for risk of bias due to a lack of assessment  
44 56 criteria. The included studies were population-based surveys (n=3), community-based cohorts  
45 57 (n=4) and cross-sectional studies of health facility data (n=3). The prevalence of multimorbidity  
46 58 was low to moderate in studies which included younger people or had a wide range of selected age  
47 59 groups (3 – 23%); and moderate to high in studies of older adults (30 – 87%). The common disease  
48 60 clusters as reported were hypertension and diabetes; hypertension and HIV, and TB and HIV.  
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51 61

52 62 **Conclusion**  
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3 63 Despite differences in settings and study types; studies indicated that multimorbidity is a norm,  
4 64 especially in older adults in South Africa. Hypertension is a driver of multimorbidity. There are  
5 65 still too few studies focused on multimorbidity in South Africa and high-quality studies are needed.  
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7 66

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9 67 **Registration:** PROSPERO (CRD42020196895)

10 68 295/ 300 words  
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For peer review only

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3 69 **Article Summary**  
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5 70 **Strengths and limitations of this study**  
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- 7  
8 71 • To our knowledge, this is the first systematic review of studies that determined the  
9 72 prevalence of multimorbidity in South Africa.  
10  
11 73 • This systematic review followed the Preferred Reporting Items for Systematic reviews and  
12 74 Meta-Analyses (PRISMA) statement.  
13  
14 75 • This study included studies conducted in general community and healthcare settings.  
15  
16 76 • This study was limited to the information reported in the included studies.  
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20 77  
21  
22 78 **Keywords:** Multimorbidity, chronic diseases, prevalence, South Africa, trends, disease clusters  
23 79  
24 80  
25 81  
26 82

## 83 INTRODUCTION

84 A third of adults residing in low and middle-income countries (LMICs) are thought to be afflicted  
85 by two or more co-existing health conditions; also known as multimorbidity.[1] The last two  
86 decades have seen an exponential growth in the number of studies about multimorbidity.[2] This  
87 can be attributed to more research into ageing populations,[2] and the recognition that  
88 multimorbidity impacts patient-care and healthcare systems.[3] Other consequences of  
89 multimorbidity include increased mortality levels,[4] lowered quality of life,[5] the risk of  
90 polypharmacy [6] and intensified utilisation of health services and associated costs.[7, 8] More  
91 recently, multimorbidity was implicated as a risk factor for COVID-19 mortality.[9, 10]

92  
93 Most research to date has been conducted in high-income countries; sparking calls for similar  
94 research in LMICs.[2, 11, 12] Research is needed into multimorbidity in LMICs, like South Africa,  
95 where disease burdens differ to those in high-income countries. South Africa has a unique disease  
96 burden – it has the largest number of people living with HIV in the world.[13] With the availability  
97 of antiretrovirals, people with HIV are living longer and developing age-related non-  
98 communicable diseases (NCDs).[14] At the same time, the burden of disease due to NCDs is  
99 increasing in the country; giving rise to a disease pattern of co-existing infectious diseases and  
100 NCDs.[15, 16]

101  
102 In resource-constrained health settings, it is imperative that we estimate the magnitude of  
103 multimorbidity as well as the nature and type of diseases cluster to more efficiently manage  
104 patients and organize health service delivery. South Africa lacks a robust national routine health  
105 information system to inform its morbidity profile. Countries with less robust routine health  
106 information systems need to rely on smaller-scale studies and surveys to better understand the  
107 scale and impact of the problem of multimorbidity. This has led to numerous studies focused on  
108 quantifying the prevalence of multimorbidity and studies focused on integrated care in South  
109 Africa.[17-21] However, many of these studies suffer from the methodological problems that tend  
110 to plague multimorbidity studies elsewhere which is a lack of standardization.[22] This makes it  
111 difficult to compare and interpret studies, given their varying estimates and methodologies. This  
112 study set out to systematically assess multimorbidity prevalence studies in South Africa, to report  
113 on common disease clusters and factors associated with multimorbidity in South Africa.



## 114 **METHODS**

### 115 **Search strategy and database search**

116 The protocol for this study was registered with PROSPERO (CRD42020196895) and published  
117 elsewhere.[23] The Preferred Reporting Items for Systematic Reviews and Meta-Analyses  
118 guidelines (PRISMA)[24] guided this study (Appendix 1). One researcher experienced in  
119 systematic review methodology (EBT), performed a systematic literature search in PubMed, Web  
120 of Science, Scopus, CINAHL, Science Direct and JSTOR to identify articles reporting  
121 epidemiology data on multimorbidity in the adult population of South Africa. The search strategy  
122 was reviewed by an expert librarian (Appendix 2). The time frame of the search was not restricted  
123 and covered a period up to December 2020.

### 124 **Study selection and data extraction**

125 The search output citations were downloaded and saved to EndNote Version X8.[25] The EndNote  
126 de-duplication function was employed, and remaining citations were uploaded into an electronic  
127 screening website, Rayyan.[26] Two researchers (RAR, EBT) independently screened the titles  
128 and abstracts and studies deemed irrelevant were discarded. A third researcher (BvW) assisted  
129 with conflicts. Case reports, reviews, editorials, letters, studies among children, studies not  
130 conducted in South Africa, study designs that were not cross-sectional or cohorts, studies where it  
131 was not possible to calculate the prevalence of multimorbidity in the general population (e.g.  
132 studies only examining multimorbidity in cancer patients) were excluded. Where multiple studies  
133 reported on the same source of data (e.g. one national survey), only the most relevant study was  
134 included.

135 The full texts for potentially eligible articles were independently assessed by two researchers  
136 (RAR, EBT) using the electronic data capture system, the Burden of Disease Review Manager  
137 (BODREVMAN).[27] BODREVMAN facilitates the independent data collection of study  
138 characteristics (study design, sample size, geographical location, whether a study is community-  
139 based or facility-based). Also, data on the definition of multimorbidity used, the disease conditions  
140 included in the study and the prevalence of multimorbidity (by age and sex where possible) were  
141 extracted. Disagreements were discussed and resolved. The reference lists of included articles were  
142 screened for additional studies.

### 143 **Quality assessment**

144 Two researchers (RAR, EBT) independently assessed and appraised each article. BODREVMAN  
145 contains a modified checklist based on the Newcastle Ottawa[28] and Hoy checklist.[29] The tool  
146 has been described elsewhere.[30] Each article was independently scored and categorised as either  
147 having a high, moderate or low risk of bias. Studies based on routine health information systems  
148 (RHIS) did not undergo a risk of bias assessment due to a lack of assessment criteria for this study  
149 type.

### 150 **Data extraction and analysis**

151 Information on multimorbidity definitions, disease conditions included and the proportion of the  
152 sample with more than one condition were extracted. Authors were contacted for data by age and  
153 sex breakdowns. Studies were categorised by study type (cohort or cross-sectional), and study  
154 setting (community or facility-based). It was noted whether disease conditions included were self-  
155 reported or biologically assessed.

156 The mean and standard deviation or the absolute number and the percentage were recorded, as  
157 appropriate. The age range and sex for each category were recorded. Where data appeared in  
158 graphical formats, authors were contacted for the original data or WebPlotDigitizer Version 4.3  
159 (California)[31] was used to extract data. STATA 15 (StataCorp, TX) was used to calculate  
160 standard errors using the sample size and prevalence estimates where possible.

### 161 **Patient and public involvement**

162 Patients and the public were not involved in this study. This study was given ethical approval by  
163 the Biomedical Science Research Ethics Committee of the University of the Western Cape  
164 (BM20/5/8).

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## 169 RESULTS

### 170 Search results

171 In total, 1081 records were screened after de-duplication (Figure 1). By screening titles and  
172 abstracts, 1041 articles were excluded. Forty-one full-text articles were assessed for eligibility, of  
173 which ten were included in a narrative synthesis.[\[32-41\]](#)

### 175 <Figure 1: PRISMA flow diagram>

#### 176 Study characteristics

177 The sample sizes of included studies ranged from 422[\[35\]](#) to 47 334 participants[\[38\]](#) (Table 1).  
178 All included studies were published after 2015 but the period of data collected ranged from  
179 2003[\[32\]](#) to 2015.[\[37, 38, 40\]](#) Three studies conducted a secondary data analysis of population-  
180 based surveys.[\[32-34\]](#) The surveys analysed were the 2003 World Health Survey (WHS),[\[32\]](#) 2007  
181 and 2010 WHO Study on global AGEing and adult health (SAGE),[\[33, 35\]](#) and the 2008 and 2012  
182 South African National Income Dynamics Survey (SANIDS).[\[34\]](#) Three studies were cross-  
183 sectional analyses of community-based cohorts and surveys.[\[36-38\]](#) The remaining three studies  
184 were of a cross-sectional nature and based in health facilities.[\[39-41\]](#)

185 Three studies were conducted nationally[\[32-34\]](#) with others conducted in Kwa-Zulu Natal  
186 province (n=3),[\[35, 36, 38\]](#) the Western Cape province (n=2) [\[40, 41\]](#) and Mpumalanga province  
187 (n=1).[\[37\]](#) One study was conducted in primary healthcare facilities in the Western Cape, North  
188 West, Northern Cape and Limpopo provinces.[\[39\]](#) Four studies were conducted in rural areas [\[35-](#)  
189 [38\]](#), two studies were conducted in urban areas[\[40, 41\]](#) and the remaining studies were conducted  
190 in both urban and rural areas.[\[32, 33, 39, 42\]](#) Six studies had a low risk of bias,[\[32-34, 37-39\]](#) three  
191 had a moderate risk of bias[\[35, 36, 40\]](#) and one based on a RHIS was not assessed for risk of bias  
192 due to a lack of assessment criteria for this study type.

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197 **Table 1: Study characteristics of included studies**

Study type	Study	Study population and size	Year	Location	Risk of bias (score)
Population-based survey	Afshar, Roderick, Kowal <i>et al</i> (2015). [32]	N= 2629. Adults 18 years and older in the 2003 World Health Survey.	2003	South Africa (Urban and rural areas included)	Low (14)
	Garin, Koyanagi, Chatterji <i>et al</i> (2016). [33]	N = 3836. Adults 50 years and older in the 2007 WHO Study on global AGEing and adult health.	2007-2008	South Africa (Urban and rural areas included)	Low (15)
	Weimann, Dai, Oni (2016). [34]	N=18526 in 2008 N=20015 in 2012 Participants 15 years and older in the National Income Dynamic Survey Wave 1 (2008) and Wave 3 (2012).	2008, 2012	South Africa (Urban and rural areas included)	Low (17)
Cross-sectional study (Community-based)	Ghose, Razak (2017). [35]	N=422. Adults 50 years and older infected and/or affected by HIV in the SAGE Well-being of Older People Study (WOPS) 2010.	2010	Hlabisa subdistrict, Kwa-Zulu Natal (Rural)	Moderate (12)
	van Heerden, Barnabas, Norris <i>et al</i> (2017). [36]	N=570. Adults older than 18 years enrolled in a cohort study to increase engagement in HIV care and testing.	Nov 2011 - Jun 2012	KwaZulu-Natal (Rural)	Moderate (13)
	Chang, Gómez-Olivé, Payne <i>et al</i> (2019). [37]	N = 3889. Adults enrolled in the Health and Ageing in Africa: A longitudinal study of an INDEPTH Community in South Africa Programme.	2014-2015	Agincourt Health and Demographic Surveillance System, Bushbuckridge subdistrict, Mpumalanga (Rural)	Low (17)
	Sharman, Bachmann (2019). [38]	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)	Low (14)
Cross-sectional study (Health facility-based)	Lalkhen, Mash (2015). [39]	N=5793 Sub-sample of primary healthcare (PHC) users where all participants had at least one NCD (Hypertension, Diabetes, Asthma, Epilepsy, COPD, Osteoarthritis).	2010	Primary healthcare facilities in the Western Cape, North West, Northern Cape and Limpopo (Urban and rural areas included)	Low (16)

Study type	Study	Study population and size	Year	Location	Risk of bias (score)
	Roche, de Vries (2017). [40]	N= 491. Consecutive admissions to an internal medicine department of a large district hospital.	2015	District hospital, Cape Town, Western Cape (Urban)	Moderate (13)
Routine Health Information Systems	Oni, Youngblood, Boulle <i>et al</i> (2015). [41]	N=14 364. Chronic disease patients (adults) with at least one disease (HIV, TB, diabetes, and hypertension) identified using the Western Cape Department of Health Data Repository and the Electronic prescription system.	Sep 2012 - May 2013	Michael Mapongwana clinic, Khayelitsha, Cape Town, Western Cape (Peri-urban)	NA

## 198 Disease conditions assessed

199 Study findings on the prevalence of multimorbidity can be influenced by i) the definition of  
200 multimorbidity used, ii) the number of disease conditions included in the study, iii) the actual  
201 disease conditions included and iv) how the disease conditions were measured.

202 All included studies used a “count” of the number of diseases to define multimorbidity i.e.  
203 multimorbidity was defined by having two or more diseases (Appendix 3). Half of these studies  
204 specified they were only focused on chronic conditions.[32-34, 37, 41] Two health facility-based  
205 studies included acute conditions such as lower respiratory infections.[39, 40] The inclusion of  
206 acute disease conditions could inflate the prevalence of multimorbidity. The full list of disease  
207 conditions included can be found in Appendix 3.

208 One study included two definitions of multimorbidity – a “count” definition (as described above)  
209 and another more detailed definition. The detailed definition specified multimorbidity as the  
210 presence of conditions from more than one of the following categories of disease: cardiometabolic  
211 conditions, mental disorders, or HIV and anaemia.[37] When using this definition, the prevalence  
212 of multimorbidity was lowered as it only includes discordant diseases (i.e. excludes diseases that  
213 belong to the same category such as hypertension and diabetes). For this review, we used their  
214 results from the “count” definition unless otherwise stated.

215 The number of disease conditions included in each study ranged from four [41] to 24.[40] (Table  
216 2). Diabetes was included as a disease condition in all ten studies. Most studies included

217 hypertension (n=9) in their assessment of multimorbidity. HIV (n=5), asthma (n=5) and heart  
218 disease (n=5) were also commonly included disease conditions.

219 The study design and setting influenced how disease conditions were measured (Appendix 3).  
220 Population-based surveys tended to use self-reported data, although some included measurements  
221 of blood pressure and obesity. Studies based on cohorts tended to use a mix of measured  
222 (biomarkers) and self-reported disease conditions. Facility-based studies tended to use medical  
223 records and biomarkers to determine the disease burden in their samples.

224 **Table 2: Ten common disease conditions reported in articles reporting on multimorbidity**

Disease conditions included	Studies										Total articles included in
	Afshar, Roderick, Kowal et al (2015)	Garin, Koyanagi, Chatterji et al (2016)	Weimann, Dai, Oni (2016)	Ghose, Razak (2017)	van Heerden, Barnabas, Norris et al (2017)	Chang, Gómez-Olivé, Payne et al (2019)	Sharman, Bachmann (2019)	Lalkhen, Mash (2015)	Roche, de Vries (2017)	Oni, Youngblood, Boule et al (2015)	
<b>Diabetes</b>	x	x	x	x	x <sup>+</sup>	x	x	x	x	x	<b>10</b>
<b>Hypertension</b>		x	x	x	x	x	x	x	x	x	<b>9</b>
<b>HIV</b>			x	x	x <sup>±</sup>	x	x		x	x	<b>5</b>
<b>Asthma</b>	x	x		x				x	x		<b>5</b>
<b>IHD / Heart disease/ Angina</b>	x	x		x		x			x		<b>5</b>
<b>Depression</b>	x <sup>^</sup>	x		x <sup>±</sup>	x	x <sup>*</sup>					<b>4</b>
<b>COPD</b>		x		x <sup>'</sup>				x	x		<b>4</b>
<b>Arthritis/ osteoarthritis</b>	x	x		x				x			<b>4</b>
<b>TB / Current TB</b>			x				x		x	x	<b>4</b>
<b>Lipid disorder</b>					x	x			x		<b>3</b>

\*Depression, post-traumatic stress disorder, alcohol dependence  
<sup>+</sup> Hyperglycaemia  
<sup>'</sup>Chronic lung disease  
<sup>^</sup> Depression, schizophrenia or psychosis  
<sup>±</sup> Assessed condition but was not able to incorporate into multimorbidity calculation based on the way study reported it  
IHD=Ischaemic Heart Disease, COPD=Chronic Obstructive Pulmonary Disease; TB= Tuberculosis

## 225 **Patterns of disease clusters observed**

226 The studies reported on common disease clusters using bubble charts of pair-wise co-morbid  
227 conditions,[[33](#), [37](#)] reporting each disease with their most common co-morbid condition,[[38](#), [39](#)]

228 or schematics detailing double and triple morbidities.[34, 37, 41] The results of the studies were  
229 difficult to compare due to how the data were reported. Four studies did not describe common  
230 disease clusters found in their study populations.[32, 35, 36, 40]

231 While it was not possible to ascertain the largest disease cluster in one study, [Garin, Koyanagi \[33\]](#)  
232 found hypertension featured strongly with diabetes, stroke, angina, cataract, cognitive impairment  
233 and all other conditions examined in their analysis. Arthritis and obesity were also commonly  
234 listed as co-morbid conditions for all other disease conditions.

235 Table 3 summarises the top five disease clusters from the five remaining studies. The number of  
236 disease combinations varied in each study with some studies reporting less than ten disease  
237 clusters[34, 41] and others reporting more than twenty disease clusters[37-39] A more detailed list  
238 of disease combinations can be found in Appendix 4.

239 Hypertension was frequently co-morbid with other diseases (Table 3). [Weimann, Dai \[34\]](#) and  
240 [Oni, Youngblood \[41\]](#) showed similar patterns of disease – with hypertension and diabetes being  
241 the most common disease cluster. In these studies, the disease cluster hypertension and HIV ranked  
242 highly, followed by TB and HIV. In terms of having three co-occurring diseases, both ranked the  
243 combination of TB, diabetes and hypertension highest; followed by the combination of  
244 hypertension, HIV and TB. [Lalkhen and Mash \[39\]](#) also found hypertension and diabetes to be the  
245 largest disease cluster in their study. While [Chang, Gómez-Olivé \[37\]](#) found the largest disease  
246 cluster was hypertension and dyslipidaemia, followed by hypertension and anaemia; and the  
247 combination of hypertension, dyslipidaemia and anaemia. Anaemia and HIV also commonly co-  
248 occurred.

249 Age and sex tend to influence the susceptibility of an individual to certain diseases. However,  
250 studies generally did not report disease clusters by these breakdowns. Two studies reported that  
251 HIV was more prevalent in their younger participants;[37, 38] while hypertension affected those  
252 over the age of 40 years and diabetes and angina affected people above the age of 60 years. One  
253 study also noted that hypertension and diabetes were more common in females compared to males,  
254 and TB was more common in males.[38] One study noted that multimorbidity was lower in patients  
255 with HIV that were on ART (compared to patients not on ART or with unknown ART status) but  
256 the association did not hold when broken down by age group.[41]



257 These results must be interpreted with caution as each study included different disease conditions  
 258 and even when the same disease conditions were included, these could differ in the way they were  
 259 measured e.g. self-reported or biologically measured (Appendix 3).

260 **Table 3: Top five disease clusters in each study**

Disease combinations / clusters			Total studies reported (n=5)	Study citation
Disease 1	Disease 2	Disease 3		
Hypertension	Diabetes		4	[34, 38, 39, 41]
Hypertension	HIV		3	[34, 38, 41]
TB	HIV		3	[34, 38, 41]
Hypertension	TB		2	[34, 41]
Diabetes	HIV		2	[38, 41]
TB	Diabetes		1	[34]
Hypertension	Osteoarthritis		1	[39]
Asthma	Hypertension		1	[39]
Hypertension	COPD		1	[39]
Hypertension	IHD		1	[39]
Hypertension	Dyslipidaemia		1	[37]
Hypertension	Anaemia		1	[37]
Hypertension	Dyslipidaemia	Anaemia	1	[37]
Anaemia	HIV		1	[37]
Hypertension	Anaemia	HIV	1	[37]

### 261 Multimorbidity prevalence

262 Due to study heterogeneity, it was not possible to do a meta-analysis. Studies reported  
 263 multimorbidity prevalence by varying age breakdowns making direct comparison difficult. Several  
 264 studies reported multimorbidity by age group and/or sex (Appendix 5). Two studies reported the  
 265 median/mean age of participants but the age range of participants was not included[39, 40] and  
 266 one did not report an overall multimorbidity prevalence for their study[36]. From the remaining  
 267 studies, multimorbidity prevalence tended to be low to moderate in studies which included younger  
 268 people or had a wide range of age groups (3% – 23%) (Figure 2); and moderate to high in studies  
 269 reporting on adults aged 50 years and older (30% – 71%) (Figure 3).

270

271



272 <Figure 2: Graph of multimorbidity prevalence estimates for studies that include younger  
273 age groups>

274

275 <Figure 3: Graph of multimorbidity prevalence in studies including persons aged 50 years  
276 and older>

277 In population-based surveys, each study reported a different age group (Table 4). In those 18 years  
278 and above, [Afshar, Roderick \[32\]](#) reported an overall prevalence of 11%, however, this was age-  
279 standardised against the WHO Standard Population which means it uses a standardised age  
280 structure rather than the one found in South Africa. Another study reported the results of a panel  
281 survey in 2008 and 2012 and showed a rather low prevalence of multimorbidity (2.7%) for those  
282 aged over 15 years old.[\[34\]](#) The study showed a negligible increase (0.1%) during a four year  
283 period. A study that only reported on those aged above 50 years of age, showed a very high overall  
284 prevalence of multimorbidity (63.4%).[\[33\]](#)

285 Among community-based cross-sectional studies, the prevalence among older adults ranged from  
286 18%[\[38\]](#) to 69%.[\[37\]](#) However, [Chang, Gómez-Olivé \[37\]](#) used two definitions of multimorbidity  
287 and when applying the second definition (categories of discordant disease groups), they estimated  
288 a lower prevalence of 54%. One study that included younger people noted a 5% increase in  
289 multimorbidity prevalence between the period 2009 to 2015.[\[37\]](#)

290 In health facilities, two studies found moderate levels of multimorbidity (14.4% and 22.6%).[\[39,](#)  
291 [41\]](#) One study based in a health facility found an extremely high prevalence of multimorbidity  
292 (87.0%), however, this study included both chronic and acute health conditions.[\[40\]](#)

293 **Table 4: Multimorbidity prevalence by age group**

	Study	Year	Age band (years)	Prevalence of multimorbidity	
				n/N	% (95% CI) <sup>a</sup>
Population-based surveys	<a href="#">Afshar (2015)</a> <sup>□</sup>	2003	Overall (18+)	-	11.2 (9.8 - 12.5)
	<a href="#">Garin (2016)</a>	2007/8	Overall (50+)	2376 / 3747*	63.4
	<a href="#">Weimann (2016)</a>	2008	Overall (15+)	-	2.7 (2.5 – 3.0)
		2012	Overall (15+)	-	2.8 (2.6 – 3.1)

	Study	Year	Age band (years)	Prevalence of multimorbidity	
				n/N	% (95% CI) <sup>a</sup>
Cross-sectional study (Community-based)	Ghose (2017)	2010	Overall (50+)	130 / 422	30.8
	Chang (2019)	2014/15	Overall (40+)	2700 / 3889	69.4
	Sharman (2019)	2009	Overall (18+)	-	8.4
		2015	Overall (40+)	-	18.4
Cross-sectional study (Health facility-based)	Lalkhen (2015)	2010	Overall (Mean age <sup>±</sup> )	2806 / 5793	48.4
	Roche (2017)	2015	Overall (Mean age 49 years)	371 / 427	87.0
Routine health information systems	Oni (2015)	2012/13	Overall (18+)	3246 / 14364	22.6

<sup>a</sup> Not all studies reported a 95% CI and there was insufficient information to calculate this.

\* Estimated from available information.

□ Reports a standardised multimorbidity prevalence.

± 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).

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## 295 Factors associated with multimorbidity

296 Most of the included studies reported on factors they found to be associated with multimorbidity  
 297 (Appendix 3). Multimorbidity was frequently associated with increasing age. [32-34, 37, 38, 41]  
 298 However, [Garin, Koyanagi \[33\]](#) noted a decrease in the prevalence in multimorbidity in the age  
 299 group 60+ years and [Chang, Gómez-Olivé \[37\]](#) noted a decrease from the age 69+ years.

300 Being female was inconsistently linked to a high prevalence of multimorbidity. The pattern was  
 301 noted in two studies;[33, 34] although another study reported it was not statistically  
 302 significant;[37] while one found no distinction between males and females.[41] One study found  
 303 that living in urban areas was a risk factor for multimorbidity[34] while another found that living  
 304 in rural areas was associated with multimorbidity.[33] Other factors found to be associated with  
 305 multimorbidity were: a lower level of education;[32, 33] being separated, divorced or  
 306 widowed;[33, 37] living in Kwa-Zulu Natal or the Eastern Cape provinces, being Indian/Asian or  
 307 being obese.[34] Socioeconomic deprivation was found to be associated with multimorbidity in  
 308 one study,[34] but another found no association between wealth and multimorbidity.[37]

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3 309 Other studies identified the effects of multimorbidity such as having memory complaints (in  
4 women), suffering from depression,[\[35\]](#) decreased well-being and self-reported health.[\[37, 38\]](#)  
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6 311 One study found that length of stay in hospital was not related to multimorbidity and also did not  
7 link lifestyle risk factors to multimorbidity.[\[40\]](#)  
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## 10 11 313 **DISCUSSION**

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13 314 This study set out to assess the prevalence of multimorbidity in adults in South Africa using  
14 systematic review methodology. This study found considerable heterogeneity among included  
15 315 articles, which stemmed from differences in study design, disease conditions assessed and how  
16 316 study results were reported. Despite this, we found a low to moderate multimorbidity prevalence  
17 317 in studies including younger people and a moderate to high prevalence in studies including older  
18 318 adults. Due to study heterogeneity, it is difficult to compare these results to the findings of a recent  
19 319 systematic review which estimated a pooled multimorbidity prevalence of 30% for low and  
20 320 middle-income countries.[\[1\]](#)  
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27 322 Three of our included studies reported fairly low levels of multimorbidity prevalence.[\[32, 34, 38\]](#)  
28 323 One study standardised the prevalence to the world population which may have resulted in a lower  
29 324 prevalence estimate (11.2%).[\[32\]](#) The other study reported an overall prevalence of less than 3%  
30 325 among people 15 years and older; and in people over the age of 65 years, they estimated a  
31 326 prevalence of only 10%.[\[34\]](#) The same 2008 dataset from a population-based survey was used in  
32 327 another study and found a similar prevalence of multimorbidity, despite using different methods  
33 328 (4.0%).[\[43\]](#) The low prevalence found in this survey could be attributed to a healthier population  
34 329 being sampled or as the authors suggested, underreporting of self-report data due to stigma around  
35 330 HIV and TB.[\[34\]](#) The study also included only four disease conditions which may have resulted  
36 331 in a lower prevalence. In contrast, a study that included many acute and chronic conditions resulted  
37 332 in a very high prevalence estimate.[\[40\]](#) This highlights the significant impact of study design on  
38 333 the estimates produced. The third study had a large sample size but may have underestimated the  
39 334 burden of multimorbidity due to the use of self-report data.[\[38\]](#) Also, they had missing data on  
40 335 HIV due to additional consent being required.

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45 336 Age is accepted to be an important predictor of multimorbidity.[\[40\]](#) Most studies showed that the  
46 337 prevalence of multimorbidity increased with age, however, two studies observed decreases in the  
47 338 oldest age groups. This needs further investigation. What also remains unclear is whether

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3 339 multimorbidity does in fact affect people at younger ages in low and middle-income countries.[12]  
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5 340 Based on this systematic review, more studies need to interrogate multimorbidity by age group as  
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7 341 the lack of reporting makes it difficult to monitor. Age and sex are both important predictors of  
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9 342 multimorbidity and multimorbidity should be reported in a disaggregated manner where  
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11 343 possible.[44]

12 344 The common diseases assessed in our included studies (diabetes and hypertension) have a high  
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14 345 prevalence in South Africa. It was surprising that only half of the studies included HIV as a  
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16 346 condition of interest; given the high prevalence of HIV in the country. However, many of the  
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18 347 studies were based on secondary data analysis and were limited to the conditions that were  
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20 348 included. Future primary studies in South Africa should plan to incorporate infectious diseases  
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22 349 (HIV and TB) into studies of multimorbidity where possible.

23 350 Despite few studies reporting on which disease clusters were largest, hypertension appeared to be  
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25 351 the biggest contributor to the burden of multimorbidity, particularly the co-occurrence of  
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27 352 hypertension with diabetes. That said, hypertension and diabetes were also among the most widely  
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29 353 included conditions in studies of multimorbidity. Hence, these findings may be biased to  
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31 354 conditions that are included in studies and not necessarily the reality of the situation. Given that  
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33 355 the prevalence of hypertension is high in South Africa (44% of men and 46% of women aged 15  
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35 356 years and older, as high as 84% in people aged above 65 years),[45] it does hold weight that it  
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37 357 would be a common co-morbid condition. A recent study on COVID-19 mortality in South Africa  
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39 358 found the combination of hypertension and diabetes was a common disease cluster in people who  
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41 359 had succumbed to the disease.[46] This cluster of disease was more prevalent than having  
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43 360 hypertension or diabetes only. Information on the prevalence of co-morbidities and  
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45 361 multimorbidities may prove very important in light of the COVID-19 pandemic.

46 362 We mainly included three types of studies in our analysis; studies based on the secondary data  
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48 363 analysis of national surveys, studies based on community cohorts and studies based in health  
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50 364 facilities. All three types of studies have strengths. National survey data can provide an overall  
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52 365 picture of what is happening in the general population. However, they tend to use self-reported  
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54 366 data which may result in an underestimation of the burden of disease; as a large percentage of  
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56 367 NCDs are underdiagnosed. Nevertheless, there are many more national surveys that could be  
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58 368 analysed to provide an overview of multimorbidity from these sources. Studies based on cohorts

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3 369 generated rich information, tended to have large sample sizes and had a mixture of self-report data  
4 and measure biological samples. These studies were mostly limited to rural areas. Whether  
5 370 multimorbidity is more common in rural or urban areas in South Africa remains unclear. Existing  
6 371 cohorts will continue to provide a good source of information on multimorbidity and we can expect  
7 372 more data to come out of planned urban cohorts.[\[47\]](#) Studies based in health facilities tended to  
8 373 include more health conditions (both acute and chronic diseases) and tended to report higher levels  
9 374 of multimorbidity. This may be due to people who require health care (ill individuals) accessing  
10 375 these facilities. However, these studies provide an important source of information that is highly  
11 376 relevant to the management and planning for multimorbidities. For example, a recent study by  
12 377 [Mannie and Kharrazi \[48\]](#) assessed the geographical distribution of comorbidities among 2.6  
13 378 million commercially insured individuals in South Africa using a comorbidity index that  
14 379 highlighted healthcare utilization. Using this score, they were able to identify areas of high  
15 380 utilization and underserved individuals; although they did not provide detail on the types of  
16 381 services needed. Multimorbidity is known to increase the costs to healthcare systems.[\[49\]](#)

17 382 This systematic review was limited to the information reported in the included studies. It was also  
18 383 limited in that it excluded studies conducted with sub-populations that had a specific disease (e.g.  
19 384 multimorbidity in cancer patients). While these studies are very important, their inclusion would  
20 385 require different search strategies. This study differed from the protocol in that it includes age  
21 386 groups of 15 years plus as the age 15 years is commonly reported as adults in population-based  
22 387 surveys.

## 39 389 **CONCLUSION**

40 390 To our knowledge, this is the first systematic review of multimorbidity on the African continent  
41 391 and one of the few focused on a LMIC. This systematic review set out to determine the prevalence  
42 392 of multimorbidity of adults in South Africa, ideally stratified by age and sex. We found that there  
43 393 was a low number of studies focused on multimorbidity in South Africa. Studies with data  
44 394 available indicated many people aged 50 years and older are afflicted with more than one long-  
45 395 term disease condition. These findings are significant as they support the notion that  
46 396 multimorbidity is the norm and not an exception which has strong implications for how healthcare  
47 397 is organised and utilised. They may also be reflective of the situation in other low and middle-  
48 398 income countries.

399 Our study found that a large component of multimorbidity appears to be attributed to hypertension.  
400 While HIV did contribute to multimorbidity, NCDs were the most common source, even in  
401 environments with a high HIV prevalence. However, these results should be interpreted with  
402 caution as many studies focused only on older adults and did not give disease clusters using age  
403 breakdowns. Heterogeneity in studies also made it difficult to observe a trend.

404 More studies are needed in low and middle-income countries to better understand the prevalence,  
405 disease burden and impact of multimorbidity. Future studies on multimorbidity should endeavour  
406 to use standardised age groups and report results by age and sex. Many more sources of secondary  
407 data could be further exploited to give a better picture of multimorbidity in South Africa.

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414 RAR, VPvW, BvW and EBT conceptualised the study. RAR and EBT conducted screening and  
415 data extraction. RAR wrote the first draft. All authors reviewed and gave input into subsequent  
416 drafts.

#### 417 **Data Sharing Statement**

418 No additional data available.

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#### 425 **Competing Interests**



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3 426 None declared.  
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10 429 **REFERENCES**  
11

- 12 430 1. Nguyen H, Manolova G, Daskalopoulou C, et al. Prevalence of multimorbidity in  
13 431 community settings: A systematic review and meta-analysis of observational studies. *Journal of*  
14 432 *comorbidity*. 2019;9:1-15. doi: 10.1177/2235042X19870934  
15 433 2. Xu X, Mishra GD, Jones M. Mapping the global research landscape and knowledge gaps  
16 434 on multimorbidity: a bibliometric study. *J Glob Health*. 2017;7(1):010414-010414. doi:  
17 435 10.7189/jogh.07.010414  
18 436 3. World Health Organization. Multimorbidity: Technical Series on Safer Primary Care.  
19 437 Geneva: World Health Organization; 2016. Report No.: 9241511656. (Date Accessed: 5 July  
20 438 2020). Available from: [http://apps.who.int/iris/bitstream/10665/252275/1/9789241511650-](http://apps.who.int/iris/bitstream/10665/252275/1/9789241511650-eng.pdf)  
21 439 [eng.pdf](http://apps.who.int/iris/bitstream/10665/252275/1/9789241511650-eng.pdf).  
22 440 4. Wei MY, Mukamal KJ. Multimorbidity, mortality, and long-term physical functioning in  
23 441 3 prospective cohorts of community-dwelling adults. *Am J Epidemiol*. 2018;187(1):103-112. doi:  
24 442 <https://doi.org/10.1093/aje/kwx198>  
25 443 5. Kanesarajah J, Waller M, Whitty JA, Mishra GD. Multimorbidity and quality of life at  
26 444 mid-life: A systematic review of general population studies. *Maturitas*. 2018;109:53-62. doi:  
27 445 10.1016/j.maturitas.2017.12.004  
28 446 6. Calderón-Larrañaga A, Poblador-Plou B, González-Rubio F, et al. Multimorbidity,  
29 447 polypharmacy, referrals, and adverse drug events: are we doing things well? *Br J Gen Pract*.  
30 448 2012;62(605):e821. doi: 10.3399/bjgp12X659295  
31 449 7. Sum G, Salisbury C, Koh GC, et al. Implications of multimorbidity patterns on health care  
32 450 utilisation and quality of life in middle-income countries: cross-sectional analysis. *J Glob Health*.  
33 451 2019;9(2):020413. doi: 10.7189/jogh.09.020413  
34 452 8. Frølich A, Ghith N, Schiøtz M, Jacobsen R, Stockmarr A. Multimorbidity, healthcare  
35 453 utilization and socioeconomic status: A register-based study in Denmark. *PLoS One*.  
36 454 2019;14(8):e0214183. doi: 10.1371/journal.pone.0214183  
37 455 9. Maddaloni E, D'Onofrio L, Alessandri F, et al. Cardiometabolic multimorbidity is  
38 456 associated with a worse Covid-19 prognosis than individual cardiometabolic risk factors: a  
39 457 multicentre retrospective study (CoViDiab II). *Cardiovasc Diabetol*. 2020;19(1):1-11. doi:  
40 458 <https://doi.org/10.1186/s12933-020-01140-2>  
41 459 10. Iaccarino G, Grassi G, Borghi C, et al. Age and multimorbidity predict death among  
42 460 COVID-19 patients: results of the SARS-RAS study of the Italian Society of hypertension.  
43 461 *Hypertension*. 2020;76(2):366-372. doi: <https://doi.org/10.1161/hypertensionaha.120.15324>  
44 462 11. The Lancet. Making more of multimorbidity: an emerging priority. *Lancet*.  
45 463 2018;391(10131):1637. doi: 10.1016/S0140-6736(18)30941-3  
46 464 12. The Academy of Medical Sciences. Multimorbidity: a priority for global health research  
47 465 2018. (Date Accessed: 20 April 2020). Available from: [https://acmedsci.ac.uk/file-](https://acmedsci.ac.uk/file-download/82222577)  
48 466 [download/82222577](https://acmedsci.ac.uk/file-download/82222577).  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3 467 13. Simbayi L, Zuma K, Moyo S, et al. South African National HIV Prevalence, Incidence,  
4 468 Behaviour and Communication Survey, 2017. Cape Town: HSRC Press; 2019. Report No.: 978-  
5 469 0-7969-2444-5. (Date Accessed: 23 December 2020). Available from:  
6 470 [https://www.hsrepress.ac.za/books/south-african-national-hiv-prevalence-incidence-behaviour-](https://www.hsrepress.ac.za/books/south-african-national-hiv-prevalence-incidence-behaviour-and-communication-survey-2017)  
7 471 [and-communication-survey-2017](https://www.hsrepress.ac.za/books/south-african-national-hiv-prevalence-incidence-behaviour-and-communication-survey-2017).  
8 472 14. Chang AY, Gómez-Olivé FX, Manne-Goehler J, et al. Multimorbidity and care for  
9 473 hypertension, diabetes and HIV among older adults in rural South Africa. *Bull World Health*  
10 474 *Organ.* 2019;97(1):10. doi: <https://dx.doi.org/10.2471%2FBLT.18.217000>  
11 475 15. Nojilana B, Bradshaw D, Pillay-van Wyk V, et al. Emerging trends in non-communicable  
12 476 disease mortality in South Africa, 1997-2010. *S Afr Med J.* 2016;106(5):477-484. doi:  
13 477 16. Mudie K, Jin MM, Tan, et al. Non-communicable diseases in sub-Saharan Africa: a  
14 478 scoping review of large cohort studies. *J Glob Health.* 2019;9(2):020409-020409. doi:  
15 479 10.7189/jogh.09.020409  
16 480 17. Oni T, McGrath N, BeLue R, et al. Chronic diseases and multi-morbidity--a conceptual  
17 481 modification to the WHO ICCC model for countries in health transition. *BMC Public Health.*  
18 482 2014;14:575. doi: 10.1186/1471-2458-14-575  
19 483 18. Mahomed OH, Asmall S. Professional nurses' perceptions and experiences with the  
20 484 implementation of an integrated chronic care model at primary healthcare clinics in South Africa.  
21 485 *Curationis.* 2017;40(1):1-6. doi: <https://dx.doi.org/10.4102%2Fcurationis.v40i1.1708>  
22 486 19. Mahomed OH, Asmall S. Development and implementation of an integrated chronic  
23 487 disease model in South Africa: lessons in the management of change through improving the quality  
24 488 of clinical practice. *Int J Integr Care.* 2015;15:e038. doi: <https://doi.org/10.5334/ijic.1454>  
25 489 20. Limbani F, Thorogood M, Gómez-Olivé FX, Kabudula C, Goudge J. Task shifting to  
26 490 improve the provision of integrated chronic care: realist evaluation of a lay health worker  
27 491 intervention in rural South Africa. *BMJ Glob Health.* 2019;4(1):e001084. doi: 10.1136/bmjgh-  
28 492 2018-001084  
29 493 21. Ameh S, Klipstein-Grobusch K, D'ambrosio L, et al. Quality of integrated chronic disease  
30 494 care in rural South Africa: user and provider perspectives. *Health Policy Plan.* 2017;32(2):257-  
31 495 266. doi: <https://dx.doi.org/10.1093%2Fheapol%2Fczw118>  
32 496 22. Fortin M, Stewart M, Poitras ME, Almirall J, Maddocks H. A systematic review of  
33 497 prevalence studies on multimorbidity: toward a more uniform methodology. *Ann Fam Med.*  
34 498 2012;10(2):142-151. doi: 10.1370/afm.1337  
35 499 23. Roomaney RA, van Wyk B, Turawa EB, Pillay-van Wyk V. Prevalence of multimorbidity  
36 500 in South Africa: a systematic review protocol. *BMJ Open.* 2020;10(12):e042889. doi:  
37 501 <https://doi.org/10.1136/bmjopen-2020-042889>  
38 502 24. Moher D, Liberati A, Tetzlaff J, Altman DG, The PG. Preferred Reporting Items for  
39 503 Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med.*  
40 504 2009;6(7):e1000097. doi: 10.1371/journal.pmed.1000097  
41 505 25. The EndNote Team. EndNote. EndNote X8 ed. Philadelphia, PA: Clarivate; 2013.  
42 506 26. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—a web and mobile app  
43 507 for systematic reviews. *Syst Rev.* 2016;5(1):210. doi: 10.1186/s13643-016-0384-4  
44 508 27. Pillay-van Wyk V, Roomaney RA, Awotiwon OF, et al. Burden of Disease Review  
45 509 Manager for Systematic Review of Observational Studies: Technical Report Version 1. Cape  
46 510 Town: South African Medical Research Council; 2017.



- 1  
2  
3 511 28. Wells GA, Tugwell P, O'Connell D, et al. The Newcastle-Ottawa Scale (NOS) for  
4 512 assessing the quality of nonrandomized studies in meta-analyses. [Internet]. 2015.  
5 513 [http://www.ohri.ca/programs/clinical\\_epidemiology/oxford.asp](http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp) (accessed 31 January 2020)  
6 514 29. Hoy D, Brooks P, Woolf A, et al. Assessing risk of bias in prevalence studies: modification  
7 515 of an existing tool and evidence of interrater agreement. *J Clin Epidemiol*. 2012;65(9):934-939.  
8 516 doi: 10.1016/j.jclinepi.2011.11.014  
9 517 30. Pheiffer C, Pillay-van Wyk V, Joubert JD, et al. The prevalence of type 2 diabetes in South  
10 518 Africa: a systematic review protocol. *BMJ Open*. 2018;8(7):e021029-e021029. doi:  
11 519 10.1136/bmjopen-2017-021029  
12 520 31. Rohatgi A. WebPlotDigitizer Version: 4.3. 2020.  
13 521 32. Afshar S, Roderick PJ, Kowal P, Dimitrov BD, Hill AG. Multimorbidity and the  
14 522 inequalities of global ageing: a cross-sectional study of 28 countries using the World Health  
15 523 Surveys. *BMC Public Health*. 2015;15(1):776. doi: <https://doi.org/10.1186/s12889-015-2008-7>  
16 524 33. Garin N, Koyanagi A, Chatterji S, et al. Global Multimorbidity Patterns: A Cross-  
17 525 Sectional, Population-Based, Multi-Country Study. *J Gerontol A Biol Sci Med Sci*.  
18 526 2016;71(2):205-214. doi: 10.1016/j.seizure.2019.06.018  
19 527 34. Weimann A, Dai D, Oni T. A cross-sectional and spatial analysis of the prevalence of  
20 528 multimorbidity and its association with socioeconomic disadvantage in South Africa: A  
21 529 comparison between 2008 and 2012. *Soc Sci Med*. 2016;163:144-156. doi:  
22 530 <https://doi.org/10.1016/j.socscimed.2016.06.055>  
23 531 35. Ghose B, Abdoul Razak MY. Memory and Learning Complaints in Relation to Depression  
24 532 among Elderly People with Multimorbidity. *Geriatrics*. 2017;2(2). doi: 10.1007/s10461-019-  
25 533 02617-2  
26 534 36. van Heerden A, Barnabas RV, Norris SA, et al. High prevalence of HIV and non-  
27 535 communicable disease (NCD) risk factors in rural KwaZulu-Natal, South Africa. *J Int AIDS Soc*.  
28 536 2017;20(2). doi: 10.1002/jia2.25012  
29 537 37. Chang AY, Gómez-Olivé FX, Payne C, et al. Chronic multimorbidity among older adults  
30 538 in rural South Africa. *BMJ Glob Health*. 2019;4(4):e001386. doi:  
31 539 <https://dx.doi.org/10.2471%2FBLT.18.217000>  
32 540 38. Sharman M, Bachmann M. Prevalence and health effects of communicable and non-  
33 541 communicable disease comorbidity in rural KwaZulu-Natal, South Africa. *Trop Med Int Health*.  
34 542 2019;24(10):1198-1207. doi: 10.1111/tmi.13297  
35 543 39. Lalkhen H, Mash R. Multimorbidity in non-communicable diseases in South African  
36 544 primary healthcare. *S Afr Med J*. 2015;105(2):134-138. doi: 10.7196/samj.8696  
37 545 40. Roche S, De Vries E. Multimorbidity in a large district hospital: A descriptive cross-  
38 546 sectional study. *S Afr Med J*. 2017;107(12):1110-1115. doi: 10.7196/SAMJ.2017.v107i12.12397  
39 547 41. Oni T, Youngblood E, Boulle A, et al. Patterns of HIV, TB, and non-communicable disease  
40 548 multi-morbidity in peri-urban South Africa- a cross sectional study. *BMC Infect Dis*. 2015;15:20.  
41 549 doi: 10.1186/s12879-015-0750-1  
42 550 42. Weimann A, Dai DJ, Oni T. A cross-sectional and spatial analysis of the prevalence of  
43 551 multimorbidity and its association with socioeconomic disadvantage in South Africa: A  
44 552 comparison between 2008 and 2012. *Soc Sci Med*. 2016;163:144-156. doi:  
45 553 10.1016/j.socscimed.2016.06.055  
46 554 43. Alaba O, Chola L. The social determinants of multimorbidity in South Africa. *Int J Equity*  
47 555 *Health*. 2013;12(1):1. doi: <https://doi.org/10.1186/1475-9276-12-63>

- 1  
2  
3 556 44. Griffith LE, Gruneir A, Fisher KA, et al. Key factors to consider when measuring  
4 557 multimorbidity: Results from an expert panel and online survey. *Journal of comorbidity*.  
5 558 2018;8(1):2235042x18795306. doi: 10.1177/2235042x18795306  
6  
7 559 45. National Department of Health, Statistics South Africa, South African Medical Research  
8 560 Council, and ICF. South Africa Demographic and Health Survey 2016. Pretoria, South Africa, and  
9 561 Rockville, Maryland, USA: NDoH, Stats SA, SAMRC, and ICF; 2019. (Date Accessed: 23  
10 562 December 2020).
- 11 563 46. Pillay-van Wyk V, Bradshaw D, Groenewald P, et al. COVID deaths in South Africa: 99  
12 564 days since South Africa's first death. *S Afr Med J*. 2020;110(10):0-0. doi:  
13 565 <https://doi.org/10.7196/SAMJ.2020.v110i11.15249>  
14 566  
15 567 47. South African Medical Research Council, Department of Science and Innovation. South  
16 568 African Population Research Infrastructure Network launches two new urban nodes to expand to  
17 569 a nationwide network and improve response to COVID-19 and other epidemics. 2020.  
18 <http://sapr.in.mrc.ac.za/1press2020.html> (accessed 3 December 2020)  
19 570  
20 571 48. Mannie C, Kharrazi H. Assessing the geographical distribution of comorbidity among  
21 572 commercially insured individuals in South Africa. *BMC Public Health*. 2020;20(1):1709. doi:  
22 573 10.1186/s12889-020-09771-6  
23 574  
24 575 49. Sum G, Hone T, Atun R, et al. Multimorbidity and out-of-pocket expenditure on medicines:  
25 576 a systematic review. *BMJ Glob Health*. 2018;3(1):e000505-e000505. doi: 10.1136/bmjgh-2017-  
26 577 000505  
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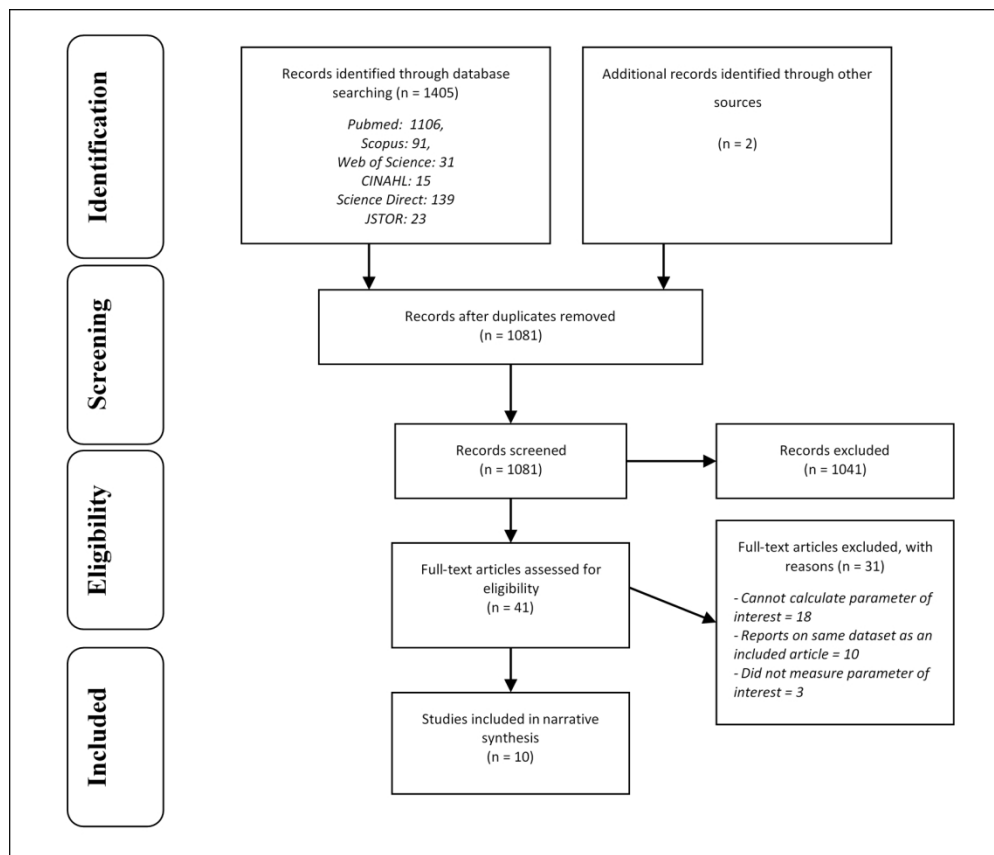


Figure 1: Study flow diagram

153x131mm (300 x 300 DPI)

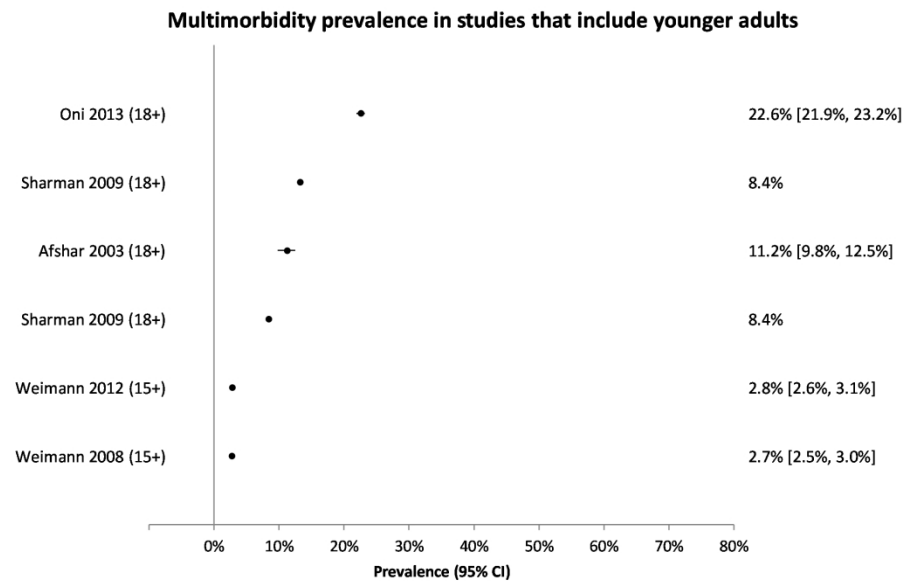


Figure 2: Graph of multimorbidity prevalence estimates for studies that include younger age groups

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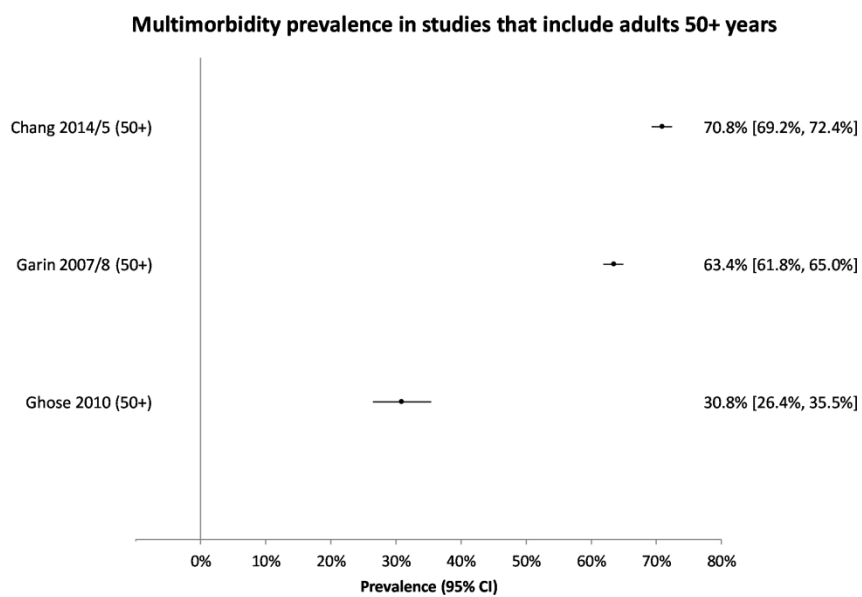


Figure 3: Graph of multimorbidity prevalence in studies including persons aged 50 years and older

209x135mm (300 x 300 DPI)

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

Appendix 1: PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
<b>TITLE</b>			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
<b>ABSTRACT</b>			
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
<b>INTRODUCTION</b>			
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
<b>METHODS</b>			
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

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
<b>RESULTS</b>			
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



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<b>DISCUSSION</b>			
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
<b>FUNDING</b>			
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](http://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.

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**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). <i>Multimorbidity and the inequalities of global ageing: a cross-sectional study of 28 countries using the World Health Surveys</i>	N= 2629. Adults 18 years and older in the 2003 World Health Survey.	2003	South Africa. (56.3% urban)	Population-based survey. WHS 2003.	<ul style="list-style-type: none"> <li>• Angina / Angina Pectoris (Heart Disease)</li> <li>• Arthritis</li> <li>• Asthma</li> <li>• Depression</li> <li>• Diabetes</li> <li>• Schizophrenia or Psychosis</li> </ul>	The presence of two or more <b>chronic</b> diseases.	Chronic conditions were chosen in this survey to reflect health system coverage and corresponded to conditions known to affect older people.	<ul style="list-style-type: none"> <li>- Increasing country GDP</li> <li>- Increasing age</li> <li>- Lower education</li> </ul>
Garin, Koyanagi, Chatterji et al (2016). <i>Global Multimorbidity Patterns: A Cross-Sectional, Population-Based, Multi-Country Study.</i>	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.	<ul style="list-style-type: none"> <li>• Angina`</li> <li>• Arthritis</li> <li>• Asthma</li> <li>• Cataract</li> <li>• Cognitive impairment`</li> <li>• COPD</li> <li>• Depression`</li> <li>• Diabetes</li> <li>• Edentulism</li> <li>• Hypertension*</li> <li>• Obesity*</li> <li>• Stroke</li> </ul>	Having at least 2 of 12 <b>chronic</b> conditions included in the study.	Selected 12 chronic conditions with high prevalence in most settings that significantly affect health	<ul style="list-style-type: none"> <li>- Generally increased with age but decreased in people over 60 years</li> <li>- Being female</li> <li>- Lower education</li> <li>- Being separated/divorced/widowed</li> <li>- Living in a rural area</li> </ul>
Weimann, Dai, Oni (2016). <i>A cross-sectional and spatial analysis of the prevalence of multimorbidity and its association with socioeconomic disadvantage in South Africa: A comparison</i>	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.	<ul style="list-style-type: none"> <li>• Diabetes</li> <li>• HIV</li> <li>• Hypertension (self-reported or measured)</li> <li>• TB</li> </ul>	The presence of two or more <b>chronic</b> 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.	<ul style="list-style-type: none"> <li>- Increasing age</li> <li>- Being female</li> <li>- Socioeconomic deprivation</li> <li>- Obesity</li> <li>- Living in urban areas</li> <li>- Living in Kwa-Zulu Natal or Eastern Cape provinces (Province)</li> <li>- Being Indian/Asian (Race)</li> </ul>

between 2008 and 2012.	(2008) and 3 (2012).							
Ghose, Razak (2017). <i>Memory and Learning Complaints in Relation to Depression among Elderly People with Multimorbidity.</i>	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.	<ul style="list-style-type: none"> <li>• Arthritis</li> <li>• Asthma</li> <li>• Cancer</li> <li>• Chronic lung disease</li> <li>• Diabetes</li> <li>• Heart Disease</li> <li>• Hypertension</li> <li>• Stroke</li> </ul>	>1 condition	Not clearly stated.	<ul style="list-style-type: none"> <li>- Memory complaints in women</li> <li>- Being diagnosed with depression</li> </ul>
van Heerden, Barnabas, Norris et al (2017). <i>High prevalence of HIV and non-communicable disease risk factors in rural KwaZulu-Natal, South Africa.</i>	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.	<ul style="list-style-type: none"> <li>• Depression</li> <li>• HIV*<sup>1</sup></li> <li>• Hyperglycaemia*</li> <li>• Hyperlipidaemia*</li> <li>• Hypertension*</li> <li>• Obesity*</li> </ul>	Not reported.	Links to study objectives to investigate HIV and NCD risk factors.	Not reported
Chang, Gómez-Olivé, Payne et al. (2019). <i>Chronic multimorbidity among older adults in rural South Africa</i>	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.	<ul style="list-style-type: none"> <li>• Alcohol Dependence<sup>1</sup></li> <li>• Anaemia*</li> <li>• Angina<sup>1</sup></li> <li>• Chronic Bronchitis</li> <li>• Depression<sup>1</sup></li> <li>• Diabetes*</li> <li>• Dyslipidaemia*</li> <li>• HIV*</li> <li>• Hypertension*</li> <li>• Post-Traumatic Stress Disorder<sup>1</sup></li> </ul>	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.	<ul style="list-style-type: none"> <li>- Increased with age until 69 years and then decreased</li> <li>- Being separated/divorced or widowed</li> <li>- HIV associated with higher levels of MM using the second definition</li> <li>- Physical functioning and well-being and self-rated health were worse with increasing numbers of conditions and categories</li> <li>-----</li> <li>- Living with more people (household size) decreased odds of multimorbidity</li> </ul>

<sup>1</sup> HIV is measured but data on HIV is presented as a sub-group and thus excluded in this analysis

								<ul style="list-style-type: none"> <li>- No relationship between wealth and multimorbidity</li> <li>- Females has higher levels of multimorbidity but it was not significantly different</li> </ul>
<p>Sharman, Bachmann (2019).</p> <p><i>Prevalence and health effects of communicable and non-communicable disease comorbidity in rural KwaZulu-Natal, South Africa.</i></p>	<p>N= 47 334.</p> <p>Participants 15 years and older enrolled in the population-based HIV and health surveillance study, conducted by the Africa Health Research Institute.</p>	2009-2015	<p>Umkhanyakude district of rural KwaZulu-Natal.</p> <p>Rural.</p>		<ul style="list-style-type: none"> <li>• Hypertension (self-reported or on treatment)</li> <li>• Diabetes</li> <li>• TB within past 12 months</li> <li>• HIV (measured or on treatment)*</li> </ul>	<p>Proportion of participants with two or more conditions (<i>termed as co-morbidity</i>)</p>	<p>Based on research gap where few studies examine the prevalence of communicable and non-communicable diseases.</p>	<ul style="list-style-type: none"> <li>- Increasing age were associated with MM</li> <li>- Self-reported health poorer with multimorbidity</li> </ul>
<p>Lalkhen, Mash (2015).</p> <p><i>Multimorbidity in non-communicable diseases in South African primary healthcare.</i></p>		2010	<p>Primary healthcare facilities in the Western Cape, North West, Northern Cape and Limpopo.</p> <p>Rural and urban.</p>	<p>Cross sectional study.</p> <p>Facility based.</p>	<ul style="list-style-type: none"> <li>• Asthma*</li> <li>• COPD*</li> <li>• Diabetes*</li> <li>• Epilepsy*</li> <li>• Hypertension*</li> <li>• Osteoarthritis*</li> <li>• And other diseases</li> </ul>	<p>The presence of two or more diseases.</p>	<p>Study aimed to examine non-communicable diseases. All conditions recorded.</p>	<p>Not reported</p>
<p>Roche, de Vries (2017).</p> <p><i>Multimorbidity in a large district hospital: A descriptive cross-sectional study.</i></p>	<p>N= 491.</p> <p>Consecutive admissions to an internal medicine department of a large district hospital.</p>	2015	<p>District hospital, Cape Town.</p> <p>Urban.</p>	<p>Cross sectional study.</p> <p>Facility based-Internal medicine department</p>	<ul style="list-style-type: none"> <li>• Anaemia*</li> <li>• Asthma*</li> <li>• Bronchiectasis*</li> <li>• Cancer*</li> <li>• Cardiac failure*</li> <li>• Cerebrovascular accident*</li> <li>• COPD*</li> <li>• Cor pulmonale*</li> <li>• Current TB*</li> <li>• Deep vein thrombosis*</li> <li>• Delirium*</li> </ul>	<p>More than one disease concurrently.</p>	<p>Not clearly stated but appears to include all conditions that were seen in the district hospital.</p>	<ul style="list-style-type: none"> <li>- Length of stay not related to multimorbidity.</li> <li>- Lifestyle risk factors were not associated with multimorbidity.</li> </ul>

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					<ul style="list-style-type: none"> <li>• Diabetes*</li> <li>• Dilated cardiomyopathy*</li> <li>• Dyslipidaemia*</li> <li>• Epilepsy*</li> <li>• Gastroenteritis*</li> <li>• HIV*</li> <li>• Hypertension*</li> <li>• Ischaemic heart disease*</li> <li>• Lower respiratory tract infection*</li> <li>• Pneumonia*</li> <li>• Renal failure*</li> <li>• Sepsis*</li> <li>• Urinary tract infection*</li> </ul>			
Oni, Youngblood, Boulle et al. (2015). <i>Patterns of HIV, TB, and non-communicable disease multi-morbidity in peri-urban South Africa- a cross sectional study.</i>	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.	<ul style="list-style-type: none"> <li>• Diabetes*</li> <li>• HIV*</li> <li>• Hypertension*</li> <li>• TB*</li> </ul>	Coexistence of more than one <b>chronic</b> 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	<ul style="list-style-type: none"> <li>• Angina`</li> <li>• Arthritis</li> <li>• Asthma</li> <li>• Cataract</li> <li>• Cognitive impairment`</li> <li>• COPD</li> <li>• Depression`</li> <li>• Diabetes</li> <li>• Edentulism</li> <li>• Hypertension*</li> <li>• Obesity*</li> <li>• Stroke</li> </ul>	<p><b>Disease Combinations</b></p> <ul style="list-style-type: none"> <li>- Hypertension was commonly present with diabetes, stroke, angina, cataract and all other conditions.</li> <li>- Obesity and diabetes commonly co-occurred.</li> </ul>
Weimann et al (2016)	2008, 2012	<ul style="list-style-type: none"> <li>• Diabetes</li> <li>• HIV</li> <li>• Hypertension (self-reported or measured)</li> <li>• TB</li> </ul>	<p>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.</p> <p><b>Disease Combinations (2008):</b></p> <p><b>Two disease conditions:</b></p> <ol style="list-style-type: none"> <li>1) Diabetes and Hypertension (70.8%)</li> <li>2) TB and Hypertension (13.2%)</li> <li>3) HIV and Hypertension (10.8%)</li> <li>4) HIV and TB (3.9%)</li> <li>5) TB and Diabetes (0.8%)</li> <li>6) HIV and Diabetes (0.3%)</li> </ol> <p><b>Three disease conditions:</b></p> <ol style="list-style-type: none"> <li>1) TB, Diabetes and Hypertension (63.9%)</li> <li>2) Hypertension, HIV and TB (36.0%)</li> </ol>
Chang et al (2019)	2014-2015	<ul style="list-style-type: none"> <li>• Alcohol Dependence`</li> <li>• Anaemia*</li> <li>• Angina`</li> <li>• Chronic Bronchitis</li> <li>• Depression`</li> <li>• Diabetes*</li> <li>• Dyslipidaemia*</li> <li>• HIV*</li> <li>• Hypertension*</li> <li>• Post-Traumatic Stress Disorder`</li> </ul>	<p>Disease clusters limited to more than 1.5% of study population.</p> <p><b>Disease profile and clusters</b></p> <ul style="list-style-type: none"> <li>- Hypertension only (11.7%)</li> <li>- Hypertension and Dyslipidaemia (9.4%)</li> <li>- None (6.9%)</li> <li>- Hypertension and Anaemia (6.4%)</li> <li>- Hypertension and Dyslipidaemia and Anaemia (4.7%)</li> <li>- Dyslipidaemia (3.9%)</li> <li>- Anaemia (3.8%)</li> <li>- Anaemia and HIV (2.6%)</li> <li>- Hypertension and Anaemia and HIV (2.6%)</li> <li>- HIV (2.4%)</li> <li>- Dyslipidaemia and Anaemia (2.1%)</li> <li>- Dyslipidaemia and Anaemia and HIV (2.0%)</li> <li>- Hypertension and HIV (1.9%)</li> <li>- Hypertension and Dyslipidaemia and Diabetes (1.8%)</li> <li>- Hypertension and Depression (1.7%)</li> <li>- Dyslipidaemia and HIV (1.6%)</li> <li>- Hypertension and Dyslipidaemia and HIV (1.6%)</li> </ul>

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



Study	Year	Conditions included	Common disease clusters identified in South Africa
			<ul style="list-style-type: none"> <li>• Diabetes (5.4%)</li> <li>• Acute bronchitis (4.7%)</li> <li>• Allergic rhinitis (3.1%)</li> <li>• TB (2.2%)</li> </ul> <p>- Of those that had COPD (n=140), people also had:</p> <ul style="list-style-type: none"> <li>• Hypertension (47.9%)</li> <li>• Osteoarthritis (12.1%)</li> <li>• Diabetes (9.3%)</li> <li>• TB (6.4%)</li> <li>• Epilepsy (3.6%)</li> <li>• Ischaemic heart disease with angina (3.6%)</li> <li>• TB (2.1%)</li> <li>• Lipid dysfunction (2.1%)</li> <li>• Tobacco abuse (2.1%)</li> <li>• Ischaemic heart disease with angina (2.1%)</li> </ul> <p>- Of those that had Osteoarthritis (n=530), people also had:</p> <ul style="list-style-type: none"> <li>• Ischaemic heart disease (2.3%)</li> </ul>
Oni et al (2015).	Sep 2012 - May 2013	<ul style="list-style-type: none"> <li>• Diabetes*</li> <li>• HIV*</li> <li>• Hypertension*</li> <li>• TB*</li> </ul>	<p>Of the 14364 participants, 21.3% had two diseases, 1.2% had three diseases and 0.1% had four diseases.</p> <p><b>Of those that had two diseases (n=3058)</b></p> <ol style="list-style-type: none"> <li>1. Hypertension and diabetes (69.1%)</li> <li>2. Hypertension and HIV (21.4%)</li> <li>3. HIV and TB (6.2%)</li> <li>4. HIV and diabetes (1.6%)</li> <li>5. Hypertension and TB (1.5%)</li> <li>6. TB and diabetes (0.2%)</li> </ol> <p><b>Of those that had three diseases (n=173)</b></p> <ol style="list-style-type: none"> <li>1. Hypertension, diabetes and HIV (63%)</li> <li>2. Hypertension, HIV and TB (26.6%)</li> </ol>

## 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	%
<b>Population-based surveys</b>								
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)	-	-	-	-
		<b>Overall (18+)</b>	-	<b>11.2 (9.8 - 12.5)</b>	-	-	-	-
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
		<b>Overall (50+)</b>	<b>2376 / 3747*</b>	<b>63.4</b>	-	-	-	-
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	-	-	-	-
		<b>Overall (15+)</b>	-	<b>2.7 (2.5 – 3.0)</b>	-	-	-	-
	2012	15 - 24	-	0.0	-	-	-	-
		25 - 34	-	0.8	-	-	-	-
		35 - 44	-	3.1	-	-	-	-
		45 - 54	-	3.1	-	-	-	-
		55 - 64	-	9.0	-	-	-	-
		65+	-	10.5	-	-	-	-
		<b>Overall (15+)</b>	-	<b>2.8 (2.6 – 3.1)</b>	-	-	-	-
Ghose, Razak (2017).	2010	<b>Overall (50+)</b>	<b>130 / 422</b>	<b>30.8</b>	-	<b>16.0</b>	-	<b>35.8</b>
<b>Community-based studies (cross-sectional study)</b>								
van Heerden,	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	%
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
	<b>Overall (40+)</b>	<b>2700 / 3889</b>	<b>69.4</b>	<b>1182 / 1758</b>	<b>67.2</b>	<b>1518 / 2130</b>	<b>71.2</b>	
Sharman, Bachmann (2019).	2009	<b>Overall (18+)</b>		<b>8.4</b>				
	2015	<b>40+</b>		<b>18.4</b>				
	2015	<b>Overall (18+)</b>		<b>13.2</b>				
<b>Health facility-based studies (cross-sectional surveys and routine health information systems)</b>								
Lalkhen, Mash (2015).	2010	<b>Overall (Mean ages±)</b>	-	<b>48.4</b>	-	-	-	-
Roche, de Vries (2017).	2015	<b>Overall (Mean age 49 years)</b>	371 / 427	<b>87.0</b>	-	-	-	-
Oni, Youngblood, Boulle et al. (2015).	2012/13	<b>Overall (18+)</b>	3246 / 14364	<b>22.6</b>	-	-	-	-

*Italicised data extracted from graphs using Webplot digitizer*

\*estimated from available information

□ standardised 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).

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**Appendix 1: PRISMA Checklist**

Section/topic	#	Checklist item	Reported on page #
<b>TITLE</b>			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
<b>ABSTRACT</b>			
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
<b>INTRODUCTION</b>			
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
<b>METHODS</b>			
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
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
<b>RESULTS</b>			
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
<b>DISCUSSION</b>			
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

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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
<b>FUNDING</b>			
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](http://www.prisma-statement.org).

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# BMJ Open

## Multimorbidity in South Africa: A systematic review of prevalence studies

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<b>Primary Subject Heading</b>:	Epidemiology
Secondary Subject Heading:	Global health, Public health
Keywords:	Public health < INFECTIOUS DISEASES, Epidemiology < TROPICAL MEDICINE, EPIDEMIOLOGY

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## Multimorbidity in South Africa: A systematic review of prevalence studies

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Total words: 3994/4000

Tables: 3

Figures: 2

1  
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3 28 **ABSTRACT**  
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5 29 **Objectives:**  
6

7 30 To review prevalence studies of multimorbidity in South Africa to identify prevalence estimates,  
8 31 common disease clusters and factors associated with multimorbidity.  
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10 32  
11 33 **Design:**

12 34 Systematic review.  
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16 36 **Setting:**

17 37 South Africa (general community and healthcare facilities).  
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21 39 **Data sources:**

22 40 Articles were retrieved from electronic databases (PubMed, Web of Science, Scopus, CINAHL,  
23 41 Science Direct and JSTOR).  
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27 43 **Eligibility criteria:**

28 44 Studies addressing the prevalence of multimorbidity in South Africa were eligible for inclusion. A  
29 45 systematic search was done in various databases up to December 2020. A risk of bias assessment  
30 46 was conducted for each article using a modified checklist.  
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34 48 **Study selection:**

35 49 Two researchers independently screened titles and abstracts; assessed the risk of bias of each study  
36 50 and extracted data. Included studies were described using a narrative synthesis.  
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40 52 **Results:**

41 53 In total, 1,407 titles were retrieved; of which ten articles were included in the narrative synthesis.  
42 54 Six studies had a low risk of bias and three had a moderate risk of bias. One study was not assessed  
43 55 for risk of bias, because there was no criteria that apply to routine health information system. Three  
44 56 of the included studies were population-based surveys, four were community-based cohorts, and  
45 57 three cross-sectional studies of health facility data. The prevalence of multimorbidity was low to  
46 58 moderate (3 – 23%) in studies that included younger people or had a wide range of selected age  
47 59 groups; and moderate to high (30 – 87%) in studies of older adults. The common disease clusters  
48 60 were hypertension and diabetes, hypertension and HIV, and TB and HIV.  
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52 62 **Conclusion**  
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3 63 All studies indicated that multimorbidity is a norm in South Africa, especially amongst older  
4 64 adults. Hypertension is the main driver of multimorbidity. Research on multimorbidity in South  
5 65 Africa need to be revitalized, and with high-quality study designs.  
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9 67 **Registration:** PROSPERO (CRD42020196895)

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3 69 **Article Summary**  
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5 70 **Strengths and limitations of this study**  
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8 71 • To our knowledge, this is the first systematic review of multimorbidity prevalence studies  
9 72 in South Africa, and of an African country.  
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11 73 • This systematic review followed the Preferred Reporting Items for Systematic reviews and  
12 74 Meta-Analyses (PRISMA) statement.  
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14 75 • This review includes studies conducted in general community and healthcare settings.  
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16 76 • A limitation of this study was that it excludes studies conducted in sub-populations with  
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18 77 one specific disease (e.g. multimorbidity in cancer patients).  
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20 78 • Grey literature (non-academic literature) was excluded.  
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26 80 **Keywords:** Multimorbidity, Chronic diseases, Prevalence, South Africa, Trends, Disease  
27 81 clusters.  
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## 86 INTRODUCTION

87 A third of adults residing in low and middle-income countries (LMICs) are thought to be afflicted  
88 by two or more co-existing health conditions; also known as multimorbidity.[1] The last two  
89 decades have seen an exponential growth in the number of studies about multimorbidity.[2] This  
90 can be attributed to more research into ageing populations,[2] and the recognition that  
91 multimorbidity impacts patient-care and healthcare systems.[3] Other consequences of  
92 multimorbidity include increased mortality levels,[4] lowered quality of life,[5] the risk of  
93 polypharmacy [6] and intensified utilisation of health services and associated costs.[7, 8] More  
94 recently, multimorbidity was implicated as a risk factor for COVID-19 mortality.[9, 10]

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96 Most research to date has been conducted in high-income countries; sparking calls for similar  
97 research in LMICs.[2, 11, 12] Research is needed into multimorbidity in LMICs, like South Africa,  
98 where disease burdens differ to those in high-income countries. South Africa has a unique disease  
99 burden – it has the largest number of people living with HIV in the world.[13] With the availability  
100 of antiretrovirals, people with HIV are living longer and developing age-related non-  
101 communicable diseases (NCDs).[14] At the same time, the burden of disease due to NCDs is  
102 increasing in the country; giving rise to a disease pattern of co-existing infectious diseases and  
103 NCDs.[15, 16]

104  
105 In resource-constrained health settings, it is imperative that we estimate the magnitude of  
106 multimorbidity as well as the nature and type of disease clusters to more efficiently manage  
107 patients and organize health service delivery. South Africa lacks a robust national routine health  
108 information system to inform its morbidity profile. Countries with less robust routine health  
109 information systems need to rely on smaller-scale studies and surveys to better understand the  
110 scale and impact of the problem of multimorbidity. This has led to numerous studies focused on  
111 quantifying the prevalence of multimorbidity and studies focused on integrated care in South  
112 Africa.[17-21] However, many of these studies suffer from the methodological problems that tend  
113 to plague multimorbidity studies elsewhere, which is a lack of standardization.[22] This makes it  
114 difficult to compare and interpret studies, given their varying estimates and methodologies. This  
115 study set out to systematically assess multimorbidity prevalence studies in South Africa, to report  
116 on common disease clusters and factors associated with multimorbidity in South Africa.

## 117 **METHODS**

### 118 **Search strategy and database search**

119 The protocol for this study was registered with PROSPERO (CRD42020196895) and published  
120 elsewhere.[\[23\]](#) The Preferred Reporting Items for Systematic Reviews and Meta-Analyses  
121 guidelines (PRISMA)[\[24\]](#) guided this study (Appendix 1). One researcher experienced in  
122 systematic review methodology (EBT), performed a systematic literature search in PubMed, Web  
123 of Science, Scopus, CINAHL, Science Direct and JSTOR to identify articles reporting  
124 epidemiological data on multimorbidity in the adult population of South Africa. The search  
125 strategy was reviewed by an expert librarian (Appendix 2). The time frame of the search was not  
126 restricted and covered a period up to December 2020.

### 127 **Study selection and data extraction**

128 The search output citations were downloaded and saved to EndNote Version X8.[\[25\]](#) The EndNote  
129 de-duplication function was employed, and remaining citations were uploaded into an electronic  
130 screening website, Rayyan.[\[26\]](#) Two researchers (RAR, EBT) independently screened the titles  
131 and abstracts and studies deemed irrelevant were discarded. A third researcher (BvW) assisted  
132 with conflicts. Case reports, reviews, editorials, letters, studies among children, studies not  
133 conducted in South Africa, study designs that were not cross-sectional or cohorts, studies where it  
134 was not possible to calculate the prevalence of multimorbidity in the general population (e.g.  
135 studies only examining multimorbidity in cancer patients) were excluded. Where multiple studies  
136 reported on the same source of data (e.g. one national survey), only the most relevant study was  
137 included.

138 The full-texts were independently assessed by two researchers (RAR, EBT) using the electronic  
139 data capture system, the Burden of Disease Review Manager (BODREVMAN).[\[27\]](#)  
140 BODREVMAN facilitates the independent data collection of study characteristics (study design,  
141 sample size, geographical location, whether a study is community-based or facility-based). Also,  
142 data on the definition of multimorbidity used, the disease conditions included in the study and the  
143 prevalence of multimorbidity (by age and sex where possible) were extracted. Disagreements were  
144 discussed and resolved. The reference lists of included articles were screened for additional  
145 studies.



### 146 **Quality assessment**

147 Two researchers (RAR, EBT) independently assessed and appraised each article. BODREVMAN  
148 contains a modified checklist based on the Newcastle Ottawa[28] and Hoy checklist.[29] The tool  
149 has been described elsewhere.[30] Each article was independently scored and categorised as either  
150 having a high, moderate or low risk of bias. Studies based on routine health information systems  
151 (RHIS) did not undergo a risk of bias assessment due to a lack of assessment criteria for this study  
152 type.

### 153 **Data extraction and analysis**

154 Information on multimorbidity definitions, disease conditions included and the proportion of the  
155 sample with more than one condition, were extracted. Authors were contacted for data by age and  
156 sex breakdowns. Studies were categorised by study type (cohort or cross-sectional), and study  
157 setting (community or facility-based). It was noted whether disease conditions included were self-  
158 reported or biologically assessed.

159 The mean and standard deviation, or the absolute number and the percentage were recorded, as  
160 appropriate. The age range and sex for each category were recorded. Where data appeared in  
161 graphical formats, authors were contacted for the original data or WebPlotDigitizer Version 4.3  
162 (California)[31] was used to extract data. STATA 15 (StataCorp, TX) was used to calculate  
163 standard errors using the sample size and prevalence estimates where possible.

### 164 **Patient and public involvement**

165 Patients and the public were not involved in this study. This study was given ethics approval by  
166 the Biomedical Research Ethics Committee of the University of the Western Cape (BM20/5/8).

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## 171 RESULTS

### 172 Search results

173 In total, 1407 titles were retrieved, and 1081 records were screened after de-duplication (Figure  
174 1). By screening titles and abstracts, 1040 articles were excluded. Forty-one full-text articles were  
175 assessed for eligibility, of which ten were included in a narrative synthesis.[\[32-41\]](#) In the title and  
176 abstract screening phase, reviewers conflicted on 2.9% of the articles. In the full-text phase, the  
177 reviewers had conflicts in 2 of the 41 articles. All conflicts were resolved.

178

179 <Figure 1: PRISMA flow diagram>

### 180 Study characteristics

181 The sample sizes of included studies ranged from 422[\[35\]](#) to 47 334 participants[\[38\]](#) (Table 1).  
182 All included studies were published after 2015 but the period of data collected ranged from  
183 2003[\[32\]](#) to 2015.[\[37, 38, 40\]](#) Three studies conducted a secondary data analysis of population-  
184 based surveys.[\[32-34\]](#) The surveys analysed were the 2003 World Health Survey (WHS),[\[32\]](#) 2007  
185 and 2010 WHO Study on global AGEing and adult health (SAGE),[\[33, 35\]](#) and the 2008 and 2012  
186 South African National Income Dynamics Survey (SANIDS).[\[34\]](#) Three studies were cross-  
187 sectional analyses of community-based cohorts and surveys.[\[36-38\]](#) The remaining three studies  
188 were of a cross-sectional nature and based in health facilities.[\[39-41\]](#)

189 Three studies were conducted nationally[\[32-34\]](#) with others conducted in Kwa-Zulu Natal  
190 province (n=3),[\[35, 36, 38\]](#) the Western Cape province (n=2) [\[40, 41\]](#) and Mpumalanga province  
191 (n=1).[\[37\]](#) One study was conducted in primary healthcare facilities in the Western Cape, North  
192 West, Northern Cape and Limpopo provinces.[\[39\]](#) Four studies were conducted in rural areas [\[35-](#)  
193 [38\]](#), two studies were conducted in urban areas[\[40, 41\]](#) and the remaining studies were conducted  
194 in both urban and rural areas.[\[32, 33, 39, 42\]](#) Six studies had a low risk of bias,[\[32-34, 37-39\]](#) three  
195 had a moderate risk of bias[\[35, 36, 40\]](#) and one based on a RHIS was not assessed for risk of bias  
196 due to a lack of assessment criteria for this study type.

197

198

199

200

201 **Table 1: Characteristics of included studies**

Study type	Study	Study population and size	Year	Location	Risk of bias (score)
Population-based survey	Afshar, Roderick, Kowal <i>et al</i> (2015). [32]	N= 2629. Adults 18 years and older in the 2003 World Health Survey.	2003	South Africa (Urban and rural areas included)	Low (14)
	Garin, Koyanagi, Chatterji <i>et al</i> (2016). [33]	N = 3836. Adults 50 years and older in the 2007 WHO Study on global AGEing and adult health.	2007-2008	South Africa (Urban and rural areas included)	Low (15)
	Weimann, Dai, Oni (2016). [34]	N=18526 in 2008. N=20015 in 2012. Participants 15 years and older in the National Income Dynamic Survey Wave 1 (2008) and Wave 3 (2012).	2008, 2012	South Africa (Urban and rural areas included)	Low (17)
Cross-sectional study (Community-based)	Ghose, Razak (2017). [35]	N=422. Adults 50 years and older infected and/or affected by HIV in the SAGE Well-being of Older People Study (WOPS) 2010.	2010	Hlabisa subdistrict, KwaZulu-Natal (Rural)	Moderate (12)
	van Heerden, Barnabas, Norris <i>et al</i> (2017). [36]	N=570. Adults older than 18 years enrolled in a cohort study to increase engagement in HIV care and testing.	Nov 2011 - Jun 2012	KwaZulu-Natal (Rural)	Moderate (13)
	Chang, Gómez-Olivé, Payne <i>et al</i> (2019). [37]	N = 3889. Adults enrolled in the Health and Ageing in Africa: A longitudinal study of an INDEPTH Community in South Africa Programme.	2014-2015	Agincourt Health and Demographic Surveillance System, Bushbuckridge subdistrict, Mpumalanga (Rural)	Low (17)
	Sharman, Bachmann (2019). [38]	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, KwaZulu-Natal (Rural)	Low (14)

Study type	Study	Study population and size	Year	Location	Risk of bias (score)
Cross-sectional study (Health facility-based)	Lalkhen, Mash (2015). [39]	N=5793 Primary healthcare (PHC) users where all participants had at least one NCD (Hypertension, Diabetes, Asthma, Epilepsy, COPD, Osteoarthritis).	2010	Primary healthcare facilities in the Western Cape, North West, Northern Cape and Limpopo  (Urban and rural areas included)	Low (16)
	Roche, de Vries (2017). [40]	N= 491. Consecutive admissions to an internal medicine department of a large district hospital.	2015	District hospital, Cape Town, Western Cape  (Urban)	Moderate (13)
Routine Health Information Systems	Oni, Youngblood, Boulle <i>et al</i> (2015). [41]	N=14 364. Chronic disease patients (adults) with at least one disease (HIV, TB, diabetes, and hypertension) identified using the Western Cape Department of Health Data Repository and the Electronic prescription system.	Sep 2012 - May 2013	Michael Mapongwana clinic, Khayelitsha, Cape Town, Western Cape  (Peri-urban)	NA

## 202 Disease conditions assessed

203 Study findings on the prevalence of multimorbidity can be influenced by i) the definition of  
204 multimorbidity used, ii) the number of disease conditions included in the study, iii) the actual  
205 disease conditions included and iv) how the disease conditions were measured.

206 All included studies used a “count” of the number of diseases to define multimorbidity i.e.  
207 multimorbidity was defined by having two or more diseases (Appendix 3). Half of these studies  
208 specified they were only focused on chronic conditions.[32-34, 37, 41] Two health facility-based  
209 studies included acute conditions such as lower respiratory infections.[39, 40] The inclusion of  
210 acute disease conditions could inflate the prevalence of multimorbidity. The full list of disease  
211 conditions included can be found in Appendix 3.

212 One study included two definitions of multimorbidity – a “count” definition (as described above)  
213 and another more detailed definition. The detailed definition specified multimorbidity as the  
214 presence of conditions from more than one of the following categories of disease: cardiometabolic  
215 conditions, mental disorders, or HIV and anaemia.[37] When using this definition, the prevalence  
216 of multimorbidity was lowered as it only includes discordant diseases (i.e. excludes diseases that

217 belong to the same category such as hypertension and diabetes). For this review, we used their  
218 results from the “count” definition, unless otherwise stated.

219 The number of disease conditions included in each study ranged from four [41] to 24.[40] (Table  
220 2). Diabetes was included as a disease condition in all ten studies. Most studies included  
221 hypertension (n=9) in their assessment of multimorbidity. HIV (n=5), asthma (n=5) and heart  
222 disease (n=5) were also commonly included disease conditions.

223 The study design and setting influenced how disease conditions were measured (Appendix 3).  
224 Population-based surveys tended to use self-reported data, although some included measurements  
225 of blood pressure and obesity. Studies based on cohorts tended to use a mix of measured  
226 (biomarkers) and self-reported disease conditions. Facility-based studies tended to use medical  
227 records and biomarkers to determine the disease burden in their samples.

228 **Table 2: Ten common disease conditions reported in articles**

Disease conditions included	Studies										Total articles included in
	Afshar, Roderick, Kowal et al (2015)	Garin, Koyanagi, Chatterji et al (2016)	Weimann, Dai, Oni (2016)	Ghose, Kazak (2017)	van Heerden, Barnabas, Norris et al (2017)	Chang, Gómez-Olivé, Payne et al (2019)	Sharman, Bachmann (2019)	Lalkhen, Mash (2015)	Roche, de Vries (2017)	Oni, Youngblood, Boule et al (2015)	
<b>Diabetes</b>	x	x	x	x	x+	x	x	x	x	x	<b>10</b>
<b>Hypertension</b>		x	x	x	x	x	x	x	x	x	<b>9</b>
<b>HIV</b>			x	x	x±	x	x		x	x	<b>5</b>
<b>Asthma</b>	x	x		x				x	x		<b>5</b>
<b>IHD / Heart disease/ Angina</b>	x	x		x		x			x		<b>5</b>
<b>Depression</b>	x^	x		x±	x	x*					<b>4</b>
<b>COPD</b>		x		x'				x	x		<b>4</b>
<b>Arthritis/ osteoarthritis</b>	x	x		x				x			<b>4</b>
<b>TB / Current TB</b>			x				x		x	x	<b>4</b>
<b>Lipid disorder</b>					x	x			x		<b>3</b>

\*Depression, post-traumatic stress disorder, alcohol dependence  
+ Hyperglycaemia  
'Chronic lung disease  
^ Depression, schizophrenia or psychosis

± Assessed condition but was not able to incorporate into multimorbidity calculation based on the way study reported it  
IHD=Ischaemic Heart Disease, COPD=Chronic Obstructive Pulmonary Disease; TB= Tuberculosis

## 229 **Patterns of disease clusters observed**

230 The studies reported on common disease clusters using bubble charts of pair-wise co-morbid  
231 conditions,[\[33, 37\]](#) reporting each disease with their most common co-morbid condition,[\[38, 39\]](#)  
232 or schematics detailing double and triple morbidities.[\[34, 37, 41\]](#) The results of the studies were  
233 difficult to compare due to how the data were reported. Four studies did not describe common  
234 disease clusters found in their study populations.[\[32, 35, 36, 40\]](#)

235 While it was not possible to ascertain the largest disease cluster in one study, [Garin, Koyanagi \[33\]](#)  
236 found hypertension featured strongly with diabetes, stroke, angina, cataract, cognitive impairment  
237 and all other conditions examined in their analysis. Arthritis and obesity were also commonly  
238 listed as co-morbid conditions for all other disease conditions.

239 Table 3 summarises the top five disease clusters from the five remaining studies. The number of  
240 disease combinations varied in each study with some studies reporting less than ten disease  
241 clusters[\[34, 41\]](#) and others reporting more than twenty disease clusters[\[37-39\]](#) (Appendix 4).

242 Hypertension was frequently co-morbid with other diseases (Table 3). [Weimann, Dai \[34\]](#) and  
243 [Oni, Youngblood \[41\]](#) showed similar patterns of disease – with hypertension and diabetes being  
244 the most common disease cluster. In these studies, the disease cluster hypertension and HIV ranked  
245 highly, followed by TB and HIV. In terms of having three co-occurring diseases, both ranked the  
246 combination of TB, diabetes and hypertension highest; followed by the combination of  
247 hypertension, HIV and TB. [Lalkhen and Mash \[39\]](#) also found hypertension and diabetes to be the  
248 largest disease cluster in their study. While [Chang, Gómez-Olivé \[37\]](#) found the largest disease  
249 cluster was hypertension and dyslipidaemia, followed by hypertension and anaemia; and the  
250 combination of hypertension, dyslipidaemia and anaemia. Anaemia and HIV also commonly co-  
251 occurred.

252 Age and sex tend to influence the susceptibility of an individual to certain diseases. However,  
253 studies generally did not report disease clusters by these breakdowns. Two studies reported that  
254 HIV was more prevalent in their younger participants;[\[37, 38\]](#) while hypertension affected those  
255 over the age of 40 years, and diabetes and angina affected people above the age of 60 years. One  
256 study also noted that hypertension and diabetes were more common in females compared to males,

257 and TB was more common in males.<sup>[38]</sup> One study noted that multimorbidity was lower in patients  
 258 with HIV that were on ART (compared to patients not on ART or with unknown ART status) but  
 259 the association did not hold when broken down by age group.<sup>[41]</sup>

260 These results must be interpreted with caution as each study included different disease conditions;  
 261 and even when the same disease conditions were included, these could differ in the way they were  
 262 measured e.g. self-reported or biologically measured.

263 **Table 3: Top five disease clusters in each study**

Disease combinations / clusters			Total studies reported (n=5)	Study citation
Disease 1	Disease 2	Disease 3		
Hypertension	Diabetes		4	[34, 38, 39, 41]
Hypertension	HIV		3	[34, 38, 41]
TB	HIV		3	[34, 38, 41]
Hypertension	TB		2	[34, 41]
Diabetes	HIV		2	[38, 41]
TB	Diabetes		1	[34]
Hypertension	Osteoarthritis		1	[39]
Asthma	Hypertension		1	[39]
Hypertension	COPD		1	[39]
Hypertension	IHD		1	[39]
Hypertension	Dyslipidaemia		1	[37]
Hypertension	Anaemia		1	[37]
Hypertension	Dyslipidaemia	Anaemia	1	[37]
Anaemia	HIV		1	[37]
Hypertension	Anaemia	HIV	1	[37]

### 264 Multimorbidity prevalence

265 Due to study heterogeneity, it was not possible to do a meta-analysis. Studies reported  
 266 multimorbidity prevalence by varying age breakdowns making direct comparison difficult. Several  
 267 studies reported multimorbidity by age group and/or sex (Appendix 5). Two studies reported the  
 268 median/mean age of participants but the age range of participants was not included<sup>[39, 40]</sup> and  
 269 one did not report an overall multimorbidity prevalence for their study<sup>[36]</sup>. From the remaining  
 270 studies, multimorbidity prevalence tended to be low to moderate in studies which included younger  
 271 people or had a wide range of age groups (3% – 23%) (Figure 2); and moderate to high in studies  
 272 reporting on adults aged 50 years and older (30% – 71%) (Figure 3).

273



274  
 275 <Figure 2: Graph of multimorbidity prevalence estimates for studies that include younger  
 276 age groups>

277  
 278 <Figure 3: Graph of multimorbidity prevalence in studies including persons aged 50 years  
 279 and older>

280 In population-based surveys, each study reported a different age group (Table 4). In those 18 years  
 281 and above, [Afshar, Roderick \[32\]](#) reported an overall prevalence of 11%, however, this was age-  
 282 standardised against the WHO Standard Population which means it uses a standardised age  
 283 structure rather than the one found in South Africa. Another study reported the results of a panel  
 284 survey in 2008 and 2012 and showed a rather low prevalence of multimorbidity (2.7%) for those  
 285 aged over 15 years old.[\[34\]](#) The study showed a negligible increase (0.1%) during a four year  
 286 period. A study that only reported on those aged above 50 years of age, showed a very high overall  
 287 prevalence of multimorbidity (63.4%).[\[33\]](#)

288 Among community-based cross-sectional studies, the prevalence among older adults ranged from  
 289 18%[\[38\]](#) to 69%.[\[37\]](#) However, [Chang, Gómez-Olivé \[37\]](#) used two definitions of multimorbidity  
 290 and when applying the second definition (categories of discordant disease groups), they estimated  
 291 a lower prevalence of 54%. One study that included younger people noted a 5% increase in  
 292 multimorbidity prevalence between the period 2009 to 2015.[\[37\]](#)

293 In health facilities, two studies found moderate levels of multimorbidity (14.4% and 22.6%).[\[39,](#)  
 294 [41\]](#) One study based in a health facility found an extremely high prevalence of multimorbidity  
 295 (87.0%), however, this study included both chronic and acute health conditions.[\[40\]](#)

296 **Table 4: Multimorbidity prevalence by age group**

	Study	Year	Age band (years)	Prevalence of multimorbidity	
				n/N	% (95% CI) <sup>a</sup>
Population-based surveys	<b>Afshar (2015)</b> <sup>□</sup>	2003	Overall (18+)	-	11.2 (9.8 - 12.5)
	<b>Garin (2016)</b>	2007/8	Overall (50+)	2376 / 3747*	63.4
	<b>Weimann (2016)</b>	2008	Overall (15+)	-	2.7 (2.5 – 3.0)



	Study	Year	Age band (years)	Prevalence of multimorbidity		
				n/N	% (95% CI) <sup>a</sup>	
		2012	Overall (15+)	-	2.8 (2.6 – 3.1)	
Cross-sectional study (Community-based)	Ghose (2017)	2010	Overall (50+)	130 / 422	30.8	
	Chang (2019)	2014/15	Overall (40+)	2700 / 3889	69.4	
	Sharman (2019)	2009	Overall (18+)	-	8.4	
			2015	Overall (40+)	-	18.4
			2015	Overall (18+)	-	13.2
Cross-sectional study (Health facility-based)	Lalkhen (2015)	2010	Overall (Mean age <sup>±</sup> )	2806 / 5793	48.4	
	Roche (2017)	2015	Overall (Mean age 49 years)	371 / 427	87.0	
Routine health information systems	Oni (2015)	2012/13	Overall (18+)	3246 / 14364	22.6	

<sup>a</sup> Not all studies reported a 95% CI and there was insufficient information to calculate this.  
\* Estimated from available information.  
□ Reports a standardised multimorbidity prevalence.  
<sup>±</sup> 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).

297

## 298 Factors associated with multimorbidity

299 Most of the included studies reported on factors they found to be associated with multimorbidity  
300 (Appendix 3). Multimorbidity was frequently associated with increasing age. [32-34, 37, 38, 41]  
301 However, [Garin, Koyanagi \[33\]](#) noted a decrease in the prevalence of multimorbidity in the age  
302 group 60+ years and [Chang, Gómez-Olivé \[37\]](#) noted a decrease from the age group 69+ years.  
303 Being female was inconsistently linked to a high prevalence of multimorbidity. The pattern was  
304 noted in two studies; [33, 34] although another study reported it was not statistically  
305 significant; [37] while one found no distinction between males and females. [41] One study found  
306 that living in urban areas was a risk factor for multimorbidity [34] while another found that living  
307 in rural areas was associated with multimorbidity. [33] Other factors found to be associated with  
308 multimorbidity were: a lower level of education; [32, 33] being separated, divorced or  
309 widowed; [33, 37] living in KwaZulu-Natal or the Eastern Cape provinces, being Indian/Asian or

1  
2  
3 310 being obese.[34] Socioeconomic deprivation was found to be associated with multimorbidity in  
4  
5 311 one study,[34] but another found no association between wealth and multimorbidity.[37]

6  
7 312 Other studies identified the effects of multimorbidity such as having memory complaints (in  
8  
9 313 women), suffering from depression,[35] decreased well-being and self-reported health.[37, 38]  
10  
11 314 One study found that length of stay in hospital was not related to multimorbidity and also did not  
12  
13 315 link lifestyle risk factors to multimorbidity.[40]

## 14 15 316 **DISCUSSION**

16  
17 317 This study set out to assess the prevalence of multimorbidity in adults in South Africa using  
18  
19 318 systematic review methodology. This study found considerable heterogeneity among included  
20  
21 319 articles, which stemmed from differences in study design, disease conditions assessed and how  
22  
23 320 study results were reported. Despite this, we found a low to moderate multimorbidity prevalence  
24  
25 321 in studies including younger people and a moderate to high prevalence in studies including older  
26  
27 322 adults. Due to study heterogeneity, it is difficult to compare these results to the findings of a recent  
28  
29 323 systematic review which estimated a pooled multimorbidity prevalence of 30% for LMICs.[1]

30 324 Three of our included studies reported fairly low levels of multimorbidity prevalence.[32, 34, 38]  
31  
32 325 One study standardised the prevalence to the world population which may have resulted in a lower  
33  
34 326 prevalence estimate (11.2%).[32] The other study reported an overall prevalence of less than 3%  
35  
36 327 among people 15 years and older; and in people over the age of 65 years, they estimated a  
37  
38 328 prevalence of only 10%.[34] The same 2008 dataset from a population-based survey was used in  
39  
40 329 another study and found a similar prevalence of multimorbidity, despite using different methods  
41  
42 330 (4.0%).[43] The low prevalence found in this survey could be attributed to a healthier population  
43  
44 331 being sampled or as the authors suggested, underreporting of self-reported data due to stigma  
45  
46 332 around HIV and TB.[34] The study also included only four disease conditions which may have  
47  
48 333 resulted in a lower prevalence. In contrast, a study that included many acute and chronic conditions  
49  
50 334 resulted in a very high prevalence estimate.[40] This highlights the significant impact of study  
51  
52 335 design on the estimates produced. The third study had a large sample size but may have  
53  
54 336 underestimated the burden of multimorbidity due to the use of self-reported data.[38] Also, they  
55  
56 337 had missing data on HIV due to additional consent being required.

1  
2  
3 338 Age is accepted to be an important predictor of multimorbidity.[40] Most studies showed that the  
4  
5 339 prevalence of multimorbidity increased with age, however, two studies observed decreases in the  
6  
7 340 oldest age groups. This needs further investigation. What also remains unclear is whether  
8  
9 341 multimorbidity does in fact affect people at younger ages in LMICs.[12] Based on this systematic  
10  
11 342 review, more studies need to interrogate multimorbidity by age group as the lack of reporting  
12  
13 343 makes it difficult to monitor. Age and sex are both important predictors of multimorbidity and  
14  
15 344 multimorbidity should be reported in a disaggregated manner where possible.[44]

16 345 The common diseases assessed in our included studies (diabetes and hypertension) have a high  
17  
18 346 prevalence in South Africa. It was surprising that only half of the studies included HIV as a  
19  
20 347 condition of interest; given the high prevalence of HIV in the country. However, many of the  
21  
22 348 studies were based on secondary data analysis and were limited to the conditions that were  
23  
24 349 included. Future primary studies in South Africa should plan to incorporate infectious diseases  
25  
26 350 (HIV and TB) into studies of multimorbidity where possible.

27 351 Despite few studies reporting on which disease clusters were largest, hypertension appeared to be  
28  
29 352 the biggest contributor to the burden of multimorbidity, particularly the co-occurrence of  
30  
31 353 hypertension with diabetes. That said, hypertension and diabetes were also among the most widely  
32  
33 354 included conditions in studies of multimorbidity. Hence, these findings may be biased to  
34  
35 355 conditions that are included in studies and not necessarily the reality of the situation. Given that  
36  
37 356 the prevalence of hypertension is high in South Africa (44% of men and 46% of women aged 15  
38  
39 357 years and older, as high as 84% in people aged above 65 years),[45] it does hold weight that it  
40  
41 358 would be a common co-morbid condition. A recent study on COVID-19 mortality in South Africa  
42  
43 359 found the combination of hypertension and diabetes was a common disease cluster in people who  
44  
45 360 had succumbed to the disease.[46] This cluster of disease was more prevalent than having  
46  
47 361 hypertension or diabetes only. Information on the prevalence of co-morbidities and  
48  
49 362 multimorbidities may prove very important in light of the COVID-19 pandemic.

50 363 We mainly included three types of studies in our analysis; studies based on the secondary data  
51  
52 364 analysis of national surveys, studies based on community cohorts and studies based in health  
53  
54 365 facilities. All three types of studies have strengths. National survey data can provide an overall  
55  
56 366 picture of what is happening in the general population. However, they tend to use self-reported  
57  
58 367 data which may result in an underestimation of the burden of disease; as a large percentage of

1  
2  
3 368 NCDs are underdiagnosed. Nevertheless, there are many more national surveys that could be  
4  
5 369 analysed to provide an overview of multimorbidity from these sources. Studies based on cohorts  
6  
7 370 generated rich information, tended to have large sample sizes and had a mixture of self-report data  
8  
9 371 and measure biological samples. These studies were mostly limited to rural areas. Whether  
10  
11 372 multimorbidity is more common in rural or urban areas in South Africa remains unclear. Existing  
12  
13 373 cohorts will continue to provide a good source of information on multimorbidity and we can expect  
14  
15 374 more data to come out of planned urban cohorts.[47] Studies based in health facilities tended to  
16  
17 375 include more health conditions (both acute and chronic diseases) and tended to report higher levels  
18  
19 376 of multimorbidity. This may be due to people who require health care (ill individuals) accessing  
20  
21 377 these facilities. However, these studies provide an important source of information that is highly  
22  
23 378 relevant to the management and planning for multimorbidities. For example, a recent study by  
24  
25 379 [Mannie and Kharrazi \[48\]](#) assessed the geographical distribution of comorbidities among 2.6  
26  
27 380 million commercially insured individuals in South Africa using a comorbidity index that  
28  
29 381 highlighted healthcare utilization. Using this score, they were able to identify areas of high  
30  
31 382 utilization and underserved individuals; although they did not provide detail on the types of  
32  
33 383 services needed. Multimorbidity is known to increase the costs to healthcare systems.[49]

34  
35 384 Prevalence estimates from systematic reviews can provide an important source of information that  
36  
37 385 is used for evidence-based health decision making - especially in LMICs that have constrained  
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39 386 health information systems. A multimorbidity prevalence systematic review conducted for South  
40  
41 387 Asia highlighted the insufficient work conducted in the area of multimorbidity and called for  
42  
43 388 greater methodological rigour to better build scientific evidence in this domain.[50] In a similar  
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45 389 vein, we also advocate for more studies to be conducted and with rigorous study designs. A recent  
46  
47 390 report by the Academy of Science of South Africa,[51] highlighted the problematic nature of  
48  
49 391 multimorbidity research in sub-Saharan Africa as: funding provided for only specific diseases;  
50  
51 392 lack of health system preparedness; and low prioritisation of multimorbidity due to a lack of  
52  
53 393 political commitment to implement concomitant health reforms. Research into multimorbidity is  
54  
55 394 crucial for better understanding of the nature of the problem in the sub-Saharan African region,  
56  
57 395 and to identify ways to introduce comprehensive health service delivery.[51]

58  
59 396  
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61 397 This systematic review was limited in that it excluded studies conducted with sub-populations that  
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63 398 had one specific disease (e.g. multimorbidity in cancer patients). While these studies are very

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3 399 important, their inclusion would require different search strategies. This study differed from the  
4  
5 400 protocol in that it includes age groups of 15 years plus as the age 15 years is commonly reported  
6  
7 401 as adults in population-based surveys.

## 8 9 402 **CONCLUSION**

10  
11 403 To our knowledge, this is the first systematic review of multimorbidity on the African continent  
12  
13 404 and one of the few focused on a LMIC. This systematic review set out to determine the prevalence  
14  
15 405 of multimorbidity of adults in South Africa, ideally stratified by age and sex. We found that there  
16  
17 406 was a low number of studies focused on multimorbidity in South Africa. Studies with data  
18  
19 407 available indicated many people aged 50 years and older are afflicted with more than one long-  
20  
21 408 term disease condition. These findings are significant as they support the notion that  
22  
23 409 multimorbidity is the norm and not an exception; which has strong implications for how healthcare  
24  
25 410 is organised and utilised. These findings may also be reflective of the situation in other LMICs.

26 411 Our study indicated that a large component of multimorbidity was attributed to hypertension.  
27  
28 412 While HIV did contribute to multimorbidity, NCDs were the most common source, even in  
29  
30 413 environments with a high HIV prevalence. However, these results should be interpreted with  
31  
32 414 caution as many studies focused only on older adults and did not give disease clusters using age  
33  
34 415 breakdowns. Heterogeneity in studies also made it difficult to detect trends.

35 416 More studies are needed in the general population to determine which disease clusters are most  
36  
37 417 prevalent and could potentially be targeted for intervention. Sources of secondary data could be  
38  
39 418 further explored to answer this question. Studies at health facilities would help to provide  
40  
41 419 information regarding multimorbidity's effect on quality of life indicators, to assess whether  
42  
43 420 people are receiving optimal treatment; and to identify the ways that multimorbidity might be  
44  
45 421 impacting healthcare utilisation.

46 422

## 47 48 423 **Acknowledgements**

49  
50  
51 424 We would like to thank Dr Annibale Cois for statistical input, Ms Elizabeth Pienaar from Cochrane  
52  
53 425 South Africa at the South African Medical Research Council for reviewing our search strategy.  
54  
55 426 Thanks to Dr Angela Y Chang for providing clarification regarding information of interest.

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3 427 **Contributorship statement**

4  
5 428 RAR, VPvW, BvW and EBT conceptualised the study. RAR and EBT conducted screening and  
6  
7 429 data extraction. RAR wrote the first draft. All authors reviewed and gave input into subsequent  
8  
9 430 drafts.

10  
11 431 **Data Sharing Statement**

12  
13 432 No additional data available.

14  
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16  
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18  
19 435 Research Council. RAR is funded by the South African Medical Research Council through the  
20  
21 436 Division of Research Capacity Development under the Internship Scholarship Programme. Grant  
22  
23 437 number: NA.

24  
25 438  
26  
27 439 **Competing Interests**

28  
29 440 None declared.

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36 443 **REFERENCES**

- 37  
38 444 1. Nguyen H, Manolova G, Daskalopoulou C, et al. Prevalence of multimorbidity in  
39 445 community settings: A systematic review and meta-analysis of observational studies. *Journal of*  
40 446 *comorbidity*. 2019;9:1-15. doi: 10.1177/2235042X19870934
- 41 447 2. Xu X, Mishra GD, Jones M. Mapping the global research landscape and knowledge gaps  
42 448 on multimorbidity: a bibliometric study. *J Glob Health*. 2017;7(1):010414-010414. doi:  
43 449 10.7189/jogh.07.010414
- 44 450 3. World Health Organization. Multimorbidity: Technical Series on Safer Primary Care.  
45 451 Geneva: World Health Organization; 2016. Report No.: 9241511656. (Date Accessed: 5 July  
46 452 2020). Available from: [http://apps.who.int/iris/bitstream/10665/252275/1/9789241511650-](http://apps.who.int/iris/bitstream/10665/252275/1/9789241511650-eng.pdf)  
47 453 [eng.pdf](http://apps.who.int/iris/bitstream/10665/252275/1/9789241511650-eng.pdf).
- 48 454 4. Wei MY, Mukamal KJ. Multimorbidity, mortality, and long-term physical functioning in  
49 455 3 prospective cohorts of community-dwelling adults. *Am J Epidemiol*. 2018;187(1):103-112. doi:  
50 456 <https://doi.org/10.1093/aje/kwx198>
- 51 457 5. Kanesarajah J, Waller M, Whitty JA, Mishra GD. Multimorbidity and quality of life at  
52 458 mid-life: A systematic review of general population studies. *Maturitas*. 2018;109:53-62. doi:  
53 459 10.1016/j.maturitas.2017.12.004



- 1  
2  
3 460 6. Calderón-Larrañaga A, Poblador-Plou B, González-Rubio F, et al. Multimorbidity,  
4 461 polypharmacy, referrals, and adverse drug events: are we doing things well? *Br J Gen Pract.*  
5 462 2012;62(605):e821. doi: 10.3399/bjgp12X659295
- 6 463 7. Sum G, Salisbury C, Koh GC, et al. Implications of multimorbidity patterns on health care  
7 464 utilisation and quality of life in middle-income countries: cross-sectional analysis. *J Glob Health.*  
8 465 2019;9(2):020413. doi: 10.7189/jogh.09.020413
- 9 466 8. Frølich A, Ghith N, Schiøtz M, Jacobsen R, Stockmarr A. Multimorbidity, healthcare  
10 467 utilization and socioeconomic status: A register-based study in Denmark. *PLoS One.*  
11 468 2019;14(8):e0214183. doi: 10.1371/journal.pone.0214183
- 12 469 9. Maddaloni E, D'Onofrio L, Alessandri F, et al. Cardiometabolic multimorbidity is  
13 470 associated with a worse Covid-19 prognosis than individual cardiometabolic risk factors: a  
14 471 multicentre retrospective study (CoViDiab II). *Cardiovasc Diabetol.* 2020;19(1):1-11. doi:  
15 472 <https://doi.org/10.1186/s12933-020-01140-2>
- 16 473 10. Iaccarino G, Grassi G, Borghi C, et al. Age and multimorbidity predict death among  
17 474 COVID-19 patients: results of the SARS-RAS study of the Italian Society of hypertension.  
18 475 *Hypertension.* 2020;76(2):366-372. doi: <https://doi.org/10.1161/hypertensionaha.120.15324>
- 19 476 11. The Lancet. Making more of multimorbidity: an emerging priority. *Lancet.*  
20 477 2018;391(10131):1637. doi: 10.1016/S0140-6736(18)30941-3
- 21 478 12. The Academy of Medical Sciences. Multimorbidity: a priority for global health research  
22 479 2018. (Date Accessed: 20 April 2020). Available from: [https://acmedsci.ac.uk/file-](https://acmedsci.ac.uk/file-download/82222577)  
23 480 [download/82222577](https://acmedsci.ac.uk/file-download/82222577).
- 24 481 13. Simbayi L, Zuma K, Moyo S, et al. South African National HIV Prevalence, Incidence,  
25 482 Behaviour and Communication Survey, 2017. Cape Town: HSRC Press; 2019. Report No.: 978-  
26 483 0-7969-2444-5. (Date Accessed: 23 December 2020). Available from:  
27 484 [https://www.hsrcpress.ac.za/books/south-african-national-hiv-prevalence-incidence-behaviour-](https://www.hsrcpress.ac.za/books/south-african-national-hiv-prevalence-incidence-behaviour-and-communication-survey-2017)  
28 485 [and-communication-survey-2017](https://www.hsrcpress.ac.za/books/south-african-national-hiv-prevalence-incidence-behaviour-and-communication-survey-2017).
- 29 486 14. Chang AY, Gómez-Olivé FX, Manne-Goehler J, et al. Multimorbidity and care for  
30 487 hypertension, diabetes and HIV among older adults in rural South Africa. *Bull World Health*  
31 488 *Organ.* 2019;97(1):10. doi: <https://dx.doi.org/10.2471%2FBLT.18.217000>
- 32 489 15. Nojilana B, Bradshaw D, Pillay-van Wyk V, et al. Emerging trends in non-communicable  
33 490 disease mortality in South Africa, 1997-2010. *S Afr Med J.* 2016;106(5):477-484. doi:  
34 491 10.7189/jogh.09.020409
- 35 492 16. Mudie K, Jin MM, Tan, et al. Non-communicable diseases in sub-Saharan Africa: a  
36 493 scoping review of large cohort studies. *J Glob Health.* 2019;9(2):020409-020409. doi:  
37 494 10.7189/jogh.09.020409
- 38 495 17. Oni T, McGrath N, BeLue R, et al. Chronic diseases and multi-morbidity--a conceptual  
39 496 modification to the WHO ICC model for countries in health transition. *BMC Public Health.*  
40 497 2014;14:575. doi: 10.1186/1471-2458-14-575
- 41 498 18. Mahomed OH, Asmall S. Professional nurses' perceptions and experiences with the  
42 499 implementation of an integrated chronic care model at primary healthcare clinics in South Africa.  
43 500 *Curationis.* 2017;40(1):1-6. doi: <https://dx.doi.org/10.4102%2Fcurationis.v40i1.1708>
- 44 501 19. Mahomed OH, Asmall S. Development and implementation of an integrated chronic  
45 502 disease model in South Africa: lessons in the management of change through improving the quality  
46 503 of clinical practice. *Int J Integr Care.* 2015;15:e038. doi: <https://doi.org/10.5334/ijic.1454>
- 47 504 20. Limbani F, Thorogood M, Gómez-Olivé FX, Kabudula C, Goudge J. Task shifting to  
48 505 improve the provision of integrated chronic care: realist evaluation of a lay health worker  
49 506

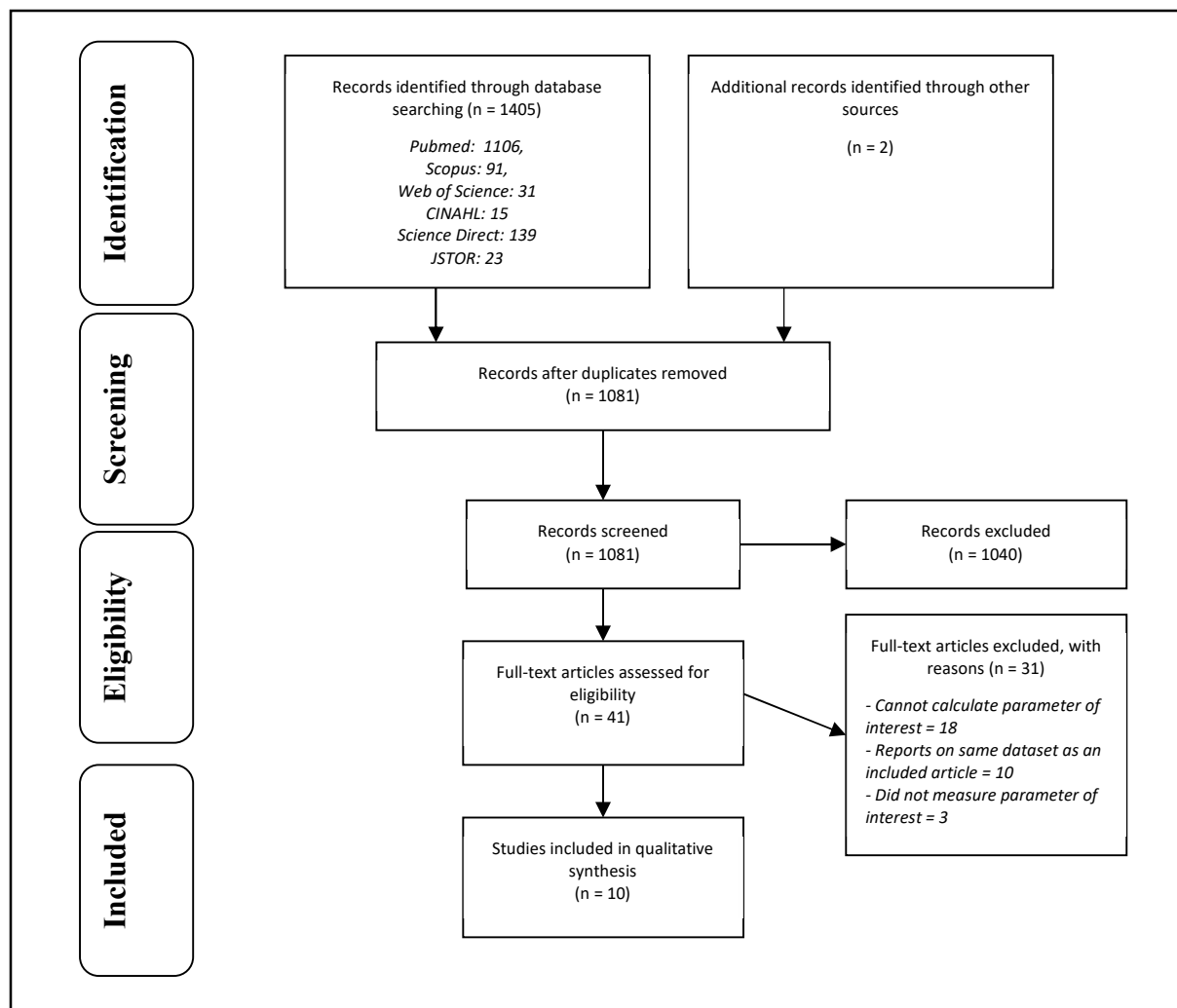
- 1  
2  
3 505 intervention in rural South Africa. *BMJ Glob Health*. 2019;4(1):e001084. doi: 10.1136/bmjgh-  
4 506 2018-001084
- 5 507 21. Ameh S, Klipstein-Grobusch K, D'ambruoso L, et al. Quality of integrated chronic disease  
6 508 care in rural South Africa: user and provider perspectives. *Health Policy Plan*. 2017;32(2):257-  
7 509 266. doi: <https://dx.doi.org/10.1093%2Fheapol%2Fczw118>
- 8 510 22. Fortin M, Stewart M, Poitras ME, Almirall J, Maddocks H. A systematic review of  
9 511 prevalence studies on multimorbidity: toward a more uniform methodology. *Ann Fam Med*.  
10 512 2012;10(2):142-151. doi: 10.1370/afm.1337
- 11 513 23. Roomaney RA, van Wyk B, Turawa EB, Pillay-van Wyk V. Prevalence of multimorbidity  
12 514 in South Africa: a systematic review protocol. *BMJ Open*. 2020;10(12):e042889. doi:  
13 515 <https://doi.org/10.1136/bmjopen-2020-042889>
- 14 516 24. Moher D, Liberati A, Tetzlaff J, Altman DG, The PG. Preferred Reporting Items for  
15 517 Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med*.  
16 518 2009;6(7):e1000097. doi: 10.1371/journal.pmed.1000097
- 17 519 25. The EndNote Team. EndNote. EndNote X8 ed. Philadelphia, PA: Clarivate; 2013.
- 18 520 26. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—a web and mobile app  
19 521 for systematic reviews. *Syst Rev*. 2016;5(1):210. doi: 10.1186/s13643-016-0384-4
- 20 522 27. Pillay-van Wyk V, Roomaney RA, Awotiwon OF, et al. Burden of Disease Review  
21 523 Manager for Systematic Review of Observational Studies: Technical Report Version 1. Cape  
22 524 Town: South African Medical Research Council; 2017.
- 23 525 28. Wells GA, Tugwell P, O'Connell D, et al. The Newcastle-Ottawa Scale (NOS) for  
24 526 assessing the quality of nonrandomized studies in meta-analyses. [Internet]. 2015.  
25 527 [http://www.ohri.ca/programs/clinical\\_epidemiology/oxford.asp](http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp) (accessed 31 January 2020)
- 26 528 29. Hoy D, Brooks P, Woolf A, et al. Assessing risk of bias in prevalence studies: modification  
27 529 of an existing tool and evidence of interrater agreement. *J Clin Epidemiol*. 2012;65(9):934-939.  
28 530 doi: 10.1016/j.jclinepi.2011.11.014
- 29 531 30. Pheiffer C, Pillay-van Wyk V, Joubert JD, et al. The prevalence of type 2 diabetes in South  
30 532 Africa: a systematic review protocol. *BMJ Open*. 2018;8(7):e021029-e021029. doi:  
31 533 10.1136/bmjopen-2017-021029
- 32 534 31. Rohatgi A. WebPlotDigitizer Version: 4.3. 2020.
- 33 535 32. Afshar S, Roderick PJ, Kowal P, Dimitrov BD, Hill AG. Multimorbidity and the  
34 536 inequalities of global ageing: a cross-sectional study of 28 countries using the World Health  
35 537 Surveys. *BMC Public Health*. 2015;15(1):776. doi: <https://doi.org/10.1186/s12889-015-2008-7>
- 36 538 33. Garin N, Koyanagi A, Chatterji S, et al. Global Multimorbidity Patterns: A Cross-  
37 539 Sectional, Population-Based, Multi-Country Study. *J Gerontol A Biol Sci Med Sci*.  
38 540 2016;71(2):205-214. doi: 10.1016/j.seizure.2019.06.018
- 39 541 34. Weimann A, Dai D, Oni T. A cross-sectional and spatial analysis of the prevalence of  
40 542 multimorbidity and its association with socioeconomic disadvantage in South Africa: A  
41 543 comparison between 2008 and 2012. *Soc Sci Med*. 2016;163:144-156. doi:  
42 544 <https://doi.org/10.1016/j.socscimed.2016.06.055>
- 43 545 35. Ghose B, Abdoul Razak MY. Memory and Learning Complaints in Relation to Depression  
44 546 among Elderly People with Multimorbidity. *Geriatrics*. 2017;2(2). doi: 10.1007/s10461-019-  
45 547 02617-2
- 46 548 36. van Heerden A, Barnabas RV, Norris SA, et al. High prevalence of HIV and non-  
47 549 communicable disease (NCD) risk factors in rural KwaZulu-Natal, South Africa. *J Int AIDS Soc*.  
48 550 2017;20(2). doi: 10.1002/jia2.25012



- 1  
2  
3 551 37. Chang AY, Gómez-Olivé FX, Payne C, et al. Chronic multimorbidity among older adults  
4 552 in rural South Africa. *BMJ Glob Health*. 2019;4(4):e001386. doi:  
5 553 <https://dx.doi.org/10.2471%2FBLT.18.217000>  
6 554 38. Sharman M, Bachmann M. Prevalence and health effects of communicable and non-  
7 555 communicable disease comorbidity in rural KwaZulu-Natal, South Africa. *Trop Med Int Health*.  
8 556 2019;24(10):1198-1207. doi: 10.1111/tmi.13297  
9 557 39. Lalkhen H, Mash R. Multimorbidity in non-communicable diseases in South African  
10 558 primary healthcare. *S Afr Med J*. 2015;105(2):134-138. doi: 10.7196/samj.8696  
11 559 40. Roche S, De Vries E. Multimorbidity in a large district hospital: A descriptive cross-  
12 560 sectional study. *S Afr Med J*. 2017;107(12):1110-1115. doi: 10.7196/SAMJ.2017.v107i12.12397  
13 561 41. Oni T, Youngblood E, Boulle A, et al. Patterns of HIV, TB, and non-communicable disease  
14 562 multi-morbidity in peri-urban South Africa- a cross sectional study. *BMC Infect Dis*. 2015;15:20.  
15 563 doi: 10.1186/s12879-015-0750-1  
16 564 42. Weimann A, Dai DJ, Oni T. A cross-sectional and spatial analysis of the prevalence of  
17 565 multimorbidity and its association with socioeconomic disadvantage in South Africa: A  
18 566 comparison between 2008 and 2012. *Soc Sci Med*. 2016;163:144-156. doi:  
19 567 10.1016/j.socscimed.2016.06.055  
20 568 43. Alaba O, Chola L. The social determinants of multimorbidity in South Africa. *Int J Equity*  
21 569 *Health*. 2013;12(1):1. doi: <https://doi.org/10.1186/1475-9276-12-63>  
22 570 44. Griffith LE, Gruneir A, Fisher KA, et al. Key factors to consider when measuring  
23 571 multimorbidity: Results from an expert panel and online survey. *Journal of comorbidity*.  
24 572 2018;8(1):2235042x18795306. doi: 10.1177/2235042x18795306  
25 573 45. National Department of Health, Statistics South Africa, South African Medical Research  
26 574 Council, and ICF. South Africa Demographic and Health Survey 2016. Pretoria, South Africa, and  
27 575 Rockville, Maryland, USA: NDoH, Stats SA, SAMRC, and ICF; 2019. (Date Accessed: 23  
28 576 December 2020). Available from: <https://dhsprogram.com/pubs/pdf/FR337/FR337.pdf>.  
29 577 46. Pillay-van Wyk V, Bradshaw D, Groenewald P, et al. COVID deaths in South Africa: 99  
30 578 days since South Africa's first death. *S Afr Med J*. 2020;110(10):0-0. doi:  
31 579 <https://doi.org/10.7196/SAMJ.2020.v110i11.15249>  
32 580 47. South African Medical Research Council, Department of Science and Innovation. South  
33 581 African Population Research Infrastructure Network launches two new urban nodes to expand to  
34 582 a nationwide network and improve response to COVID-19 and other epidemics. 2020.  
35 583 <http://sapr.in.mrc.ac.za/1press2020.html> (accessed 3 December 2020)  
36 584 48. Mannie C, Kharrazi H. Assessing the geographical distribution of comorbidity among  
37 585 commercially insured individuals in South Africa. *BMC Public Health*. 2020;20(1):1709. doi:  
38 586 10.1186/s12889-020-09771-6  
39 587 49. Sum G, Hone T, Atun R, et al. Multimorbidity and out-of-pocket expenditure on medicines:  
40 588 a systematic review. *BMJ Glob Health*. 2018;3(1):e000505-e000505. doi: 10.1136/bmjgh-2017-  
41 589 000505  
42 590 50. Pati S, Swain S, Hussain MA, et al. Prevalence and outcomes of multimorbidity in South  
43 591 Asia: a systematic review. *BMJ Open*. 2015;5(10):e007235. doi: 10.1136/bmjopen-2014007235  
44 592 51. Academy of Science of South Africa. Improving the prevention and management of  
45 593 multimorbidity in sub-Saharan Africa. 2020. (Date Accessed: 16 August 2021). Available from:  
46 594 [https://research.assaf.org.za/bitstream/handle/20.500.11911/139/2020\\_assaf\\_ams\\_multimorbidity\\_subsaharan\\_africa.pdf?sequence=1&isAllowed=y](https://research.assaf.org.za/bitstream/handle/20.500.11911/139/2020_assaf_ams_multimorbidity_subsaharan_africa.pdf?sequence=1&isAllowed=y).  
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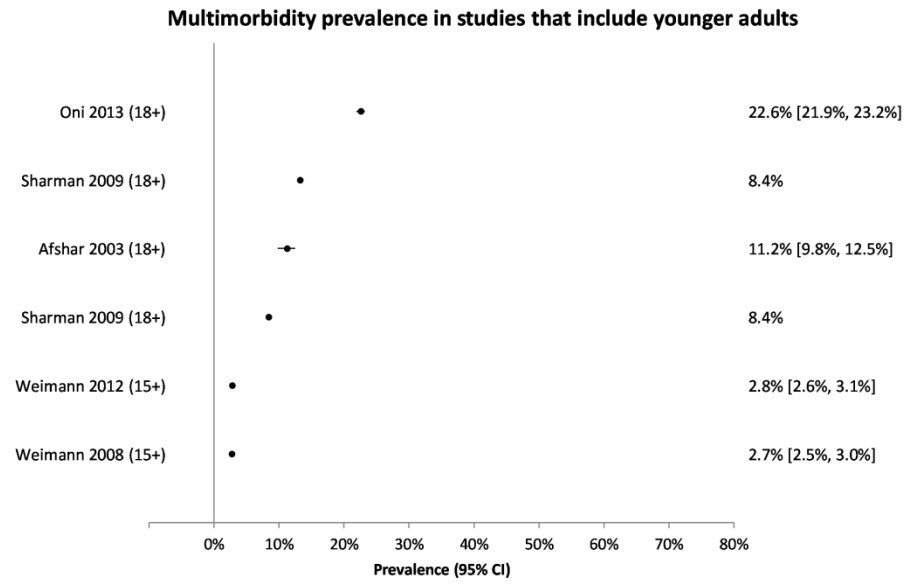


Figure 2: Graph of multimorbidity prevalence estimates for studies that include younger age groups  
209x134mm (300 x 300 DPI)

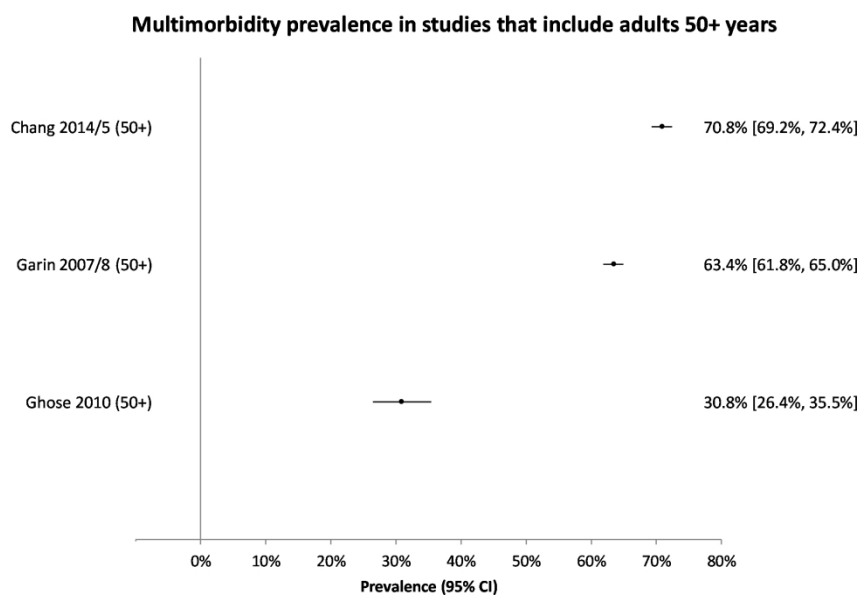


Figure 3: Graph of multimorbidity prevalence in studies including persons aged 50 years and older

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3 **Supplementary file to *Multimorbidity in South Africa: A systematic review of prevalence studies***  
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8 **Appendix 1: PRISMA Checklist**  
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Section/topic	#	Checklist item	Reported on page #
<b>TITLE</b>			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
<b>ABSTRACT</b>			
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
<b>INTRODUCTION</b>			
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
<b>METHODS</b>			
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

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
<b>RESULTS</b>			
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

<b>DISCUSSION</b>			
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
<b>FUNDING</b>			
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](http://www.prisma-statement.org).

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## 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.

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**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). <i>Multimorbidity and the inequalities of global ageing: a cross-sectional study of 28 countries using the World Health Surveys</i>	N= 2629. Adults 18 years and older in the 2003 World Health Survey.	2003	South Africa. (56.3% urban)	Population-based survey. WHS 2003.	<ul style="list-style-type: none"> <li>• Angina / Angina Pectoris (Heart Disease)</li> <li>• Arthritis</li> <li>• Asthma</li> <li>• Depression</li> <li>• Diabetes</li> <li>• Schizophrenia or Psychosis</li> </ul>	The presence of two or more <b>chronic</b> diseases.	Chronic conditions were chosen in this survey to reflect health system coverage and corresponded to conditions known to affect older people.	<ul style="list-style-type: none"> <li>- Increasing country GDP</li> <li>- Increasing age</li> <li>- Lower education</li> </ul>
Garin, Koyanagi, Chatterji et al (2016). <i>Global Multimorbidity Patterns: A Cross-Sectional, Population-Based, Multi-Country Study.</i>	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.	<ul style="list-style-type: none"> <li>• Angina`</li> <li>• Arthritis</li> <li>• Asthma</li> <li>• Cataract</li> <li>• Cognitive impairment`</li> <li>• COPD</li> <li>• Depression`</li> <li>• Diabetes</li> <li>• Edentulism</li> <li>• Hypertension*</li> <li>• Obesity*</li> <li>• Stroke</li> </ul>	Having at least 2 of 12 <b>chronic</b> conditions included in the study.	Selected 12 chronic conditions with high prevalence in most settings that significantly affect health	<ul style="list-style-type: none"> <li>- Generally increased with age but decreased in people over 60 years</li> <li>- Being female</li> <li>- Lower education</li> <li>- Being separated/divorced/widowed</li> <li>- Living in a rural area</li> </ul>
Weimann, Dai, Oni (2016). <i>A cross-sectional and spatial analysis of the prevalence of multimorbidity and its association with socioeconomic disadvantage in South Africa: A comparison</i>	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.	<ul style="list-style-type: none"> <li>• Diabetes</li> <li>• HIV</li> <li>• Hypertension (self-reported or measured)</li> <li>• TB</li> </ul>	The presence of two or more <b>chronic</b> 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.	<ul style="list-style-type: none"> <li>- Increasing age</li> <li>- Being female</li> <li>- Socioeconomic deprivation</li> <li>- Obesity</li> <li>- Living in urban areas</li> <li>- Living in Kwa-Zulu Natal or Eastern Cape provinces (Province)</li> <li>- Being Indian/Asian (Race)</li> </ul>

between 2008 and 2012.	(2008) and 3 (2012).							
Ghose, Razak (2017). <i>Memory and Learning Complaints in Relation to Depression among Elderly People with Multimorbidity.</i>	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.	<ul style="list-style-type: none"> <li>• Arthritis</li> <li>• Asthma</li> <li>• Cancer</li> <li>• Chronic lung disease</li> <li>• Diabetes</li> <li>• Heart Disease</li> <li>• Hypertension</li> <li>• Stroke</li> </ul>	>1 condition	Not clearly stated.	<ul style="list-style-type: none"> <li>- Memory complaints in women</li> <li>- Being diagnosed with depression</li> </ul>
van Heerden, Barnabas, Norris et al (2017). <i>High prevalence of HIV and non-communicable disease risk factors in rural KwaZulu-Natal, South Africa.</i>	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.	<ul style="list-style-type: none"> <li>• Depression</li> <li>• HIV*<sup>1</sup></li> <li>• Hyperglycaemia*</li> <li>• Hyperlipidaemia*</li> <li>• Hypertension*</li> <li>• Obesity*</li> </ul>	Not reported.	Links to study objectives to investigate HIV and NCD risk factors.	Not reported
Chang, Gómez-Olivé, Payne et al. (2019). <i>Chronic multimorbidity among older adults in rural South Africa</i>	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.	<ul style="list-style-type: none"> <li>• Alcohol Dependence`</li> <li>• Anaemia*</li> <li>• Angina`</li> <li>• Chronic Bronchitis</li> <li>• Depression`</li> <li>• Diabetes*</li> <li>• Dyslipidaemia*</li> <li>• HIV*</li> <li>• Hypertension*</li> <li>• Post-Traumatic Stress Disorder`</li> </ul>	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.	<ul style="list-style-type: none"> <li>- Increased with age until 69 years and then decreased</li> <li>- Being separated/divorced or widowed</li> <li>- HIV associated with higher levels of MM using the second definition</li> <li>- Physical functioning and well-being and self-rated health were worse with increasing numbers of conditions and categories</li> <li>-----</li> <li>- Living with more people (household size) decreased odds of multimorbidity</li> </ul>

<sup>1</sup> HIV is measured but data on HIV is presented as a sub-group and thus excluded in this analysis

								<ul style="list-style-type: none"> <li>- No relationship between wealth and multimorbidity</li> <li>- Females has higher levels of multimorbidity but it was not significantly different</li> </ul>
<p>Sharman, Bachmann (2019). <i>Prevalence and health effects of communicable and non-communicable disease comorbidity in rural KwaZulu-Natal, South Africa.</i></p>	<p>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.</p>	<p>2009-2015</p>	<p>Umkhanyakude district of rural KwaZulu-Natal. Rural.</p>		<ul style="list-style-type: none"> <li>• Hypertension (self-reported or on treatment)</li> <li>• Diabetes</li> <li>• TB within past 12 months</li> <li>• HIV (measured or on treatment)*</li> </ul>	<p>Proportion of participants with two or more conditions (<i>termed as co-morbidity</i>)</p>	<p>Based on research gap where few studies examine the prevalence of communicable and non-communicable diseases.</p>	<ul style="list-style-type: none"> <li>- Increasing age were associated with MM</li> <li>- Self-reported health poorer with multimorbidity</li> </ul>
<p>Lalkhen, Mash (2015). <i>Multimorbidity in non-communicable diseases in South African primary healthcare.</i></p>		<p>2010</p>	<p>Primary healthcare facilities in the Western Cape, North West, Northern Cape and Limpopo. Rural and urban.</p>	<p>Cross sectional study. Facility based.</p>	<ul style="list-style-type: none"> <li>• Asthma*</li> <li>• COPD*</li> <li>• Diabetes*</li> <li>• Epilepsy*</li> <li>• Hypertension*</li> <li>• Osteoarthritis*</li> <li>• And other diseases</li> </ul>	<p>The presence of two or more diseases.</p>	<p>Study aimed to examine non-communicable diseases. All conditions recorded.</p>	<p>Not reported</p>
<p>Roche, de Vries (2017). <i>Multimorbidity in a large district hospital: A descriptive cross-sectional study.</i></p>	<p>N= 491. Consecutive admissions to an internal medicine department of a large district hospital.</p>	<p>2015</p>	<p>District hospital, Cape Town. Urban.</p>	<p>Cross sectional study. Facility based-Internal medicine department</p>	<ul style="list-style-type: none"> <li>• Anaemia*</li> <li>• Asthma*</li> <li>• Bronchiectasis*</li> <li>• Cancer*</li> <li>• Cardiac failure*</li> <li>• Cerebrovascular accident*</li> <li>• COPD*</li> <li>• Cor pulmonale*</li> <li>• Current TB*</li> <li>• Deep vein thrombosis*</li> <li>• Delirium*</li> </ul>	<p>More than one disease concurrently.</p>	<p>Not clearly stated but appears to include all conditions that were seen in the district hospital.</p>	<ul style="list-style-type: none"> <li>- Length of stay not related to multimorbidity.</li> <li>- Lifestyle risk factors were not associated with multimorbidity.</li> </ul>

					<ul style="list-style-type: none"> <li>• Diabetes*</li> <li>• Dilated cardiomyopathy*</li> <li>• Dyslipidaemia*</li> <li>• Epilepsy*</li> <li>• Gastroenteritis*</li> <li>• HIV*</li> <li>• Hypertension*</li> <li>• Ischaemic heart disease*</li> <li>• Lower respiratory tract infection*</li> <li>• Pneumonia*</li> <li>• Renal failure*</li> <li>• Sepsis*</li> <li>• Urinary tract infection*</li> </ul>			
<p>Oni, Youngblood, Boulle et al. (2015). <i>Patterns of HIV, TB, and non-communicable disease multi-morbidity in peri-urban South Africa—a cross sectional study.</i></p>	<p>N=14364. Chronic disease patients (adults) with at least one disease (HIV, TB, diabetes, and hypertension) identified on electronic databases.</p>	<p>Sep 2012 - May 2013</p>	<p>Michael Mapongwana clinic, Khayelitsha, Cape Town.</p> <p>Peri-urban area.</p>	<p>Facility based RHIS. Western Cape Department of Health Data Repository, electronic prescription system.</p>	<ul style="list-style-type: none"> <li>• Diabetes*</li> <li>• HIV*</li> <li>• Hypertension*</li> <li>• TB*</li> </ul>	<p>Coexistence of more than one <b>chronic</b> condition in one person.</p>	<p>Informed by the research gap between NCDs and communicable diseases.</p>	<p>- Increasing age associated with MM.</p> <p>-----</p> <p>- No significant differences between males and females.</p>

#### Appendix 4: Common disease conditions / disease clusters

Study	Year	Conditions included	Common disease clusters identified in South Africa
Garin, et al (2016)	2007-2008	<ul style="list-style-type: none"> <li>• Angina`</li> <li>• Arthritis</li> <li>• Asthma</li> <li>• Cataract</li> <li>• Cognitive impairment`</li> <li>• COPD</li> <li>• Depression`</li> <li>• Diabetes</li> <li>• Edentulism</li> <li>• Hypertension*</li> <li>• Obesity*</li> <li>• Stroke</li> </ul>	<p><b>Disease Combinations</b></p> <ul style="list-style-type: none"> <li>- Hypertension was commonly present with diabetes, stroke, angina, cataract and all other conditions.</li> <li>- Obesity and diabetes commonly co-occurred.</li> </ul>
Weimann et al (2016)	2008, 2012	<ul style="list-style-type: none"> <li>• Diabetes</li> <li>• HIV</li> <li>• Hypertension (self-reported or measured)</li> <li>• TB</li> </ul>	<p>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.</p> <p><b>Disease Combinations (2008):</b></p> <p><b>Two disease conditions:</b></p> <ol style="list-style-type: none"> <li>1) Diabetes and Hypertension (70.8%)</li> <li>2) TB and Hypertension (13.2%)</li> <li>3) HIV and Hypertension (10.8%)</li> <li>4) HIV and TB (3.9%)</li> <li>5) TB and Diabetes (0.8%)</li> <li>6) HIV and Diabetes (0.3%)</li> </ol> <p><b>Three disease conditions:</b></p> <ol style="list-style-type: none"> <li>1) TB, Diabetes and Hypertension (63.9%)</li> <li>2) Hypertension, HIV and TB (36.0%)</li> </ol>
Chang et al (2019)	2014-2015	<ul style="list-style-type: none"> <li>• Alcohol Dependence`</li> <li>• Anaemia*</li> <li>• Angina`</li> <li>• Chronic Bronchitis</li> <li>• Depression`</li> <li>• Diabetes*</li> <li>• Dyslipidaemia*</li> <li>• HIV*</li> <li>• Hypertension*</li> <li>• Post-Traumatic Stress Disorder`</li> </ul>	<p>Disease clusters limited to more than 1.5% of study population.</p> <p><b>Disease profile and clusters</b></p> <ul style="list-style-type: none"> <li>- Hypertension only (11.7%)</li> <li>- Hypertension and Dyslipidaemia (9.4%)</li> <li>- None (6.9%)</li> <li>- Hypertension and Anaemia (6.4%)</li> <li>- Hypertension and Dyslipidaemia and Anaemia (4.7%)</li> <li>- Dyslipidaemia (3.9%)</li> <li>- Anaemia (3.8%)</li> <li>- Anaemia and HIV (2.6%)</li> <li>- Hypertension and Anaemia and HIV (2.6%)</li> <li>- HIV (2.4%)</li> <li>- Dyslipidaemia and Anaemia (2.1%)</li> <li>- Dyslipidaemia and Anaemia and HIV (2.0%)</li> <li>- Hypertension and HIV (1.9%)</li> <li>- Hypertension and Dyslipidaemia and Diabetes (1.8%)</li> <li>- Hypertension and Depression (1.7%)</li> <li>- Dyslipidaemia and HIV (1.6%)</li> <li>- Hypertension and Dyslipidaemia and HIV (1.6%)</li> </ul>

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

Study	Year	Conditions included	Common disease clusters identified in South Africa
			<ul style="list-style-type: none"> <li>• Diabetes (5.4%)</li> <li>• Acute bronchitis (4.7%)</li> <li>• Allergic rhinitis (3.1%)</li> <li>• TB (2.2%)</li> </ul> <p>- Of those that had COPD (n=140), people also had:</p> <ul style="list-style-type: none"> <li>• Hypertension (47.9%)</li> <li>• Osteoarthritis (12.1%)</li> <li>• Diabetes (9.3%)</li> <li>• TB (6.4%)</li> <li>• Epilepsy (3.6%)</li> <li>• Ischaemic heart disease with angina (3.6%)</li> <li>• TB (2.1%)</li> <li>• Lipid dysfunction (2.1%)</li> <li>• Tobacco abuse (2.1%)</li> <li>• Ischaemic heart disease with angina (2.1%)</li> </ul> <p>- Of those that had Osteoarthritis (n=530), people also had:</p> <ul style="list-style-type: none"> <li>• Ischaemic heart disease (2.3%)</li> </ul>
Oni et al (2015).	Sep 2012 - May 2013	<ul style="list-style-type: none"> <li>• Diabetes*</li> <li>• HIV*</li> <li>• Hypertension*</li> <li>• TB*</li> </ul>	<p>Of the 14364 participants, 21.3% had two diseases, 1.2% had three diseases and 0.1% had four diseases.</p> <p><b>Of those that had two diseases (n=3058)</b></p> <ol style="list-style-type: none"> <li>1. Hypertension and diabetes (69.1%)</li> <li>2. Hypertension and HIV (21.4%)</li> <li>3. HIV and TB (6.2%)</li> <li>4. HIV and diabetes (1.6%)</li> <li>5. Hypertension and TB (1.5%)</li> <li>6. TB and diabetes (0.2%)</li> </ol> <p><b>Of those that had three diseases (n=173)</b></p> <ol style="list-style-type: none"> <li>1. Hypertension, diabetes and HIV (63%)</li> <li>2. Hypertension, HIV and TB (26.6%)</li> </ol>



## 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	%
<b>Population-based surveys</b>								
Afshar, Roderick, Kowal et al. (2015) <sup>1</sup>	2003	18 - 49	-	5.0 (3.9 – 6.0)	-	-	-	-
		50 - 64	-	21.6 (16.6 – 26.0)	-	-	-	-
		65+	-	30.1 (20.6- 39.7)	-	-	-	-
		<b>Overall (18+)</b>	-	<b>11.2 (9.8 - 12.5)</b>	-	-	-	-
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
		<b>Overall (50+)</b>	<b>2376 / 3747*</b>	<b>63.4</b>	-	-	-	-
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	-	-	-	-
		<b>Overall (15+)</b>	-	<b>2.7 (2.5 – 3.0)</b>	-	-	-	-
	2012	15 - 24	-	0.0	-	-	-	-
		25 - 34	-	0.8	-	-	-	-
		35 - 44	-	3.1	-	-	-	-
		45 - 54	-	3.1	-	-	-	-
		55 - 64	-	9.0	-	-	-	-
		65+	-	10.5	-	-	-	-
		<b>Overall (15+)</b>	-	<b>2.8 (2.6 – 3.1)</b>	-	-	-	-
Ghose, Razak (2017).	2010	<b>Overall (50+)</b>	<b>130 / 422</b>	<b>30.8</b>	-	<b>16.0</b>	-	<b>35.8</b>
<b>Community-based studies (cross-sectional study)</b>								
	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
		<b>Overall (40+)</b>	<b>2700 / 3889</b>	<b>69.4</b>	<b>1182 / 1758</b>	<b>67.2</b>	<b>1518 / 2130</b>	<b>71.2</b>
Sharman, Bachmann (2019).	2009	<b>Overall (18+)</b>		<b>8.4</b>				
	2015	<b>40+</b>		<b>18.4</b>				
	2015	<b>Overall (18+)</b>		<b>13.2</b>				
<b>Health facility-based studies (cross-sectional surveys and routine health information systems)</b>								
Lalkhen, Mash (2015).	2010	<b>Overall (Mean ages±)</b>	-	<b>48.4</b>	-	-	-	-
Roche, de Vries (2017).	2015	<b>Overall (Mean age 49 years)</b>	<b>371 / 427</b>	<b>87.0</b>	-	-	-	-
Oni, Youngblood, Boulle et al. (2015).	2012/13	<b>Overall (18+)</b>	<b>3246 / 14364</b>	<b>22.6</b>	-	-	-	-

*Italicised data extracted from graphs using Webplot digitizer*  
 \*estimated from available information  
 †standardised 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).

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