The Effect of Multimorbidity Patterns and the Impact of Comorbid Anxiety and Depression on Primary Health Service Use: The Men Androgen Inflammation Lifestyle Environment and Stress (MAILES) Study

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Abstract

This study sought to determine patterns of multimorbidity and quantify their impact on use of primary health services in the presence and absence of anxiety and depression among a cohort of urban community-dwelling men in Australia. The analytic sample consisted of men (n = 2039; age 38–85) from the follow-up wave of a prospective cohort study of all participants of the Florey Adelaide Male Ageing Study (FAMAS; Stage 2 [2007–2010]) and age-matched men from the North-West Adelaide Health Study (NWAHS; Stage 3 [2008–2010]). Self-reported data and linkage with a national universal health coverage scheme (Medicare) provided information on the prevalence of eight chronic conditions and health service utilization information (including annual GP visits). Obesity and cardiovascular disease (CVD) were associated with the highest number of comorbid conditions. Two nonrandom multimorbidity "clusters" emerged: "CVD, Obesity, Diabetes" and "CVD, Obesity, Osteoarthritis." Participants with conditions comorbid with CVD were more likely to have 10 or more annual GP visits, compared to multimorbidity involving other conditions. In comparison to participants without CVD, the presence of CVD increased the chance of having 10 or more annual GP visits (adjusted risk ratio: 3.7; 95% CI [2.8, 4.8]). When CVD was comorbid with anxiety and depression, having 10 or more annual GP visits was more common (adjusted risk ratio: 1.8; 95% CI [1.2, 2.5]). Multimorbidity patterns involving CVD, especially for multimorbidity that includes CVD with comorbid anxiety and depression, should be considered in developing clinical trials to better inform medical decision-making and care for patients with CVD and comorbid conditions.

Keywords

multimorbidity, primary health services use, anxiety, depression, cardiovascular disease, cohort studies, men's health

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Background

Multimorbidity has recently been identified as one of the greatest challenges facing the global health system (Pearson-Stuttard et al., 2019). Estimates from the World Health Organization (WHO) demonstrate that between 40% and 60% of the adult population in developed countries have two or more chronic conditions (World Health Organization, 2016). The presence of multimorbidity has been associated with lower quality of life (Fortin et al., 2004), increased mortality (Nunes et al., 2016), and higher utilization of hospital and primary care

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services (McRae et al., 2013; Salisbury et al., 2011; Westert et al., 2001; Zulman et al., 2015). Despite this, the study of multimorbidity—distinct from earlier studies that focused on comorbidity (Feinstein, 1967)—is relatively new. Multimorbidity is particularly applicable to the primary care setting, where the general practitioner (GP) tends to focus on the whole care of the patient rather than one particular condition (Harrison & Siriwardena, 2018). In contrast to the United States, where a range of specialists provides primary care and for some conditions patients may only see a specialist (Jones et al., 2011), the Australian health-care system requires that the starting point and ongoing continuity of care is vested with GPs who are the gateway to other health-care services.

Recent editorials in *Lancet* (Lancet editorial, 2018), *British Journal of General Practice* (Mair & Gallacher, 2017), and *Journal of Comorbidity* (Navickas et al., 2016) have detailed major gaps in our knowledge around multimorbidity, especially its effect on primary care services. For instance, while the prevalence of multimorbidity is known to increase with age (Singer et al., 2019), the higher number of absolute cases of multimorbidity in those aged under 65 and the limited opportunities for intervention in elderly patients have motivated a life course approach to multimorbidity in primary care (Schafer et al., 2012). Despite this, there remains an absence of studies that examine multimorbidity in younger to middle-aged cohorts (Mair & Gallacher, 2017). The burden of comorbid mental health conditions on multimorbidity patterns, particularly anxiety and depression, has also been highlighted as requiring further study, with around one in three patients with multimorbidity having a concomitant mental health disorder (Gallo, 2017; Pearson-Stuttard et al., 2019; Rice et al., 2018). A recent U.K. Academy of Medical Sciences report (Academy of Medical Sciences, 2018) has recommended, as a research priority, the need to better understand the biopsychosocial determinants of multimorbidity clusters. However, most evidence on multimorbidity to date has been derived from large disease surveillance systems that have limited capacity to understand multimorbidity as "a non-random series of predictable clusters" (Pearson-Stuttard et al., 2019), and identify modifiable targets for intervention in primary care (Smith et al., 2016).

Given these knowledge gaps, our study involves two main objectives. The first objective is to examine the patterns of multimorbidity of eight chronic conditions (anxiety, asthma, CVD, depression, diabetes, obesity, osteoarthritis, rheumatoid arthritis). The second objective concerns studying the impact of comorbid anxiety and depression on the utilization of GP services for urban-dwelling, middle-aged to elderly men.

Methods

Setting and Population

The Men Androgen Inflammation Lifestyle Environment and Stress (MAILES) study was established in 2009 to investigate the associations of sex steroids, inflammation, and environmental and psychosocial factors with cardio-metabolic disease risk in men. The study population consisted of 2568 men aged 35–80 years at baseline from two cohort studies: all participants of the Florey Adelaide Male Ageing Study (FAMAS) and age-matched male participants of the North-West Adelaide Health Study (NWAHS). Data were collected on a number of chronic conditions as well as linked Medicare data about individual health service claims and utilization information. Medicare in Australia is a universal health insurance scheme serving all Australians for a wide range of health and hospital services. This contrasts with Medicare in the United States that primarily serves people over 65 years of age and younger disabled people and dialysis patients. All protocols were approved by the (Blinded, for review) and written, informed consent was obtained from all participants. Detailed information on recruitment and follow-up process is reported elsewhere (Grant et al., 2014). The data in the MAILES Stage 2 study contained 2039 men (FAMAS Stage 2: 2007–2010; NWAHS Stage 3: 2008–2010), representing data collected at clinics approximately 5 years after baseline visits in the two studies.

Chronic Conditions

Data on chronic disease status (CVD, diabetes, arthritis, depression, anxiety, asthma) were collected through self-report to the question "Have you ever been told by a doctor that you have any of the following conditions?" Classification of diabetes was by self-report and biomedical measures (fasting blood glucose ≥ 7.0 mmol/L and/or HbA1c ≥ 6.5; see Grant et al., 2014). Obesity was indicated by a waist circumference ≥ 100 cm as measured at the clinic visit. Depressive symptoms were assessed using the Beck Depression Inventory (BDI-Ia; Beck & Beck, 1972) for FAMAS men and the Center for Epidemiologic Studies-Depression Scale (CES-D; Radloff, 1977) for NWAHS men. Cutoff scores of 10 and 16 for the BDI-1a and CES-D, respectively, were employed to classify into the depression categories (Yes/No). Both the BDI-1a and CES-D show comparable specificities from the classification of major depression in residential, older men (Shafer, 2006). Anxiety symptoms were assessed using the seven-item Generalized Anxiety Disorder (GAD-7) scale (Spitzer et al., 2006). A cutoff score of 10 was used for the anxiety category (Yes/No). The GAD-7 shows good overall specificity for GAD in comparable men (Spitzer et al.,

2006). The BDI, CES-D, and GAD-7 are not formal clinical diagnostic assessments for depression or anxiety. They are screening instruments for depression or anxiety for research in the general population.

Health Service Usage

Health service use was obtained from a self-reported, piloted, health service utilization questionnaire. The number of GP visits in 1 year during the follow-up period was categorized into four categories (0, 1–4, 5–9, and 10+). Information was also obtained regarding participants' main reason for visiting the GP, their overall rating of the visit, whether other health issues were raised, and the use of other health service providers. GP and health utilization data were also verified through consented linkage into Medicare, the Australian Government's nationwide medical services program. There were data available on specialist or allied health consultations (including services provided by psychologists and psychiatrists). However, the number of participants who reported the use of such services is relatively small (only around 3%), and thus such data were not considered in the analyses. This study focuses on GP services only.

Demographic and Lifestyle Factors

Age, marital status, household income, education and qualifications, work status, smoking, alcohol consumption, and physical activity were utilized as collected by self-reported questionnaires at MAILES Stage 2. Information about country of birth was taken from the baseline.

Statistical Analysis

The analysis of chronic conditions was conducted based on the clustering method of pairwise concordance statistics (Ng et al., 2012), which adopts the asymmetric Somers' D statistic to quantify the degree of multimorbidity beyond chance (Ng, 2015; Ng et al., 2018). The identification of significant (nonrandom) multimorbidity between conditions, also known as "associative multimorbidity" (Prados-Torres et al., 2014), is more informative to view disease patterns for a potential sharing of risk factors of the diseases (Batstra et al., 2002; Baty et al., 2013; Ng, 2015; Ng et al., 2019). The clustering method adopts the Benjamini–Hochberg procedure to control for the false discovery rate at $\alpha = .05$ (Benjamini & Hochberg, 1995).

A χ^2 analysis (for categorical variables) or analysis of variance (ANOVA; for quantitative variables) was used to test for significant differences in participants' characteristics and multimorbidity patterns between the four groups according to the number of GP visits in 1 year. A

multinomial logistic regression method was adopted to assess the impact of depression and anxiety on the frequencies of GP visits via additive interaction terms, separately for obesity, CVD, and diabetes, with adjustment for participants' demographic and lifestyle characteristics. Adjusted relative risk ratios (RRRs) of GP visits relative to the reference category of 1–4 GP visits were obtained, along with their 95% confidence intervals (CIs). Predicted probabilities of 10+ annual GP visits were calculated to illustrate the effects from either obesity, CVD, or diabetes alone as well as the impact of comorbid anxiety or depression. It is well recognized that any factor that is caused in part by the exposure (incidence of chronic condition) and is associated with outcome of interest (frequency of GP visits) should not be treated as a confounder or adjusted for in the regression analysis (Weinberg, 1993). Bias can result from adjusting for this "intermediate factor" as the estimated exposure-related risk will be markedly reduced. On the basis of literature and clinical evidence, medication was hypothesized to be part of the causal pathway between multimorbidity and GP visits; that is, multimorbidity is associated with more medications (Masnoon et al., 2017; Vogeli et al., 2007) and in turn more medications have been shown to be associated with increased health service utilization (Milton et al., 2008; Nishtala et al., 2014). Therefore, medication was not adjusted for in the multinomial logistic regression analysis.

The comparison analysis and logistic regression analysis were performed using STATA (SE 13.1; StataCorp, College Station, Texas) on the basis of 1904 participants (93.4% of 2039) with complete information on the annual frequency of GP visits. Sensitivity analyses were conducted regarding the definitions of anxiety and depression based on either assessment instruments (GAD-7 for anxiety; BDI-1a/CES-D for depression) or medications for anxiety and/or depression, compared to the self-reported questionnaire.

Results

Multimorbidity of Chronic Conditions

Prevalence rates in decreasing order of the eight chronic conditions among the MAILES Stage 2 cohort were: obesity ($n = 933$ out of 1870; 49.9%), diabetes ($n = 389$ of 1969; 19.8%), asthma ($n = 256$ of 1951; 13.1%), CVD ($n = 235$ of 1988; 11.8%), osteoarthritis ($n = 221$ of 1988; 11.1%), depression ($n = 171$ of 1865; 9.2%), anxiety ($n = 134$ of 1865; 7.2%), and rheumatoid arthritis ($n = 74$ of 1988; 3.7%). Figure 1 displays the multimorbidity patterns among these chronic conditions, along with seven pairs of conditions with significant nonrandom multimorbidity. As shown in Figure 1, obesity and CVD have the highest number of associated comorbid
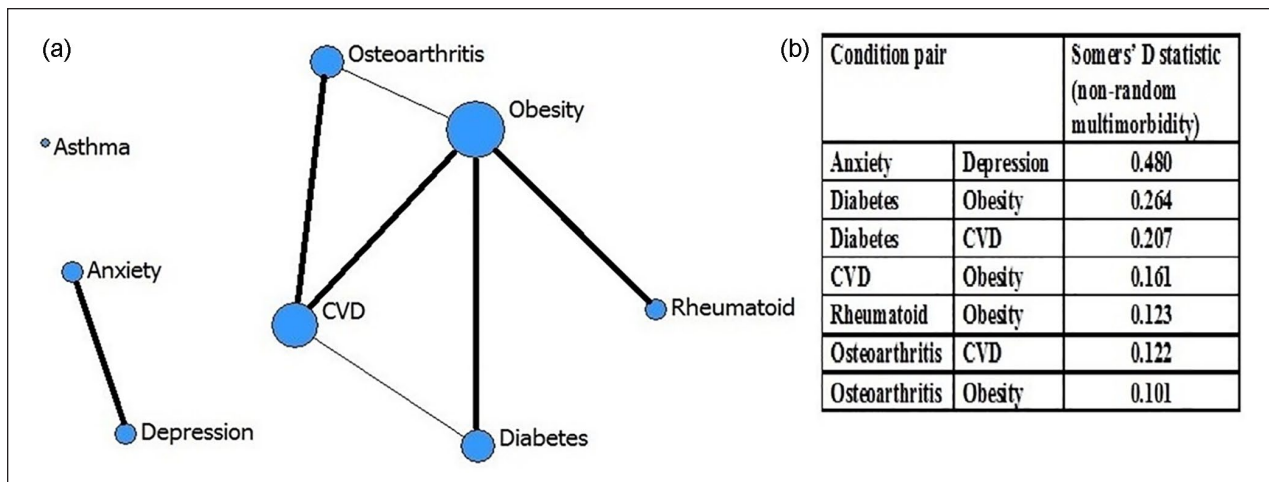
Figure 1. Multimorbidity analysis. (a) Significant nonrandom multimorbidity between eight chronic conditions (nodal size is proportional to the number of conditions that are significantly comorbid with the condition; lines connect two conditions when their pairwise Somers' D statistic is significant; lines will be bolded if they represent the "closest" pairs of conditions, with which the pairwise Somers' D statistic is maximum and significant). (b) Significant comorbid chronic conditions (higher Somers' D statistic [maximum is 1.0] represents a higher degree of nonrandom multimorbidity, where the strength of multimorbidity is measured through the number of concordant pairs indicating the presence of both conditions).

conditions. A nonrandom multimorbidity "cluster" is formed when all members are significantly associated with one another (Ng et al., 2012). Two nonrandom multimorbidity clusters were identified: "CVD, Obesity, and Diabetes" and "CVD, Obesity, and Osteoarthritis."

Primary Health Service Use

The demographic and lifestyle characteristics of all participants ($N = 2039$) and separately for participants with completed or missing information on the annual frequency of GP visits are shown in supplemental Table S1. Overall, the mean age of participants was 59.8; 77.8% were married; 67.0% were born in Australia; and 14.8% had a degree. About 55.4% of participants were employed, and 36.9% were retired. Majority of participants were nonsmokers (85.0%) and consumed less than two standard alcoholic drinks per day (79.7%). Participants who had complete information on GP visits were more likely younger (mean age of 59.6 versus 62.6, $p = .005$), born in Australia ($p = .016$), and employed ($p = .045$). Other demographic and lifestyle characteristics were not different significantly between participants with completed or missing information on GP visits.

Among 1904 participants with GP service utilization information, 156 (8.2%) did not visit a GP in the last 12 months, 1084 (57.0%) visited 1–4 times, 416 (21.8%) visited 5–9 times, and 248 (13.0%) participants had 10 or more GP visits. The median range of GP visits was 3–4 times in a year. Participants' characteristics among the four categories of GP visits are provided in Table 1. Those

attending their GP more frequently tended to be older (there is a trend of increasing mean ages from 51.7 to 66.6 years, $p < .001$). Related to this, the category of 10+ GP visits has significantly higher proportions of people being separated/widowed ($p = .006$), of lower income ($p < .001$), and retired ($p < .001$). As shown in Table 1, it is also observed that the category of 10+ GP visits contains significantly fewer Australian-born people ($p = .021$) and fewer smokers ($p = .002$). As described in the "Statistical Analysis" section, Table 1 shows the trend of increasing mean number of medications from 0.11 to 3.17 ($p < .001$), indicating a positive association between medication and the frequency of GP visits. There are no differences between the four categories of GP visits in education qualification and alcohol consumption.

Impact of Multimorbidity on Primary Health Service Use

Table 2 displays the differences in nine types of comorbid conditions (identified from Figure 1) among the four categories of GP visits. From Table 2, participants with comorbid conditions have generally more GP visits compared to those without any comorbid conditions (namely, decrease in proportions of 0 GP visit and 1–4 GP visits but increase in proportions of 5–9 or 10+ GP visits; see also supplemental Figure S1). Men with comorbid conditions that include CVD were more likely to have 10 or more annual GP visits. For those participants with neither anxiety nor depression, 54.1% of participants with CVD, obesity, and diabetes; 50.0% of participants with CVD

Table 1. Demographic and Lifestyle Characteristics of Participants in the Four Categories of GP Visits ($N = 1904$).

	Frequency (%) or Mean (SD)				
Characteristics[a]	0 GP Visit (n =156) (8.2%)	1–4 GP Visits (n = 1084) (57.0%)	5–9 GP Visits (n = 416) (21.8%)	10+ GP Visits (n = 248) (13.0%)	Total (N = 1904)
Age[b]	51.7 (8.3)	57.8 (10.9)	63.2 (11.2)	66.6 (10.6)	59.6 (11.5)
Marital status[b]					
Married	118 (76.6%)	860 (80.2%)	315 (76.6%)	172 (69.6%)	1465 (77.7%)
Separated/widowed	23 (14.9%)	148 (13.8%)	74 (18.0%)	58 (23.5%)	303 (16.1%)
Never married	13 (8.4%)	65 (6.1%)	22 (5.4%)	17 (6.9%)	117 (6.2%)
Missing	2	11	5	1	19
Country of birth[b]					
Australia	104 (66.7%)	754 (69.6%)	284 (68.3%)	146 (59.1%)	1288 (67.7%)
UK/Ireland	27 (17.3%)	196 (18.1%)	83 (20.0%)	52 (21.1%)	358 (18.8%)
Europe	18 (11.5%)	91 (8.4%)	38 (9.1%)	40 (16.2%)	187 (9.8%)
Asia/Other	7 (4.5%)	43 (4.0%)	11 (2.6%)	9 (3.6%)	70 (3.7%)
Missing	0	0	0	1	1
Household income[b]					
Up to $20 K	8 (5.5%)	99 (9.6%)	74 (18.9%)	72 (31.7%)	253 (14.0%)
$20–$60 K	47 (32.2%)	431 (41.6%)	198 (50.5%)	121 (53.3%)	797 (44.2%)
$60–$80 K	26 (17.8%)	154 (14.9%)	56 (14.3%)	19 (8.4%)	255 (14.2%)
>$80 K	65 (44.5%)	353 (34.0%)	64 (16.3%)	15 (6.6%)	497 (27.6%)
Missing	10	47	24	21	102
Education qualification					
High school	39 (25.2%)	279 (26.0%)	132 (31.8%)	79 (32.2%)	529 (28.0%)
Trade	39 (25.2%)	254 (23.6%)	98 (23.6%)	61 (24.9%)	452 (23.9%)
Cert./Diploma	51 (32.9%)	369 (34.3%)	125 (30.1%)	84 (34.3%)	629 (33.3%)
Degree	26 (16.8%)	173 (16.1%)	60 (14.5%)	21 (8.6%)	280 (14.8%)
Missing	1	9	1	3	14
Work status[b]					
Employed	128 (83.7%)	702 (65.1%)	165 (40.1%)	56 (22.6%)	1051 (55.6%)
Unemployed	5 (3.3%)	20 (1.9%)	6 (1.5%)	4 (1.6%)	35 (1.9%)
Retired	15 (9.8%)	311 (28.8%)	218 (53.0%)	147 (59.3%)	691 (36.6%)
Other	5 (3.3%)	45 (4.2%)	22 (5.4%)	41 (16.5%)	113 (6.0%)
Missing	3	6	5	0	14
Smoking[b]					
Yes/Occasionally	32 (21.1%)	167 (16.0%)	37 (9.3%)	34 (14.4%)	270 (14.8%)
No	120 (78.9%)	876 (84.0%)	359 (90.7%)	203 (85.7%)	1558 (85.2%)
Missing	4	41	20	11	76
Alcohol					
<2 drinks	118 (77.1%)	810 (78.4%)	315 (80.4%)	191 (84.5%)	1434 (79.5%)
3–4 drinks	18 (11.8%)	115 (11.1%)	45 (11.5%)	19 (8.4%)	197 (10.9%)
5–8 drinks	10 (6.5%)	73 (7.1%)	18 (4.6%)	10 (4.4%)	111 (6.2%)
>8 drinks	7 (4.6%)	35 (3.4%)	14 (3.6%)	6 (2.7%)	62 (3.4%)
Missing	3	51	24	22	100
Number of medications[b]	0.11 (0.6)	0.76 (1.6)	2.04 (3.0)	3.17 (4.2)	1.30 (2.6)

Note. GP = general practitioner.
[a]Differences in frequencies among the four categories were tested using χ^2; differences in means were tested using ANOVA.
[b]Significant differences among the four categories of GP visits ($p < .05$).

and osteoarthritis; 43.8% of participants with CVD, obesity, and osteoarthritis; 42.9% of participants with CVD and diabetes; and 36.1% of participants with CVD and obesity had 10 or more annual GP visits. Table 2 also shows the increased proportions of participants with 10+ GP visits when symptoms of anxiety or depression

Table 2. Frequency of GP Visits for Nine Types of Comorbid Conditions.

	Count (Row %)				
Multimorbidity	0 GP Visit *n* =156 (8.2%)	1–4 GP Visits *n* = 1084 (57.0%)	5–9 GP Visits *n* = 416 (21.8%)	10+ GP Visits *n* = 248 (13.0%)	Total
Anxiety and depression	1 (1.4%)	**27 (38.0%)**	19 (26.8%)	24 (33.8%)	71
Nil	136 (8.7%)	933 (59.7%)	330 (21.1%)	163 (10.4%)	1562
Diabetes and obesity (anx, dep, or both)	1 (2.9%)	9 (25.7%)	8 (22.9%)	**17 (48.6%)**	35
Diabetes and obesity (no anx or dep)	8 (4.2%)	**84 (43.5%)**	55 (28.5%)	46 (23.8%)	193
Nil	92 (11.7%)	505 (64.0%)	131 (16.6%)	61 (7.7%)	789
Diabetes and CVD (anx, dep, or both)	0 (0%)	1 (9.1%)	3 (27.3%)	**7 (63.6%)**	11
Diabetes and CVD (no anx or dep)	0 (0%)	12 (21.4%)	20 (35.7%)	**24 (42.9%)**	56
Nil	138 (10.2%)	849 (62.9%)	259 (19.2%)	103 (7.6%)	1349
CVD and obesity (anx, dep, or both)	1 (5.6%)	1 (5.6%)	6 (33.3%)	**10 (55.6%)**	18
CVD and obesity (no anx or dep)	0 (0%)	**36 (37.1%)**	26 (26.8%)	35 (36.1%)	97
Nil	96 (11.8%)	515 (63.3%)	146 (18.0%)	56 (6.9%)	813
Rheumatoid arthritis and obesity (anx, dep, or both)	0 (0%)	3 (33.3%)	2 (22.2%)	**4 (44.4%)**	9
Rheumatoid arthritis and obesity (no anx or dep)	2 (4.9%)	**14 (45.2%)**	9 (29.0%)	6 (19.4%)	31
Nil	96 (11.2%)	531 (61.9%)	158 (18.4%)	73 (8.5%)	858
Osteoarthritis and CVD (anx, dep, or both)	0 (0%)	0 (0%)	1 (14.3%)	**6 (85.7%)**	7
Osteoarthritis and CVD (no anx or dep)	0 (0%)	9 (30.0%)	6 (20.0%)	**15 (50.0%)**	30
Nil	148 (9.7%)	932 (61.3%)	305 (20.1%)	135 (8.9%)	1520
Osteoarthritis and obesity (anx, dep, or both)	1 (6.3%)	1 (6.3%)	**7 (43.8%)**	**7 (43.8%)**	16
Osteoarthritis and obesity (no anx or dep)	1 (1.2%)	**40 (46.0%)**	25 (28.7%)	21 (24.1%)	87
Nil	94 (11.7%)	503 (62.5%)	149 (18.5%)	59 (7.3%)	805
Diabetes, CVD, and obesity[a] (anx, dep, or both)	0 (0%)	0 (0%)	1 (14.3%)	**6 (85.7%)**	7
Diabetes, CVD, and obesity[a] (no anx or dep)	0 (0%)	9 (24.3%)	8 (21.6%)	**20 (54.1%)**	37
Nil	91 (12.3%)	482 (65.2%)	122 (16.5%)	44 (6.0%)	739
Osteoarthritis, CVD, and obesity[a] (anx, dep, or both)	0 (0%)	0 (0%)	1 (33.3%)	**2 (66.7%)**	3
Osteoarthritis, CVD, and obesity[a] (no anx or dep)	0 (0%)	6 (37.5%)	3 (18.8%)	**7 (43.8%)**	16
Nil	93 (12.4%)	480 (64.0%)	130 (17.3%)	47 (6.3%)	750

Note. Data are counts (row percentages) in each category of GP visits. Comparison is between participants with the specific type of comorbid conditions (split by those with comorbid anxiety and/or depression [anx, dep, or both] and those with no anxiety or depression [no anx or dep]) relative to those participants without any of the specific comorbid conditions (denoted as "Nil"); participants with either of the specific comorbid conditions were excluded from the comparisons.

Values in bold indicate the highest-frequency category of GP visits for each pattern of comorbid conditions. CVD = cardiovascular disease.

[a]The multimorbidity group corresponds to a multimorbidity cluster identified from Figure 1.

were also present (e.g., from 54.1% to 85.7% and from 43.8% to 66.7% for participants, respectively, with "CVD, Obesity, and Diabetes" and "CVD, Obesity, and Osteoarthritis," the two nonrandom multimorbidity clusters identified).

The results of multinomial logistic regression models assessing the impact of anxiety and/or depression (defined by the self-reported questionnaire) on the frequencies of GP visits are provided in Table 3, separately for Conditions A (obesity), B (CVD), and C (diabetes). As described in

the "Methods" section, these results are based on the use of screening instruments and do not indicate formal diagnostic assessments for depression or anxiety. Besides age, household income, and work status, other demographic and lifestyle characteristics were not significant.

The presence of obesity was associated with an increase in the frequency of GP visits (adjusted RRRs: 1.4 for 5–9 GP visits and 2.3 for 10+ GP visits over 1–4 GP visits) for participants without anxiety and depression. For participants with obesity, the presence

Table 3. Multinomial Logistic Regression on the Four Categories of GP Visits.

Characteristics	0 GP Visit (n = 138) Versus 1–4 GP Visits (n = 952)	5–9 GP Visits (n = 363) Versus 1–4 GP Visits (n = 952)	10+ GP Visits (n = 200) Versus 1–4 GP Visits (n = 952)
Condition A (for obesity)[a]			
Obesity effect for participants without anx or dep	0.7 (0.5–1.1)	1.4* (1.1–1.9)	2.3* (1.5–3.5)
Extra effect from anx, dep, or both for participants with obesity	0.9 (0.3–2.7)	2.2* (1.3–3.7)	3.8* (2.2–6.6)
Age	0.9* (0.9–1.0)	1.0 (1.0–1.0)	1.1* (1.0–1.1)
Household income			
Up to $20 K	Reference	Reference	Reference
$20–$60 K	0.9 (0.3–2.3)	0.8 (0.6–1.2)	0.7 (0.5–1.1)
$60–$80 K	0.9 (0.3–2.7)	1.1 (0.6–1.8)	0.6 (0.3–1.3)
>$80 K	1.0 (0.4–2.7)	0.6 (0.4–1.0)	0.3* (0.1–0.6)
Work status			
Employed	Reference	Reference	Reference
Unemployed	1.6 (0.5–5.2)	0.9 (0.3–2.5)	1.0 (0.3–3.9)
Retired	0.7 (0.3–1.6)	2.2* (1.5–3.4)	1.6 (0.9–2.9)
Other	0.8 (0.3–2.2)	1.5 (0.8–2.8)	6.3* (3.4–11.6)
Condition B (for CVD)[a]			
CVD effect for participants without anx or dep	N/A	1.7* (1.1–2.6)	4.8* (3.0–7.6)
Extra effect from anx, dep, or both for participants with CVD		4.2* (1.0–16.8)	5.0* (1.3–19.7)
Age		1.0 (1.0–1.0)	1.0* (1.0–1.1)
Household income			
Up to $20 K		Reference	Reference
$20–$60 K		0.8 (0.6–1.2)	0.6* (0.4–1.0)
$60–$80 K		1.0 (0.6–1.6)	0.5* (0.3–1.0)
>$80 K		0.5* (0.3–0.9)	0.2* (0.1–0.5)
Work status			
Employed		Reference	Reference
Unemployed		0.8 (0.3–2.3)	1.0 (0.3–3.7)
Retired		2.2* (1.5–3.3)	1.6 (0.9–2.7)
Other		1.5 (0.8–2.7)	5.8* (3.2–10.5)
Condition C (for diabetes)[a]			
Diabetes effect for participants without anx or dep	0.8 (0.4–1.6)	1.9* (1.4–2.7)	3.1* (2.1–4.8)
Extra effect from anx, dep, or both for participants with diabetes	1.7 (0.3–8.9)	1.2 (0.5–2.8)	3.0* (1.3–6.8)
Age	0.9* (0.9–1.0)	1.0 (1.0–1.0)	1.1* (1.0–1.1)
Household income			
Up to $20 K	Reference	Reference	Reference
$20–$60 K	0.8 (0.3–2.0)	0.9 (0.6–1.3)	0.7 (0.5–1.1)
$60–$80 K	0.8 (0.3–2.3)	1.0 (0.6–1.8)	0.6 (0.3–1.3)
>$80 K	0.9 (0.3–2.2)	0.6* (0.4–1.0)	0.3* (0.1–0.6)
Work status			
Employed	Reference	Reference	Reference
Unemployed	1.9 (0.6–5.5)	0.8 (0.3–2.3)	0.9 (0.2–3.5)
Retired	0.7 (0.3–1.6)	2.1* (1.4–3.2)	1.5 (0.9–2.6)
Other	0.8 (0.3–2.1)	1.5 (0.8–2.8)	5.8* (3.2–10.7)

Note. Data are adjusted relative risk ratios (RRRs) with 95% CI (significant results marked with *). Extra effect refers to the interaction term of the condition and anxiety/depression; it compares the frequency of GP visits between the patients with the condition and those with the condition and anxiety/depression. N/A for Model B because there are no participants with comorbid conditions involving CVD in the category of 0 GP visit. Other work status includes student and people with home duties. CVD = cardiovascular disease.
[a]Number of medications was not adjusted in the models; see text for details.

of anxiety or depression was associated with a further increase in the frequency of GP visits (adjusted RRRs: 2.2 for 5–9 GP visits and 3.8 for 10+ GP visits relative to 1–4 GP visits). The predicted probabilities of 10+ GP visits, comparing men without obesity, anxiety, or depression to those with obesity but no anxiety or depression, and to those with obesity and anxiety, depression, or both, are displayed in Figure 2(A). The corresponding predicted probabilities of 10+ GP visits for these three groups were 4.5%, 9.1%, and 22.3%, respectively. The adjusted risk ratio of 10+ GP visits for obesity alone was 2.0 = 9.1/4.5 (95% CI [1.5, 2.8]), whereas that attributed to anxiety or depression was 2.4 = 22.3/9.1 (95% CI [1.9, 3.2]).

The presence of CVD was associated with an increase in the frequency of GP visits (adjusted RRRs: 1.7 for 5–9 GP visits and 4.8 for 10+ GP visits) for participants without anxiety and depression. For participants with CVD, the presence of anxiety or depression was associated with a further increase in the frequency of GP visits (adjusted RRRs: 4.2 for 5–9 GP visits and 5.0 for 10+ GP visits relative to 1–4 GP visits). The predicted probabilities of 10+ GP visits were 5.7%, 21.0%, and 36.8% for the groups without CVD anxiety or depression, CVD without anxiety or depression, and CVD with anxiety and/or depression, respectively (Figure 2B). The adjusted risk ratio of 10+ GP visits for CVD alone was 3.7 (95% CI [2.8, 4.8]), whereas that attributed to anxiety or depression was 1.8 (95% CI [1.2, 2.5]).

The presence of diabetes was associated with an increase in the frequency of GP visits (adjusted RRRs: 1.9 for 5–9 GP visits and 3.1 for 10+ GP visits) for participants without anxiety and depression. For participants with diabetes, the presence of anxiety or depression was associated with a further increase in the chance of 10+ GP visits over 1–4 GP visits, with an adjusted RRR of 3.0. The predicted probabilities of 10+ GP visits were 5.5%, 13.5%, and 30.1% for the groups without diabetes, anxiety or depression, diabetes without anxiety and depression, and diabetes with anxiety and/or depression, respectively. The adjusted risk ratio of 10+ GP visits for diabetes alone was 2.4 (95% CI [1.9, 3.2]), whereas that attributed to anxiety or depression was 2.2 (95% CI [1.6, 3.1]) (Figure 2C).

Additional results of the sensitivity analyses on the definition of anxiety and depression based on formal clinical diagnosis (GAD-7 for anxiety; BDI-1a/CES-D for depression) or medications for anxiety and/or depression are provided in supplemental Tables S2 and S3. The results indicate the same conclusion as above that the presence of clinically diagnosed or medication-based anxiety and/or depression was significantly associated with a further increase in the chance of 10+ GP visits.

Discussion

This study presents findings about the utilization of GP services by older-aged community-dwelling men (38–85 years) in relation to their patterns of multimorbidity, where two nonrandom multimorbidity "clusters" of "CVD, Obesity, Diabetes" and "CVD, Obesity, Osteoarthritis" were identified, as well as the impact of comorbid anxiety and depression. There is a common misperception that "men don't go to the doctors." In 2014–2015, an estimated 7.4 million males aged ≥15 years (78%) in Australia had seen a GP at least once in the previous year; the proportion increased with age (from 80.4% at age 45–54 to 96.3% at age ≥65). In 2013–2014, expenditure on primary health-care and hospital services was 38% and 40%, respectively, of the total health funding in Australia (Australian Institute of Health and Welfare, 2015). We previously reported that >90% of men in our cohort attended their GP at least once in the preceding year (Wittert et al., 2011). The current study shows higher proportions of at least one GP visit in the previous year for men with comorbid conditions (e.g., 96% for men with diabetes and obesity; 100% for men with diabetes, obesity, and CVD). Specifically, this study revealed that men with chronic conditions comorbid with CVD are more likely to have 10 or more annual GP visits, compared to multimorbidity involving other conditions such as diabetes, obesity, arthritis, or depression and anxiety, in the absence of CVD. Primary health service use has previously been shown to be frequent in men with multimorbidity involving heart failure in older men (Robertson et al., 2012) or congenital heart disease in younger men (mean age 28.1 years; Billett et al., 2008). Our study quantified the impact of multimorbidity involving obesity, CVD, or diabetes on the relative risks of higher frequencies in annual GP visits, showing again higher impact from CVD compared to multimorbidity involving obesity or diabetes without CVD, after adjustment for demographic factors. Furthermore, there is a two to three-fold increase in the chance of having 10 or more GP services annually for Australian men with CVD alone.

Another significant driver of primary health-care service use among men is mental health disorders. Data from the FAMAS cohort (men aged 35–80) showed an adjusted odds ratio (*OR*) of 3.9 of 10+ annual GP visits versus none for depressed men (Atlantis et al., 2011). Based on a national survey (aged 16–85), approximately 27.5% of men with mental disorders made use of any services for mental health problems in a year, compared to 8.8% of the general Australian men population (Burgess et al., 2009). Our study found that 33.8% of men with anxiety and depression had 10 or more annual GP visits, compared to 10.4% of men without anxiety
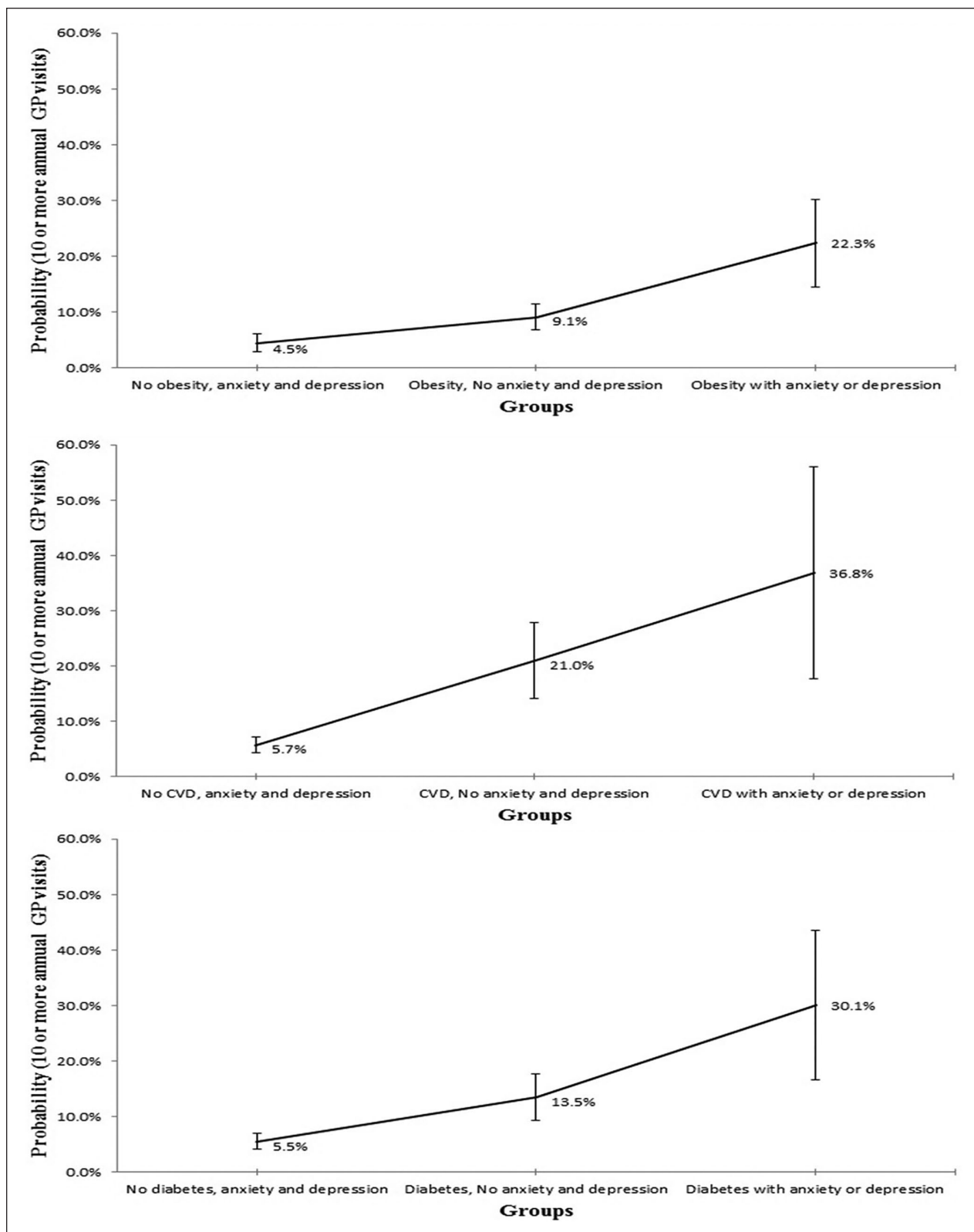
Figure 2. Adjusted predictions of 10 or more annual GP visits with 95% CIs for (A) obesity, (B) CVD, and (C) diabetes conditions. CVD = cardiovascular disease.

and depression. Primary health service use particularly in community-dwelling men with anxiety and/or depression in addition to other chronic health conditions was less researched. Without accounting for gender difference, it has been documented that comorbid depression in persons with diabetes is associated with increased health-care utilization for a Hungarian population aged >18 and a sample of African American patients aged ≥40 (Husaini et al., 2004; Vamos et al., 2009). Our study revealed for the first time the synergistic effect of comorbid anxiety and/or depression with either obesity, CVD, or diabetes on primary health service use for older-aged men. The likelihood of having 10 or more annual GP visits increased by 140%, 80%, and 120%, respectively, for comorbid obesity, CVD, or diabetes due to anxiety and/ or depression. But the overall effect is still the largest (the predicted probability of 10+ GP visits was 36.8%) for anxiety and/or depression with comorbid CVD compared to obesity (22.3%) and diabetes (30.1%). The significance of comorbid depression and anxiety is not just a matter of increased use of primary care services (Atlantis et al., 2012; Roy-Byrne et al., 2008; Van der Kooy et al., 2007). Nabi et al. (2010) reported that depression symptoms are associated with an increased risk of all-cause death for middle-aged men and women with comorbid coronary heart disease and depression (the British Whitehall-II study), and May et al. (2017) found, using a large cohort of patients who underwent angiography (aged ≥18), that a depression diagnosis at any time following coronary artery disease diagnosis was the strongest predictor of all-cause death, emphasizing the need for continual screening of depression among patients with heart diseases.

The prevalence of anxiety/depression is significantly higher in patients with comorbid conditions than in the general population (Husaini et al., 2004; Pearson-Stuttard et al., 2019; Roy-Byrne et al., 2008), and the combination is associated with poorer health outcomes. These observations are generalizable across a variety of populations, including the United States (Li et al., 2019; Voinov et al., 2013). There is also, on an almost global basis, a higher prevalence of preexisting comorbidities and poorer health outcomes among men compared to women (Rovito et al., 2017; World Health Organization Regional Office for Europe, 2018). It is no longer tenable to assert that inequitable burden of poor health experienced by men is the consequence of failure to use health services (Schlichthorst et al., 2016). One possible explanation may relate to the markedly lower frequency with which depression is diagnosed in men (World Health Organization, 2019), possibly because of the failure to recognize a "male type" presentation typified by somatization of symptoms, irritability, anger, and substance abuse (Martin et al., 2013). Effective management

of depression has long been shown to reduce primary care visit frequency and costs (Simon et al., 2001). It is also clear that an optimal outcome for chronic conditions occurs when comorbid depression and/or anxiety is recognized and effectively managed (Atlantis et al., 2013; Bhattacharya et al., 2016; DeJean et al., 2013; Tully & Baumeister, 2015). The implication of these data is that to reduce the disproportionate burden of poor health among men, a focus on strategies to efficiently recognize and manage multiple concurrent chronic diseases with a low threshold to consider depression and anxiety, particularly in men who are frequent users of health care, is required.

The major strength of the MAILES study is its value-added benefit of combining selected participants from two high-quality cohort studies to provide a wealth of measured and self-reported information about multiple chronic conditions, together with the data collected on a wide range of biomedical and sociodemographic variables as well as linked information about primary health service utilization from Medicare data. The MAILES study has a sound epidemiological base, a comparatively large sample of randomly selected community-dwelling men, and a high overall response rate, allowing its findings to be generalized to the broader population (Grant et al., 2014). As with most cohort studies, the key limitation of the MAILES study is its reliance on self-reported information for some lifestyle and medical factors, such as rheumatic diseases (Gill & Hill, 2017). However, De-Loyde et al. (2015) reported that the use of patient self-reported questionnaires to ascertain comorbid conditions remains a valid method for health services research, as shown in the sensitivity analyses, which indicated the same conclusion for using clinically diagnosed or medication-based anxiety and depression. Moreover, self-reports of cardiac and stroke events have been reported to be accurate (Bergmann et al., 1998; Kriegsman et al., 1996). There is accumulating evidence for a male-specific phenotype of depression (e.g., increased anger and risk-taking) that is not captured by the BDI or CES-D. The use of specific questionnaires such as the Male Depression Risk Scale-22 (MDRS-22; Rice et al., 2013, 2018) provides a better understanding depression (and anxiety) in men and associated service use in men. Another limitation of the study is the lack of information on the severity of the disease and type of treatment. Although the study participants were representative of its target population, they were also predominantly Caucasian, aged 35–80 years (at recruitment), and community-dwelling (Grant et al., 2014). Also, the BDI, CES-D, and GAD-7 are not formal clinical diagnostic assessments for depression or anxiety. This point should be considered when interpreting the results that are based on the use of screening instruments.

Conclusions

Our study strengthens the evidence-based information about the nature of multimorbidity in men and its impact on primary health services use, which is critical to inform guidelines and health management for effective and efficient care of men with multimorbidity and comorbid anxiety and/or depression. Coexisting conditions may also influence the effectiveness of therapies or modify patients' priorities concerning their health care (Boyd et al., 2011). Effective management of this patient group thus requires effective management of other comorbid conditions as well (Boult, 2010; Caughey & Roughead, 2011), bearing on the different patterns in men's health service use (Smith et al., 2006). More importantly, multimorbidity patterns involving CVD should be considered in the development of clinical trials and guidelines to better inform medical decision-making and provide comprehensive or collaborative care for patients with CVD and comorbid conditions including anxiety and/or depression (Assari et al., 2013; Boyd et al., 2011; Glynn et al., 2008; Morgan et al., 2009).

Declaration of Conflicting Interests

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Ethical Approval and Consent to Participate

All protocols were approved by the Royal Adelaide Hospital and the Queen Elizabeth Hospital Research Ethics Committees, with written, informed consent obtained from all participants.

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Supplemental Material

Supplemental material for this article is available online.

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