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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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

Background: Multimorbidity has been identified as a serious challenge on global health system, closely associated with lower quality of life, poorer health outcomes, and higher utilisation of health services. However, there are major gaps in our knowledge around multimorbidity, especially its effect on primary care services and the burden of comorbid mental health conditions on multimorbidity patterns. 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.

Methods: This was a prospective cohort study with Australian population. The study population consisted of 2,039 men aged ≥40, who were enrolled either in the Florey Adelaide Male Ageing Study (FAMAS) Stage 2 between 2007-2010 or in the North-West Adelaide Health Study (NWAHS) Stage 3 between 2008-2010. Data have been collected on the prevalence of 8 chronic conditions and linked Medicare data about individual health service utilization information on annual GP visits. Multinomial logistic regression was adopted to quantify the impact of anxiety and depression on the frequencies of GP visits, with adjustment for participant's demographic and lifestyle characteristics.

Results: Obesity and cardiovascular disease (CVD) were associated with the highest number of comorbid conditions. Two non-random 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. Comparing 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).

Conclusions: In Australian, community-dwelling men, multimorbidity is associated with a high use of GP services; especially for multimorbidity that includes CVD with comorbid anxiety and depression. Multimorbidity patterns involving CVD 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

Background

Multimorbidity has recently been identified as one of the greatest challenges facing the global health system [1]. Estimates from the WHO demonstrate that between 40-60% of the adult population in developed countries have two or more chronic conditions [2]. The presence of multimorbidity has been associated with lower quality of life [3], increase mortality [4], and higher utilisation of hospital and primary care services [5-8]. Despite this, the study of multimorbidity, as distinct from earlier studies focussed on comorbidity [9], is only relatively new. Multimorbidity is particularly applicable to the primary care setting, where the focus of the general practitioner tends to focus on the whole care of the patient rather than one particular condition [10].

Recent editorials [11-13] have detailed major gaps in our knowledge around multimorbidity, and especially its effect on primary care services. For instance, while the prevalence of multimorbidity is known to increase with age [14] the higher number of absolute cases of multimorbidity in those aged under 65 and the limited opportunities for intervention in elderly patients has motivated a life course approach to multimorbidity in primary care [15]. Despite this, there remains an absence of studies that examine multimorbidity in younger to middle-aged cohorts [12]. 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 [1, 16]. The recent UK Academy of Medical Sciences report [17] has recommended as a research priority the need to better understand the biopsychosocial determinants of multimorbidity clusters. However to date most evidence on multimorbidity is derived from large disease surveillance systems that have limited capacity to understand multimorbidity as “a non-random series of predictable clusters” [1], and identify modifiable targets for intervention in primary care [18].

Given this, the objectives of our study are to examine: (a) the patterns of multimorbidity of eight chronic conditions (anxiety, asthma, CVD, depression, diabetes, obesity, osteoarthritis,

rheumatoid arthritis), and (b) the impact of comorbid anxiety and depression, on the utilization of general practitioner services for urban-dwelling, middle-aged to elderly men.

Methods

Setting and population

The MAILES study was established in 2009 to investigate the associations of sex steroids, inflammation, environmental and psychosocial factors with cardio-metabolic disease risk in men. The study population consists of 2,568 men 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 have been collected on a number of chronic conditions, as well as linked Medicare data about individual health service claims and utilization information. 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. Detailed information on recruitment and follow-up process was reported elsewhere [19]. The data in MAILES Stage 2 study contain 2,039 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.

Health service usage

Health service use was obtained from a self-reported, piloted, health service utilization questionnaire. The number of general practitioner (GP) visits in one year was categorized into four categories (zero, 1-4, 5-9, and 10 or more). Information was also obtained regarding a participant's 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.

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 ≥7.0mmol/L and/or HbA1c ≥6.5) [19]. Obesity is indicated by a waist circumference ≥100cm as measured at the clinic visit. Depressive symptoms were assessed using the Beck Depression Inventory (BDI-Ia) [20] for FAMAS men and the Center for Epidemiologic Studies - Depression Scale (CES-D) [21] for NWAHS men. Cut-off scores of 10 and 16 for the BDI-1a & CES-D, respectively, were employed to classify into depression categories (Yes/No). Both the BDI-1a and CES-D show comparable specificities from the classification of major depression in residential, older men [22]. Anxiety symptoms were assessed using the Generalised Anxiety Disorder 7 item (GAD-7) scale [23]. A cut-off score of 10 was used to categorise into anxiety categories (Yes/No). The GAD-7 shows good overall specificity for generalised anxiety disorder in comparable men [23].

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 from baseline.

Statistical analysis

Analysis of chronic conditions was conducted based on the clustering method of pairwise concordance statistics [24], which adopts the asymmetric Somers' D statistic to quantify the degree of multimorbidity beyond chance [25-26]. Identification of significant (non-random) multimorbidity between conditions, also known as "associative multimorbidity" [27], is more informative to view disease patterns for a potential sharing of risk factors of the diseases [25, 28-30]. The clustering method adopts the Benjamini-Hochberg procedure to control for the false discovery rate at α=0.05 [31].

Chi-square analysis (for categorical variables) or ANOVA (for quantitative variables) were used to test for significant differences in participant's characteristics and multimorbidity patterns between the four groups according to the number of GP visits in one year. Multinomial logistic

regression 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 participant's 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, which 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 and should not be adjusted for in the regression analysis [32]. 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; i.e., multimorbidity is associated with more medications [33-34] and in turn more medications have been shown to increase the health service utilization [35-36]. Therefore, medication was not adjusted for in the multinomial logistic regression analysis.

Comparison analysis and logistic regression were performed using STATA (SE 13.1; StataCorp, College Station, Texas) on the basis of 1,904 participants (93.4% of 2,039) with complete information on the annual frequency of GP visits. Sensitivity analyses were conducted regarding the definitions of anxiety and depression based on either formal clinical diagnosis (GAD7 for anxiety; BDI-1a/CES-D for depression) or medications for anxiety and/or depression, compared to 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 (49.9%), Diabetes (19.8%), Asthma (13.1%), CVD (11.8%), Osteoarthritis

(11.1%), Depression (9.2%), Anxiety (7.2%), and Rheumatoid arthritis (3.7%). Fig. 1 displays the multimorbidity patterns among these chronic conditions, along with seven pairs of conditions with significant non-random multimorbidity. From Fig. 1, obesity and CVD have the highest number of associated comorbid conditions. Two non-random 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=2,039) and separately for participants with completed or missing information on the annual frequency of GP visits are shown in Supplementary Table S1. Overall, the mean age of participants was 59.8, 77.8% married, 67.0% born in Australia, and 14.8% with a degree. About 55.4% of participants were employed, with 36.9% retired. Majority of participants were non-smokers (85.0%) and consumed <2 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=0.005), born in Australia (p=0.016), and employed (p=0.045). Other demographic and lifestyle characteristics were not different significantly between participants with completed or missing information on GP visits.

Among 1,904 participants with GP service utilization information, 156 (8.2%) did not visit a GP in last 12 months, 1,084 (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. Participant's 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<0.001). Related to this, the category of 10+ GP visits has significantly higher proportions of people being separated/widowed (p=0.006), of lower income (p<0.001), and retired (p<0.001). From Table 1, it is also observed that the category of 10+ GP visits contains significantly less Australian born people (p=0.021) and less smokers (p=0.002). 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<0.001), 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 Fig. 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 zero GP visit and 1-4 GP visits but increase in proportions of 5-9 or 10+ GP visits); see also Supplementary Fig. S1. Men with comorbid conditions that include CVD were more likely to have 10 or more annual GP visits. For those participants without neither anxiety nor depression, 54.1% of participants with CVD, obesity, and diabetes, 50.0% of participants with CVD 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 was also present (for example, from 54.1% to 85.7% and from 50.0% to 85.7% for participants, respectively, with (CVD, Obesity, and Diabetes) and with (CVD and Osteoarthritis).

The results of multinomial logistic regression models assessing the impact of anxiety and/or depression (defined by self-reported questionnaire) on the frequencies of GP visits are provided in Table 3, separately for Conditions A (obesity), B (CVD), and C (diabetes). Besides age, household income and work status, other demographic and lifestyle characteristics were not significant.

The presence of obesity increased 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 of anxiety or depression further increased 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 those with obesity and also

anxiety, depression or both, are displayed in Fig. 2(a). The corresponding predicted probabilities of 10+ GP visits for these 3 groups were 4.5%, 9.1%, and 22.3%, respectively. The adjusted risk ratios of 10+ GP visits for obesity alone was 2.0 (95% CI: 1.5-2.8), whereas those attributed to anxiety or depression was 2.4 (95% CI: 1.9-3.2).

The presence of CVD increased 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 further increased 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, CVD with anxiety and/or depression, respectively (Fig. 2b). The adjusted risk ratios of 10+ GP visits for CVD alone was 3.7 (95% CI: 2.8-4.8), whereas those attributed to anxiety or depression was 1.8 (95% CI: 1.2-2.5).

The presence of diabetes increased 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 further increased the chance of 10+ GP visits over 1-4 GP visits, with 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 ratios of 10+ GP visits for diabetes alone was 2.4 (95% CI: 1.9-3.2), whereas those attributed to anxiety or depression was 2.2 (95% CI: 1.6-3.1) (Fig. 2(c)).

Additional results of the sensitivity analyses on the definition of anxiety and depression based on formal clinical diagnosis (GAD7 for anxiety; BDI-1a/CES-D for depression) or medications for anxiety and/or depression were provided in Supplementary Tables S2-S3, which indicated the same conclusion as above that the presence of clinically-diagnosed or medication-based anxiety and/or depression further increased significantly the chance of 10+ GP visits.

Discussion

This study presents findings about the utilization of GP services by older-aged community-dwelling men (≥40 years) in relation to their patterns of multimorbidity, where two non-random multimorbidity "clusters" of (CVD, Obesity, Diabetes) and (CVD, Obesity, Osteoarthritis) were identified, and the impact of comorbid anxiety and depression. There is a common misperception that "men don't go to the doctors". In 2014-15, 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 of 45-54 to 96.3% at age ≥65). In 2013-14, expenditure on primary healthcare and hospital services was 38% and 40% of total health funding respectively in Australia [37]. We have previously reported that >90% of men in our cohort attended their GP at least once in the preceding year [38]. The current study shows higher proportions of at least one GP visit in 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 [39] or congenital heart disease in younger men (mean age 28.1 years) [40]. 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 OR of 3.9 of 10+ annual GP visits versus none for depressed men [41]. 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 [42]. 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 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 healthcare utilization for a Hungarian population aged >18 and a sample of African-American patients age ≥40 [43-44]. 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 were 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 only a matter of increased use of primary care services [45-47]. Nabi et al. [48] 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. [49] found using a large cohort of patients underwent angiography (aged ≥18) that a depression diagnosis at any time following coronary artery disease diagnosis was the strongest predictor of all-cause death, emphasising the need for continual screening of depression among patients with heart diseases.

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 socio-demographic 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 [19]. 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 [50]. However, De-Loyde et al. [51] 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 [52-53]. Another limitation of the study was 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 [19].

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 [54]. Effective management of this patient group thus requires effective management of other comorbid conditions as well [55-56], bearing on different pattern in men's health service use [57]. 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 [54, 58-60].

Additional file

Additional file 1 contains supplementary material including Tables S1-S3 and Fig. S1.

Abbreviations

ANOVA: Analysis of variance; CI: confidence interval; CVD: Cardiovascular disease;

FAMAS: Florey Adelaide Male Ageing Study; GP: General practitioner;

MAILES: Men Androgen Inflammation Lifestyle Environment and Stress;

NWAHS: North-West Adelaide Health Study; OR: odds ratio; RRR: Relative risk ratio

Ethics 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.

Consent for publication

Not applicable.

Availability of data and material

The data that support the findings of this study are available from the MAILES cohort study team but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of the MAILES cohort study team.

Competing interests

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Authors' contributions

SN, SM, RA, GW conceptualised and designed the research project. SN was responsible for the statistical analysis. SN, SM, GW interpreted the results and drafted the first version of the manuscript. All authors (SN, SM, RA, PO, GW) critically revised, read and approved the manuscript.

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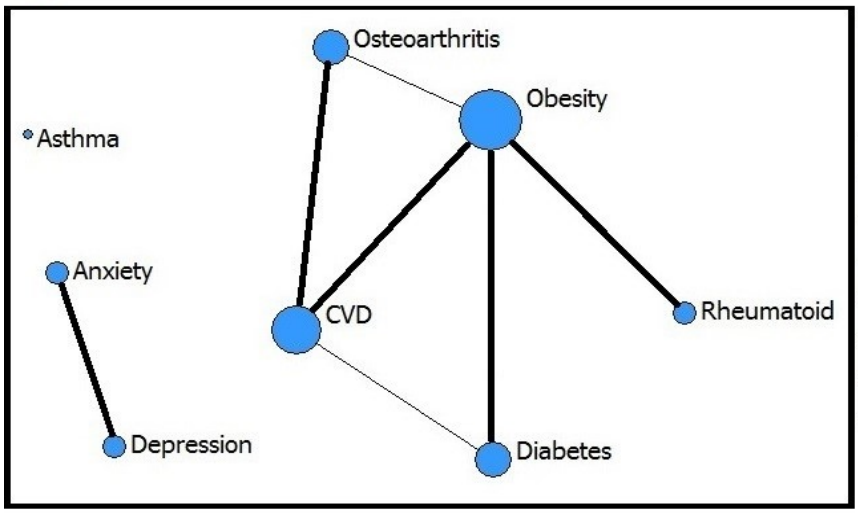
(a)



(b)

Condition pair		Somers' D statistic (non-random multimorbidity)
Anxiety	Depression	0.480
Diabetes	Obesity	0.264
Diabetes	CVD	0.207
CVD	Obesity	0.161
Rheumatoid	Obesity	0.123
Osteoarthritis	CVD	0.122
Osteoarthritis	Obesity	0.101

Fig. 1 Multimorbidity analysis: (a) Significant non-random multimorbidity between 8 chronic conditions (nodal size is proportional to the number of conditions that are significantly comorbid with the condition; bolded lines link 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 non-random multimorbidity, where the strength of multimorbidity is measured through the number of concordant pairs indicating the presence of both conditions [24].

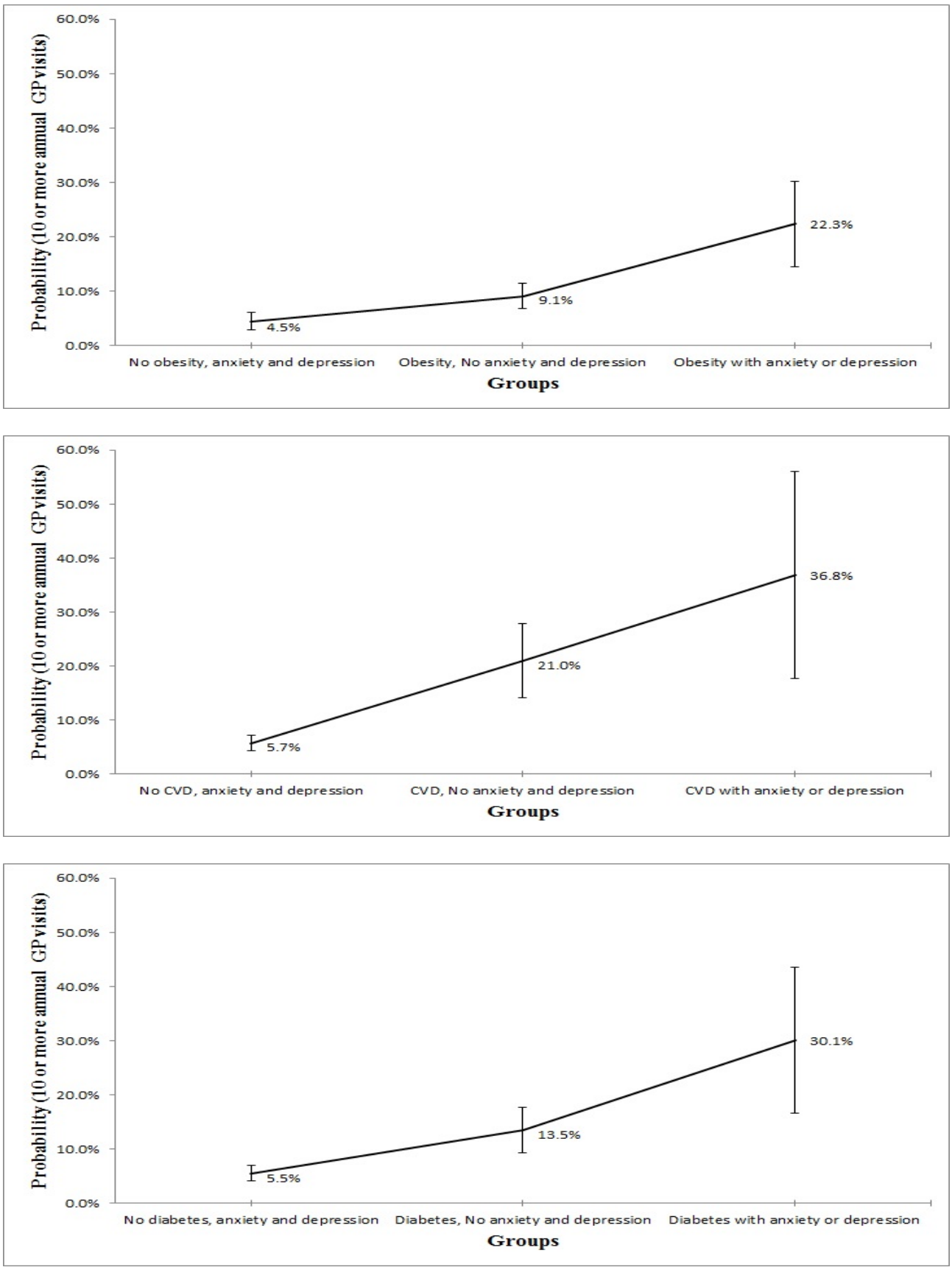


Fig. 2 Adjusted predictions of 10 or more annual GP visits with 95% CIs for Conditions (a) Obesity; (b) CVD; and (c) Diabetes.

Table 1 Demographic and lifestyle characteristics of participants in the four categories of GP visits (N = 1,904)

Characteristics[a]	Frequency (%) or Mean (SD)				Total (n=1,904)
	Zero 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%)	
Age*	51.7 (8.3)	57.8 (10.9)	63.2 (11.2)	66.6 (10.6)	59.6 (11.5)
Marital status*					
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*					
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*					
Up to $20K	8 (5.5%)	99 (9.6%)	74 (18.9%)	72 (31.7%)	253 (14.0%)
$20 - $60K	47 (32.2%)	431 (41.6%)	198 (50.5%)	121 (53.3%)	797 (44.2%)
$60 - $80K	26 (17.8%)	154 (14.9%)	56 (14.3%)	19 (8.4%)	255 (14.2%)
>$80K	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*					
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*					
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*	0.11 (0.6)	0.76 (1.6)	2.04 (3.0)	3.17 (4.2)	1.30 (2.6)

[a] Test for differences in frequencies among the four categories using chi-square tests; test for differences in means using ANOVA.

* Significant differences among the four categories of GP visits ($p<0.05$).

Table 2 Frequency of GP visits for nine types of comorbid conditions

Multimorbidity	Count (row %)				Total
	Zero 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%)	
Anxiety & 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 & Obesity (anx, dep or both)	1 (2.9%)	9 (25.7%)	8 (22.9%)	17 (48.6%)	35
Diabetes & Obesity (no anx nor 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 & CVD (anx, dep or both)	0 (0%)	1 (9.1%)	3 (27.3%)	7 (63.6%)	11
Diabetes & CVD (no anx nor 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 & Obesity (anx, dep or both)	1 (5.6%)	1 (5.6%)	6 (33.3%)	10 (55.6%)	18
CVD & Obesity (no anx nor 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 & Obesity (anx, dep or both)	0 (0%)	3 (33.3%)	2 (22.2%)	4 (44.4%)	9
Rheumatoid & Obesity (no anx nor 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 & CVD (anx, dep or both)	0 (0%)	0 (0%)	1 (14.3%)	6 (85.7%)	7
Osteoarthritis & CVD (no anx nor 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 & Obesity (anx, dep or both)	1 (6.3%)	1 (6.3%)	7 (43.8%)	7 (43.8%)	16
Osteoarthritis & Obesity (no anx nor 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
Diab & CVD & Obesity (anx, dep or both)	0 (0%)	0 (0%)	1 (14.3%)	6 (85.7%)	7
Diab & CVD & Obesity (no anx nor 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
Arth & CVD & Obesity (anx, dep or both)	0 (0%)	0 (0%)	1 (33.3%)	2 (66.7%)	3
Arth & CVD & Obesity (no anx nor 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

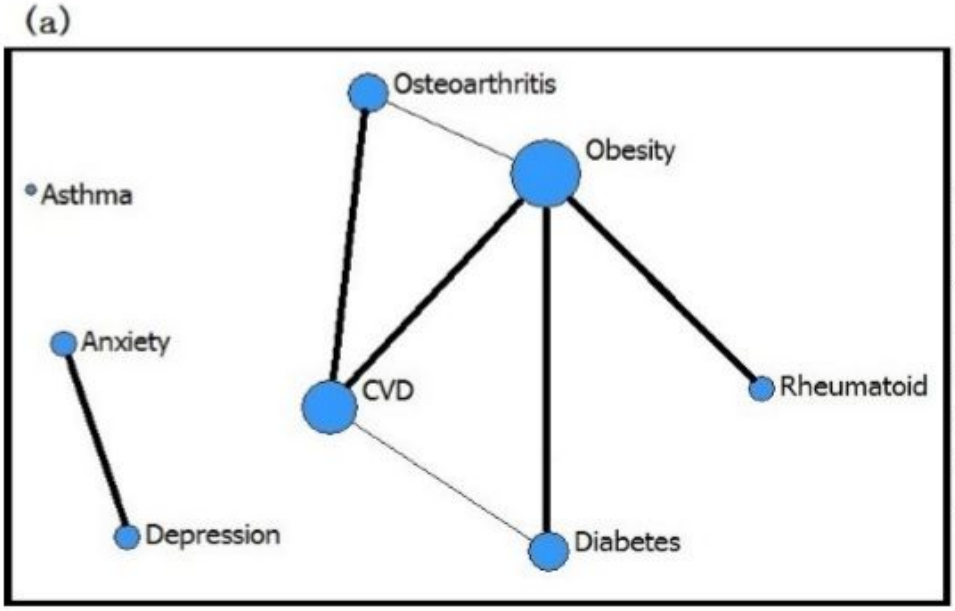
Data are counts (row percentages) in each category of GP visits.
Comparison is between participants with the specific type of comorbid conditions (split by those with comorbid anxiety and/or depression (anx, dep or both) and those with no anxiety nor depression (no anx nor dep)) relative to those participants without any of the specific comorbid conditions (denoted as Nil); participants with either of the specific comorbid conditions were excluded from the comparisons).
The highest-frequency category of GP visits is highlighted for each pattern of comorbid conditions.

Table 3 Multinomial logistic regression on the four categories of GP visits

Characteristics	Zero 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 $20K	Reference	Reference	Reference
$20 - $60K	0.9 (0.3-2.3)	0.8 (0.6-1.2)	0.7 (0.5-1.1)
$60 - $80K	0.9 (0.3-2.7)	1.1 (0.6-1.8)	0.6 (0.3-1.3)
>$80K	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 $20K		Reference	Reference
$20 - $60K		0.8 (0.6-1.2)	0.6* (0.4-1.0)
$60 - $80K		1.0 (0.6-1.6)	0.5* (0.3-1.0)
>$80K		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 $20K	Reference	Reference	Reference
$20 - $60K	0.8 (0.3-2.0)	0.9 (0.6-1.3)	0.7 (0.5-1.1)
$60 - $80K	0.8 (0.3-2.3)	1.0 (0.6-1.8)	0.6 (0.3-1.3)
>$80K	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)

Data are adjusted relative risk ratios (RRRs) with 95% CI (significant results marked with an *).
N/A for Model B because there are no participants with comorbid conditions involving CVD in the category of zero GP visit. Other work status includes student and people with home duties.
[a] Number of medications was not adjusted in the models; see text for details.

Figures



(b)

Condition pair		Somers' D statistic (non-random multimorbidity)
Anxiety	Depression	0.480
Diabetes	Obesity	0.264
Diabetes	CVD	0.207
CVD	Obesity	0.161
Rheumatoid	Obesity	0.123
Osteoarthritis	CVD	0.122
Osteoarthritis	Obesity	0.101

Figure 1

Multimorbidity analysis: (a) Significant non-random multimorbidity between 8 chronic conditions (nodal size is proportional to the number of conditions that are significantly comorbid with the condition; bolded lines link 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 non-random multimorbidity, where the strength of multimorbidity is measured through the number of concordant pairs indicating the presence of both conditions [24].

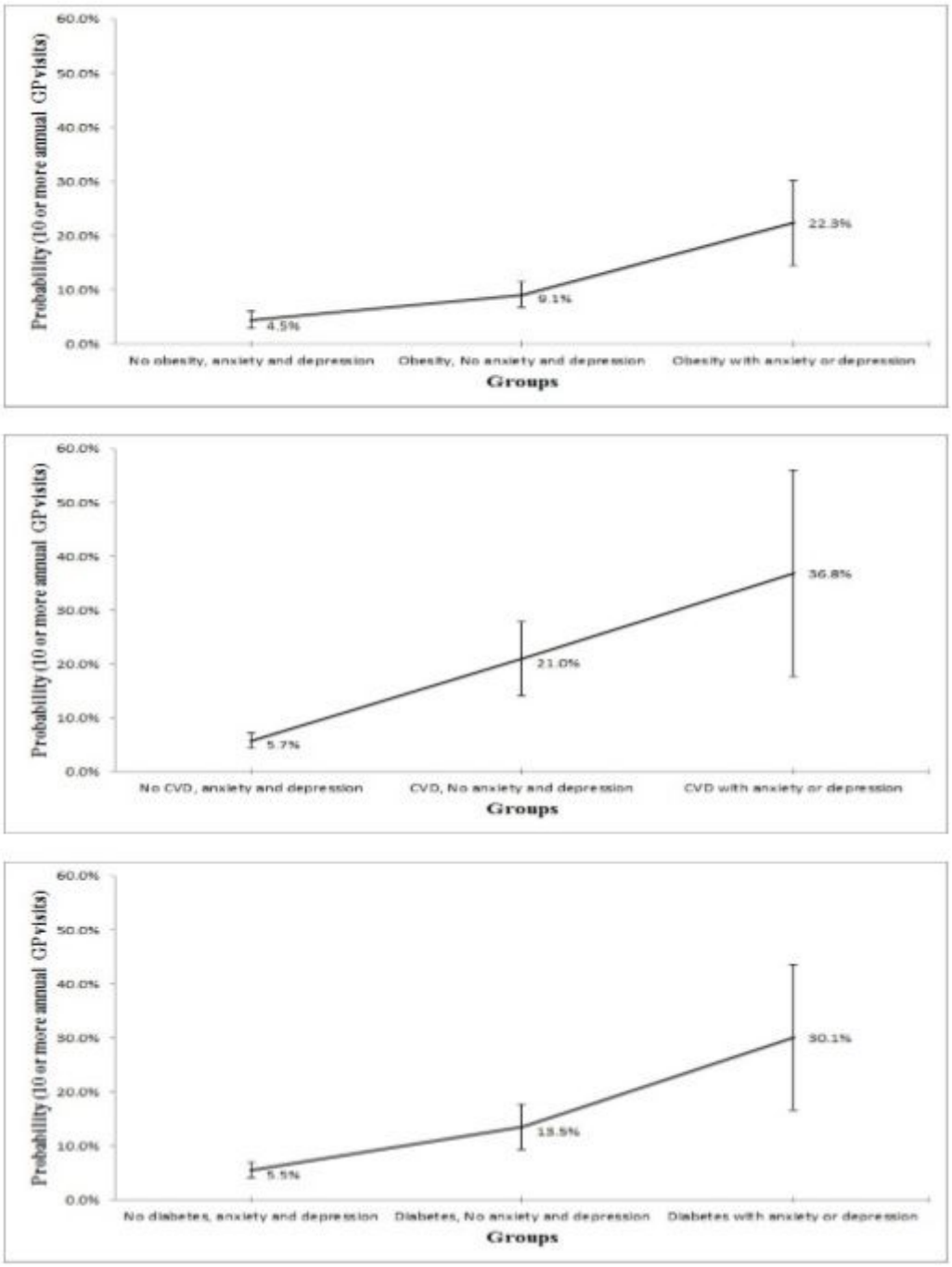


Figure 2

Adjusted predictions of 10 or more annual GP visits with 95% CIs for Conditions (a) Obesity; (b) CVD; and (c) Diabetes.

Supplementary Files

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