

# Associations between Gastro-oesophageal Reflux Disease, Generalised Anxiety Disorder, Major Depressive Episodes, and Healthcare Utilisation: a Community-based Study

ADP Mak, JCY Wu, Y Chan, YK Tse, S Lee

## Abstract

**Objective:** To examine the prevalence and comorbidity of gastro-oesophageal reflux disease (GORD) with generalised anxiety disorder (GAD) and major depressive episodes (MDE) in a general population using DSM-IV, and to evaluate the associations between these conditions and healthcare utilisation.

**Methods:** A random population-based telephone survey was conducted to record frequency of GORD symptoms, symptoms of GAD and MDE based on DSM-IV, and healthcare utilisation.

**Results:** Of 2011 respondents, 4.2% had weekly GORD and 13.9% had monthly GORD, whereas 3.8% reported GAD and 12.4% reported MDE. Those with monthly GORD had higher risk of GAD ( $p = 0.01$ ) and MDE ( $p < 0.001$ ). GORD symptom frequency was independently correlated with MDE and GAD in a dose-response manner. The number of psychiatric diagnoses was independently correlated with GORD. GORD symptom frequency, GAD, and MDE were correlated with consultation frequency. GORD symptom frequency was correlated with high investigation expenditure.

**Conclusion:** GORD had a strong dose-response relationship with GAD and MDE in a Hong Kong population. Excessive healthcare utilisation should alert clinicians to the risk of psychiatric comorbidity.

**Key words:** Anxiety disorders; Depressive disorder, major; Gastroesophageal reflux

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## Introduction

Gastro-oesophageal reflux disease (GORD) is characterised by troublesome reflux symptoms of heartburn and regurgitation as well as complications such as esophagitis.<sup>1</sup> In Western populations, 15% to 25% have been reported to have GORD at least weekly.<sup>2</sup>

Generalised anxiety disorder (GAD) and major depressive episodes (MDE) are the most common mental disorders globally.<sup>3</sup> GORD is often associated with anxiety and depression,<sup>4</sup> with a bidirectional link.<sup>5</sup> However, most

evidence is derived from patient samples.<sup>5</sup> For example, a study reported association between GORD and mental disorders (such as schizophrenia and major depression) in patients,<sup>6</sup> but selection bias may have distorted the association,<sup>7</sup> as only 38% of people with GORD seek care.<sup>8</sup> In addition, studies on psychiatric comorbidity of GORD have failed to measure mental disorders using standardised diagnostic criteria such as the DSM-IV-TR.<sup>9</sup> All population studies on psychiatric comorbidity of GORD used rating scales such as the Hospital Anxiety and Depressive Scale<sup>4,8</sup> instead of diagnostic interviews. These symptom rating scales do not capture the clinically relevant symptoms, symptom duration, and functional impairment required for the DSM-IV<sup>9</sup> diagnoses of GAD or MDE. Therefore, existing community data do not provide adequate evidence on the association of GORD with mental disorders such as GAD and MDE.

Anxiety and depressive symptoms result in increased healthcare utilisation in GORD.<sup>8</sup> Treatment of anxiety and depression may alleviate comorbid gastrointestinal symptoms.<sup>10</sup> It remains uncertain how GORD may interact with specific mental disorders, for which effective interventions exist. We conducted a community survey to evaluate the association between GORD of various symptom frequencies and GAD and MDE. Sociodemographic and diagnostic indicators of healthcare utilisation were also investigated.

## Methods

This study was approved by the Chinese University of Hong Kong research ethics committee. Verbal consent was obtained from each respondent. The Hong Kong Institute of Asia-Pacific Studies of the Chinese University of Hong Kong was commissioned to conduct a telephone survey about 'digestive problems and emotional health' of a random selection of the general population aged 15 to 65 years. Interviews were conducted from 22 April to 13 May 2009. Interviewers were university students with 1 to 3 years of part-time experience in telephone interviews. They were trained on questionnaire administration and skills involved in eliciting symptoms of GORD, GAD, and MDE. Interviews were conducted in Cantonese and took approximately 20 minutes.

Sampling telephone lines should generate a representative sample of households, as >99% of households have a telephone line.<sup>11</sup> Phone calls were made in the evening (6-10 pm) to access the working population.

### Instrument

A 40-item questionnaire was used to record demographics, frequency of GORD symptoms (troublesome reflux symptoms of heartburn and/or regurgitation over the past 3 months) using the Rome III Classification of Dyspepsia module pertaining to the Montreal definition,<sup>1</sup> symptoms of GAD and MDE based on DSM-IV, and healthcare utilisation.

The questionnaire has been used in previous telephone surveys and has reported the 12-month prevalence to be 4.1% for GAD<sup>12</sup> and 8.4% for MDE.<sup>13</sup> Clinical re-appraisal for diagnoses of MDE and GAD using the Structured Clinical Interview for DSM-IV Axis I Disorders yielded good agreement.<sup>14,15</sup> In Hong Kong, the prevalence of Rome III irritable bowel syndrome was reported to be 5.4% and Rome III dyspepsia to be 8%, comparable with overseas estimates.<sup>16,17</sup>

Respondents were also asked "how much did you spend over the past 5 years on investigations for your gastrointestinal problems?" to assess investigation expenditure and "how frequent did you see a doctor for your health problems" to assess frequency of consultations over the past 5 years. Frequent consulting behaviour was arbitrarily defined as more than monthly consultations; high investigation expenditure was defined as  $\geq$ HK\$50 000 over the past 5 years, with both indexes representing unusually high levels of healthcare utilisation.

### Study power

With an overall sample of 2011, a logistic regression of binary response variable of GORD (monthly) [ $n = 254$ , 13.1% GORD (monthly) without GAD] on the binary independent variable of GAD ( $n = 77$ , 3.8%), to achieve 80% power at a significance level of 0.05, would have a minimum detectable odds ratio of 2.23.<sup>18</sup>

## Analysis

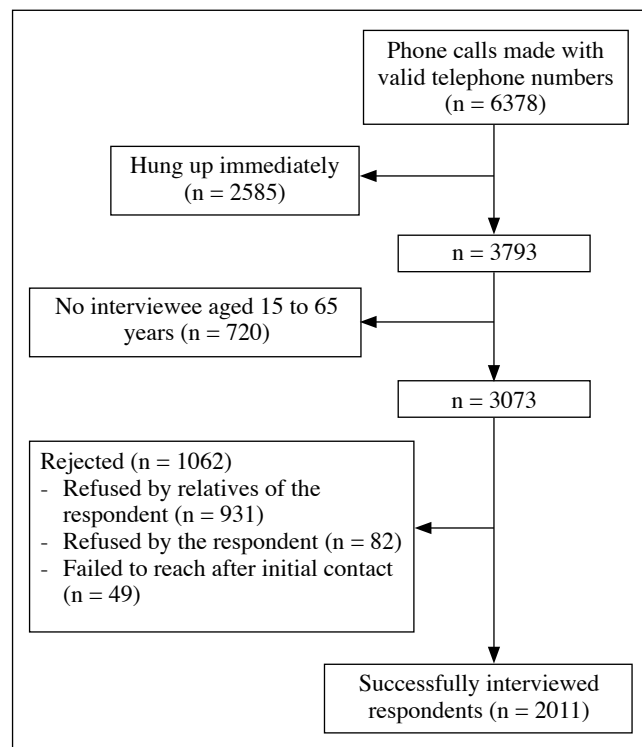
The study sample was weighted according to age and sex distribution of the Hong Kong general population based on the 2008 Census data.<sup>11</sup> The current prevalence of GERD and 12-month prevalence of GAD and MDE were presented as percentages. All variables were put into logistic regression analysis to determine variables that were independent associated with high investigation expenditure (arbitrarily defined as  $\geq$ HK\$50,000 over the past 5 years) and frequent medical consultations (arbitrarily defined as monthly or more). Statistical analysis was performed using SPSS (Windows version 16; SPSS Inc., Chicago [IL], US). All  $p$  values were two-tailed with the significance level at 0.05.

## Results

### Prevalence

Of the 6378 valid home telephone numbers randomly selected, 2585 hung up immediately, 720 had no interviewees aged 15 to 65 years, and 3073 were successful contacts. Of these contacts, 1062 were turned down by relatives of the respondent ( $n = 931$ ) or the respondent ( $n = 82$ ) or contact could not be made to the respondent after initial contact ( $n = 49$ ) [Figure]. The final sample comprised 2011 respondents (937 men and 1074 women), with a participation rate of 65.4%, which has been reported in a study.<sup>19</sup> The age distribution of respondents is comparable to that of the general population in Census 2008 (Table 1).<sup>11</sup>

Of the 2011 respondents over the past 3 months, 4.2% and 13.9% reported at least weekly and monthly GORD



**Figure.** Flow diagram showing numbers of respondents and enrolment criteria.

**Table 1. Sociodemographic data of respondents and Census 2008 data<sup>11</sup>.**

	%	
	Total respondents (n = 2011)	General population in Census 2008 <sup>11</sup>
Gender		
Male	46.6	47.2
Female	53.4	52.8
Age, y		
15-24	16.9	17.0
25-34	20.4	20.4
35-44	22.6	22.6
45-54	24.3	24.2
55-65	15.8	15.8
Education		
Primary or below	11.2	-
Secondary	45.0	-
Pre-college	10.3	-
College or above	33.2	-
Missing	0.3	-
Work status		
Employed	60.3	-
Unemployed	6.4	-
Retired	7.0	-
Student	12.0	-
Homemaker	13.8	-
Missing	0.5	-
Marital status		
Single	38.2	-
Married/living together	59.2	-
Previously married	2.1	-
Missing	0.5	-
Income level, HK\$		
≤10000	19.3	-
10001-30000	43.2	-
30001-60000	20.7	-
>60000	9.5	-
Missing	7.2	-

symptoms, respectively, whereas 3.6% and 12.8% reported at least weekly and monthly regurgitation, respectively; 1.6% and 4.1% reported at least weekly and monthly heartburn, respectively (Table 2). The 12-month prevalence of GAD has previously been reported to be 3.8%, and that of MDE to be 12.4%.<sup>16</sup>

### Comorbidities of GORD

GORD was associated with both GAD and MDE in terms of symptoms and disorder level. MDE was reported more frequently by respondents with regurgitation than by those without (21% vs 10.2%,  $p < 0.001$ ) and by those with heartburn than by those without (31% vs 11.1%,  $p < 0.001$ ).

**Table 2. Prevalence of gastro-oesophageal reflux disease symptoms (regurgitation and/or heartburn) in 2011 respondents.**

Gastro-oesophageal reflux disease symptoms	Prevalence, %
Weekly	
Regurgitation and/or heartburn	4.2
Regurgitation	3.6
Heartburn	1.6
Monthly	
Regurgitation and/or heartburn	13.9
Regurgitation	12.8
Heartburn	4.1

GAD was reported more frequently by respondents with regurgitation than by those without (7.6% vs 2.9%,  $p < 0.001$ ) and by those with heartburn than by those without (14.7% vs 3.1%,  $p < 0.001$ ).

On univariate analysis, respondents with either MDE or GAD were more likely to report at least monthly GORD symptoms, and respondents with at least monthly GORD symptoms were more likely to report either MDE or GAD. On multivariate analysis, both GAD and MDE were independently associated with at least monthly GORD symptoms (Table 3).

### Association with concomitant MDE and GAD

More respondents with both MDE and GAD reported GORD than did those with either or no psychiatric diagnosis (32.1% vs 27.4% vs 11.7%,  $p < 0.001$ ). On multivariate analysis, respondents with at least monthly GORD symptoms more commonly reported having one or both psychiatric diagnoses, with odds ratios increasing with the number of psychiatric diagnoses (Table 4).

### GORD frequency and psychiatric comorbidity

Odds ratios for having GAD and/or MDE increased with GORD frequency in a dose-response manner, even after adjusting for all sociodemographic variables (Table 4).

### Frequent medical consultations

Approximately 25% of respondents with at least monthly GORD symptoms reported medical consultations at least once per month over the past year, compared with those without the condition (12.4%). In addition, the proportion of respondents who reported more frequent consultations increased with GORD symptom frequency. Respondents with GAD or MDE also reported more frequent consultations, and the likelihood increased in respondents with both diagnoses. On multivariate analysis, frequent medical consultations were positively associated with at least monthly GORD symptoms, GAD, MDE, both psychiatric diagnoses, GORD frequency, and female sex, whereas frequent medical consultations were negatively associated with work status of respondents (Table 3).

**Table 3. Sociodemographic and psychiatric comorbidity variables in respondents with at least monthly GORD, respondents with frequent consultations, and respondents with high investigation expenditure.\***

	Respondents with at least monthly GORD (n = 280)				
	No. (%)	Crude OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Gender					
Male (n = 937)	135 (14.4)	1		1	
Female (n = 1074)	145 (13.5)	0.93 (0.72-1.20)	0.57	0.87 (0.65-1.18)	0.38
Age, y					0.11
15-24 (n = 341)	50 (14.7)	1		1	
25-34 (n = 411)	47 (11.4)	0.74 (0.48-1.14)	0.17	0.53 (0.27-1.02)	0.06
35-44 (n = 454)	54 (11.9)	0.78 (0.52-1.18)	0.24	0.45 (0.22-0.92)	0.03
45-54 (n = 488)	71 (14.5)	0.98 (0.66-1.45)	0.93	0.55 (0.27-1.13)	0.10
55-65 (n = 317)	59 (18.6)	1.31 (0.87-1.99)	0.19	0.73 (0.33-1.61)	0.44
Education					0.83
Primary or below (n = 226)	35 (15.6)	1.31 (0.85-2.00)	0.22	0.78 (0.44-1.36)	0.38
Secondary (n = 905)	132 (14.6)	1.21 (0.90-1.62)	0.21	0.93 (0.65-1.32)	0.69
Pre-college (n = 206)	27 (13.1)	1.08 (0.68-1.72)	0.75	0.88 (0.53-1.46)	0.61
College or above (n = 667)	83 (12.4)	1		1	
No response (n = 7)	-	-	-	-	-
Work status					0.56
Employed (n = 1212)	156 (12.9)	0.94 (0.64-1.38)	0.76	1.00 (0.63-1.59)	0.99
Unemployed (n = 129)	25 (19.4)	1.50 (0.86-2.62)	0.15	1.44 (0.76-2.70)	0.26
Retired (n = 141)	23 (16.4)	1.27 (0.72-2.23)	0.41	1.04 (0.52-2.07)	0.91
Student (n = 241)	33 (13.7)	1.03 (0.62-1.70)	0.92	0.74 (0.33-1.67)	0.47
Homemaker (n = 278)	38 (13.6)	1		1	
No response (n = 10)	-	-	-	-	-
Marital status					0.06
Single (n = 769)	92 (12.0)	1		1	
Married/living together (n = 1190)	177 (14.9)	1.28 (0.98-1.68)	0.07	1.68 (1.10-2.58)	0.02
Previously married (n = 43)	8 (16.6)	1.58 (0.70-3.57)	0.27	1.61 (0.65-4.03)	0.31
No response (n = 9)	-	-	-	-	-
Income level, HK\$					0.09
≤10000 (n = 389)	57 (14.7)	1.58 (0.91-2.74)	0.11	1.37 (0.73-2.56)	0.33
10001-30000 (n = 869)	134 (15.4)	1.67 (1.002-2.78)	0.05	1.65 (0.95-2.88)	0.08
30001-60000 (n = 416)	46 (11.1)	1.14 (0.65-2.01)	0.65	1.07 (0.60-1.92)	0.82
>60000 (n = 192)	19 (9.9)	1		1	
No response (n = 144)	-	-	-	-	-
GERD					
At least monthly (n = 280)	-	-	-	-	-
Less than monthly (n = 1731)	-	-	-	-	-
GERD frequency					
Less than monthly (n = 1731)	-	-	-	-	-
Monthly to less than weekly (n = 196)	-	-	-	-	-
Weekly or more (n = 84)	-	-	-	-	-
Psychiatric diagnoses (GAD and/or MDE)					
With GAD (n = 77)	26 (33.8)	3.38 (2.07-5.53)	<0.001	2.06 (1.16-3.68)	0.01
Without GAD (n = 1934)	254 (13.1)	1		1	
With MDE (n = 249)	69 (27.7)	2.80 (2.06-3.83)	<0.001	2.71 (1.88-3.90)	<0.001
Without MDE (n = 1762)	211 (12.0)	1		1	
No. of psychiatric diagnoses					<0.001
None (n = 1739)	203 (11.7)	1		1	
One (n = 219)	60 (27.4)	2.84 (2.04-3.96)	<0.001	3.09 (2.16-4.41)	<0.001
Two (n = 53)	17 (32.1)	3.70 (2.05-6.68)	<0.001	4.40 (2.31-8.36)	<0.001

Abbreviations: GAD = generalised anxiety disorder; GORD = gastro-oesophageal reflux disease; MDE = major depressive episode  
 \* % is equal to the number of respondents in each row corresponding to category specified in column head divided by the total number of respondents in each row times 100. All group sizes are weighted according to age and sex distribution of the Hong Kong general population based on the 2008 Census data and do not represent raw values

Respondents with frequent consultations (n = 287 )					Respondents with high investigation expenditure (n = 30)				
No. (%)	Crude OR (95% CI)	P value	Adjusted OR (95% CI)	P value	No. (%)	Crude OR (95% CI)	P value	Adjusted OR (95% CI)	P value
102 (10.9)	1		1		15 (1.6)	1		1	
185 (17.3)	1.72 (1.32-2.23)	<0.001	1.67 (1.24-2.26)	0.001	15 (1.6)	0.89 (0.43-1.84)	0.74	0.83 (0.34-1.99)	0.67
				0.11					0.68
29 (8.5)	1		1		1 (0.3)	1		1	
65 (15.8)	0.39 (0.24-0.63)	<0.001	0.53 (0.27-1.02)	0.06	5 (1.2)	5.50 (0.45-67.17)	0.18	9.52 (0.04-2558.97)	0.43
68 (15.0)	0.79 (0.54-1.16)	0.23	0.45 (0.22-0.92)	0.03	8 (1.8)	8.34 (0.73-95.41)	0.09	10.80 (0.04-3229.93)	0.41
66 (13.6)	0.74 (0.50-1.08)	0.12	0.55 (0.27-1.13)	0.10	12 (2.5)	11.68 (1.06-129.23)	0.05	14.78 (0.05-4372.25)	0.35
60 (19.0)	0.66 (0.45-0.97)	0.03	0.73 (0.33-1.61)	0.44	4 (1.3)	6.72 (0.54-83.06)	0.14	6.16 (0.02-2068.87)	0.54
				0.21			0.85		0.24
44 (19.6)	1.49 (1.00-2.20)	0.051	1.19 (0.69-2.06)	0.53	4 (1.8)	1.28 (0.42-3.91)	0.67	3.92 (0.83-18.41)	0.08
126 (14.0)	0.98 (0.74-1.31)	0.89	0.92 (0.64-1.31)	0.64	12 (1.3)	0.84 (0.37-1.94)	0.69	1.22 (0.43-3.46)	0.71
22 (10.6)	0.71 (0.43-1.16)	0.17	0.59 (0.33-1.05)	0.07	2 (1.0)	0.69 (0.16-2.92)	0.61	0.61 (0.10-3.89)	0.60
95 (14.3)	1		1		10 (1.5)	1	-	1	-
-	-	-	-	-	-	-	-	-	-
				0.02			0.64		0.92
180 (14.9)	0.76 (0.54-1.07)	0.12	1.07 (0.70-1.64)	0.74	21 (1.7)	1.47 (0.45-4.83)	0.52	1.07 (0.70-1.64)	0.74
18 (14.1)	0.72 (0.41-12.9)	0.28	1.02 (0.53-1.95)	0.95	2 (1.6)	1.45 (0.25-8.25)	0.68	1.02 (0.53-1.95)	0.95
24 (17.1)	0.89 (0.52-1.52)	0.66	1.09 (0.56-2.11)	0.80	3 (2.2)	1.65 (0.32-8.53)	0.55	1.09 (0.56-2.11)	0.80
12 (5.0)	0.23 (0.12-0.45)	<0.001	0.25 (0.10-0.63)	0.05	1 (0.4)	0.25 (0.02-3.34)	0.30	0.25 (0.10-0.63)	0.05
52 (18.8)	1		1		3 (1.1)	1	-	1	-
-	-	-	-	-	-	-	-	-	-
				0.22			0.03		0.22
83 (10.8)	1		1		4 (0.5)	1		1	
194 (16.4)	1.63 (1.24-2.14)	0.001	1.41 (0.95-2.10)	0.09	25 (2.1)	4.02 (1.41-11.51)	0.01	2.22 (0.58-8.51)	0.24
9 (20.9)	2.33 (1.09-4.97)	0.03	1.50 (0.63-3.55)	0.36	0 (0)	0	1	-	1
-	-	-	-	-	-	-	-	-	-
				0.46			0.06		0.04
52 (13.5)	1.07 (0.64-1.78)	0.81	0.87 (0.47-1.59)	0.64	3 (0.8)	0.38 (0.08-1.83)	0.23	0.21 (0.03-1.40)	0.11
124 (14.3)	1.14 (0.72-1.81)	0.59	1.16 (0.69-1.95)	0.56	8 (0.9)	0.50 (0.14-1.74)	0.28	0.41 (0.10-1.74)	0.23
63 (15.1)	1.21 (0.73-2.00)	0.46	1.18 (0.70-1.99)	0.54	11 (2.7)	1.47 (0.45-4.87)	0.53	1.51 (0.43-5.30)	0.52
25 (13.0)	1		1		4 (2.1)	1	-	1	-
-	-	-	-	-	-	-	-	-	-
70 (25.1)	2.32 (1.71-3.15)	<0.001	1.98 (1.41-2.79)	<0.001	10 (3.7)	3.18 (1.46-6.96)	0.004	2.67 (1.07-6.67)	0.04
217 (12.6)	1		1		20 (1.2)	1		1	
				<0.001			<0.001		0.01
217 (12.6)	1		1		20 (1.2)	1		1	
40 (20.5)	1.79 (1.23-2.60)	0.002	1.67 (1.11-2.50)	0.02	3 (1.6)	1.55 (0.49-4.97)	0.46	1.28 (0.33-5.00)	0.72
30 (35.7)	3.87 (2.42-6.18)	<0.001	2.74 (1.61-4.64)	<0.001	6 (7.5)	7.36 (2.91-18.64)	<0.001	5.55 (1.85-16.65)	0.002
28 (36.8)	3.69 (2.27-6.00)	<0.001	1.92 (1.01-3.27)	0.05	4 (5.6)	4.25 (1.42-12.74)	0.01	3.58 (0.92-13.98)	0.07
260 (13.5)	1		1		25 (1.3)	1		1	
75 (30.4)	3.19 (2.35-4.34)	<0.001	2.44 (1.68-3.53)	<0.001	6 (2.5)	1.9 (0.77-4.70)	0.17	1.51 (0.50-4.62)	0.47
212 (12.1)	1		1		23 (1.3)	1		1	
							0.03		0.03
205 (11.8)	1		1		20 (1.2)	1		1	
61 (27.9)	2.90 (2.09-4.03)	<0.001	2.55 (1.76-3.70)	<0.001	8 (3.7)	3.17 (1.38-7.30)	0.01	3.63 (1.41-9.36)	0.01
21 (40.4)	4.95 (2.80-8.78)	<0.001	3.91 (2.05-7.49)	<0.001	1 (2.1)	1.77 (0.23-13.45)	0.58	2.13 (0.26-17.80)	0.49

**Table 4. GORD frequency and prevalence of GAD and MDE.\***

GORD frequency	GAD (n = 77)					MDE (n = 249)				
	No. (%)	OR (95% CI)	P value	Adjusted OR (95% CI)	P value	No. (%)	OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Less than monthly (n = 1731)	51 (2.9)	1		1	0.03	180 (10.4)	1		1	<0.001
Monthly to less than weekly (n = 196)	16 (8.2)	3.01 (1.69-5.34)	<0.001	1.94 (0.97-3.89)	0.06	45 (23)	2.58 (1.79-3.72)	<0.001	2.63 (1.72-4.01)	<0.001
Weekly or more (n = 84)	10 (16.2)	4.29 (2.07-8.88)	<0.001	2.78 (1.16-6.67)	0.02	24 (28.6)	3.37 (2.04-5.56)	<0.001	2.90 (1.59-5.28)	0.001

Abbreviations: GAD = generalised anxiety disorder; GORD = gastro-oesophageal reflux disease; MDE = major depressive episode  
 \* % is equal to the number of respondents in each row corresponding to category specified in column head divided by the total number of respondents in each row times 100. The study sample is weighted according to age and sex distribution of the Hong Kong general population based on the 2008 Census data and do not represent raw values

### High investigation expenditure

Only 1.4% of respondents spent  $\geq$ HK\$50,000 in investigation expenditure over past 5 years, but this proportion was overrepresented in those with at least monthly GORD symptoms (especially those with at least weekly symptoms), GAD, having one (but not both) psychiatric diagnosis, those aged 45 to 54 years, and those married/living together with a partner. On univariate analysis, high investigation expenditure was weakly associated with income. On multivariate analysis, high investigation expenditure was associated with at least monthly GORD symptoms, GORD frequency, income, and work status of respondents (Table 3).

### Discussion

The participation rate of the present study is comparable to previously reported telephone surveys.<sup>15</sup> GORD was found to be strongly associated with GAD and MDE in this random, representative sample using standardised diagnostic criteria. This indicates that the association found in clinical studies is not a consequence of help-seeking bias.

In the present study, GORD was independently associated with MDE and GAD; whereas only symptom scores have been reported previously.<sup>4,8</sup> In particular, a dose-response relationship between GORD and GAD or MDE appeared to be bidirectional. This suggests that mental disorders such as GAD and MDE may have different biological correlates (eg, association with serotonin dysfunction, serotonin transporter genetic associations) than the common experience of stress. The association between the pathologies of brain and oesophagus warrants biological and psychosocial research on the mechanisms linking these mental disorders with GORD. In addition, the dose-response relationship suggests a possible causal relationship between GORD and mental disorders, which should be confirmed by longitudinal studies in representative and well-characterised samples. Moreover, the bidirectionality is consistent with the 'two-way traffic' of the brain-gut axis. Epidemiological evidence has been

found for functional dyspepsia in a population-based cohort study.<sup>20</sup> Chronic psychosocial adversities and psychiatric disorders have been associated with reduced pain threshold for reflux symptoms,<sup>6,21</sup> altered oesophageal motility,<sup>6</sup> and gastric secretion.<sup>22</sup> Individuals with depressive and anxiety disorders may tend to feel burdened by more troublesome reflux symptoms.<sup>23</sup> The dose-response relationship mirrors evidence from the psychosomatic literature that suggests a dose-response relationship between somatic symptom load and psychopathology.<sup>23</sup> Oesophageal acid stimulation has been shown to sensitise the cingulate gyrus and insula to non-painful mechanical stimulations on functional magnetic resonance imaging.<sup>24</sup> However, it remains unclear how GORD increases the risk of mental disorders in addition to the anxiety and depressive disorders caused by distress and functional impairment from GORD symptoms.<sup>25</sup> There may also be common psychosocial aetiological factors, such as chronic experience of life stress that predisposes individuals to anxiety and depressive disorders as well as GORD.<sup>26</sup> This warrants further biopsychosocial research on the bidirectional dynamic in the brain-gut axis in the context of mental disorders.

Our study found unusually high levels of healthcare utilisation. GORD frequency was associated with frequent medical consultations and high investigation expenditure in a dose-response manner. In addition, both GAD and MDE were independently associated with frequent consultations. The lack of correlation between mental disorders and high investigation expenditure could be related to the small proportion of individuals with the extreme level of expenditure arbitrarily selected as a cut-off for the present study. Other possible reasons include more severe occupational impairment from mental disorders that may limit the respondents' ability to pay as well as reduced motivation and pessimistic tendencies in individuals with MDE that may limit help-seeking behaviour.

Our study has several limitations. First, endoscopy was not performed to confirm erosive or non-erosive diseases and study their disparate relationship with mental



disorders. Second, brief telephone surveys were used instead of detailed face-to-face interviews. However, telephone surveys may avoid psychiatric stigma and facilitate disclosure of sensitive information.<sup>27</sup> In particular, Chinese people tend to be inhibited about disclosure of psychological distress.<sup>28</sup> Third, other potentially important factors associated with GORD were not recorded, such as medication use. However, medication use is unlikely to play a major role in this association, as few respondents with mental disorders had access to treatment.<sup>13</sup> Fourth, recall bias and the cross-sectional design limited the study of causality. Prospective illness course studies in the community can better inform causality.<sup>20</sup> However, the bidirectional link suggests a complex relationship between mental disorders and GORD. Last, assessment of 12-month prevalence of GAD and MDE may lead to an optimistic result compared with current prevalence of GORD.

## Conclusion

GORD is strongly associated with MDE and GAD, with substantial effects on healthcare utilisation. Common anxiety and depressive disorders should be routinely screened when assessing GORD, especially in patients with high healthcare utilisation. Clinicians treating patients with GORD and comorbid GAD or MDE should consider help-seeking behaviour as an important part of the illness experience. Both GAD and MDE respond to psychobehavioural and/or pharmacological therapies. A holistic approach combining gastroenterologists and mental health professionals is recommended.

## Disclosure

The authors have no conflicts of interests to disclose.

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