

Depression and physical co morbidity in primary care- asthma and coronary heart disease

Prof Andre Tylee

Section of Primary Care Mental Health,
Health Services and Population Research
Dept, Institute of Psychiatry, Kings College
London.

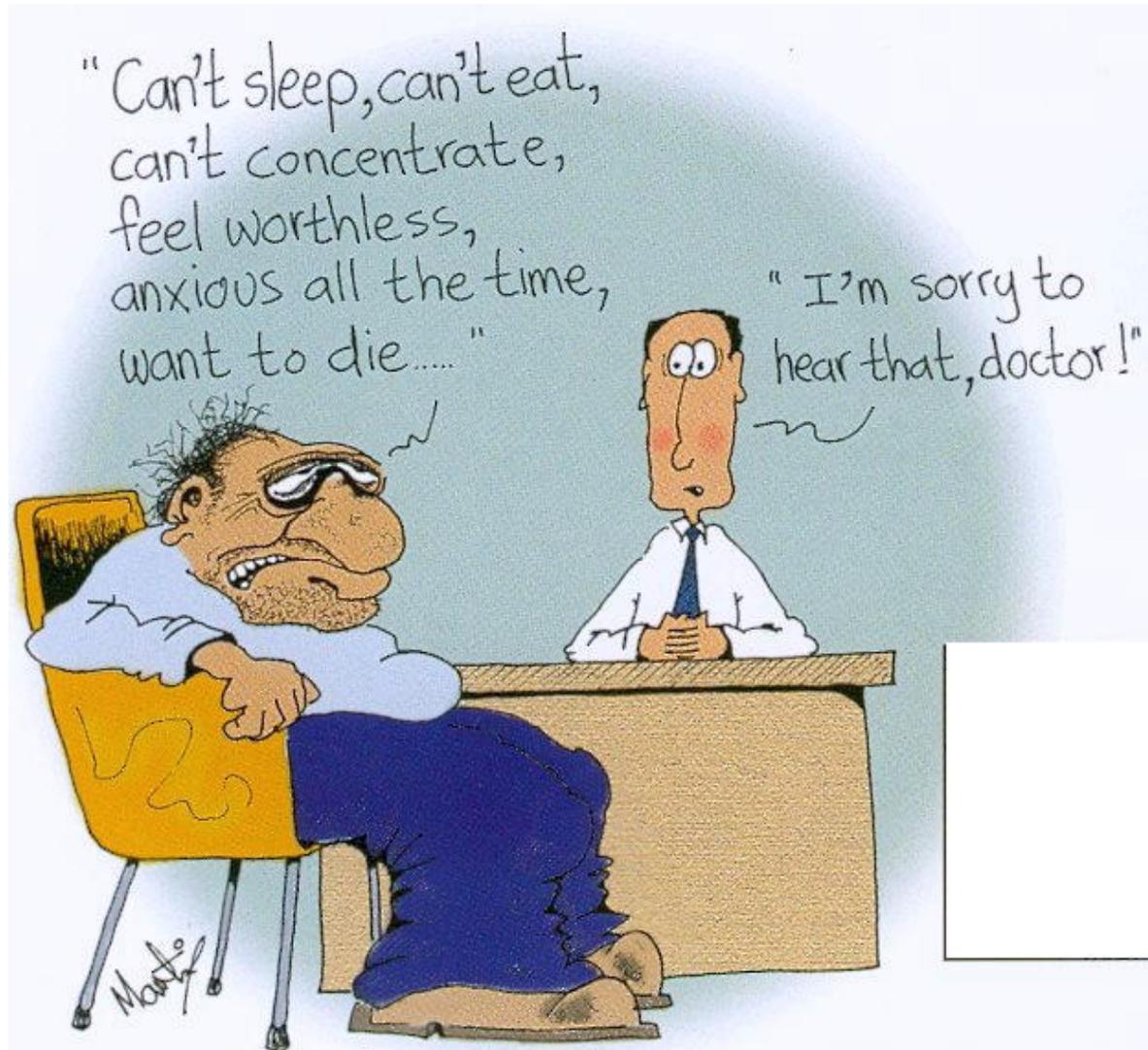
**Institute of
Psychiatry**

at The Maudsley

KING'S
College
LONDON
Founded 1829

University of London

No-one is immune



Depression in Primary Care Patients with Asthma

- Professor Andre Tylee (KCL) Principal Investigator
- Dr Paul Walters (KCL)
- Mr Peter Schofield (KCL)
- Dr Louise Howard (KCL)
- Dr Mark Ashworth (KCL)
- Dr Richard Hubbard (Uni of Nottingham)

Funded by grants from:

- SLAM/IOP NIHR Biomedical Research Centre for Mental Health
- Medical Research Council

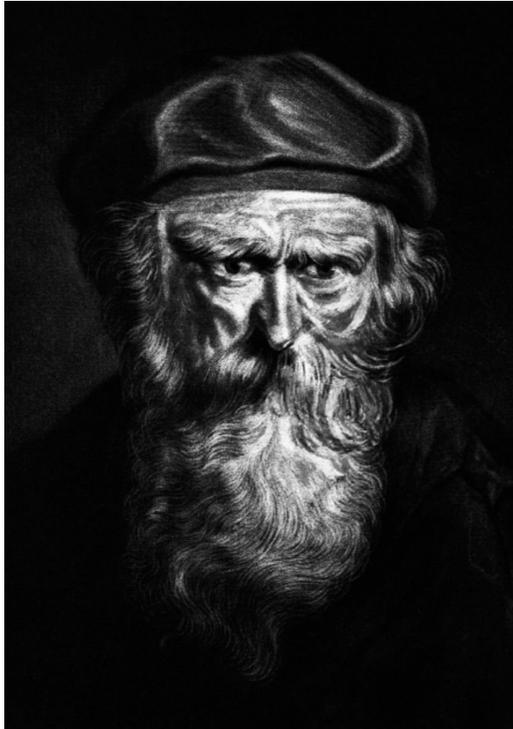
**Institute of
Psychiatry**

at The Maudsley

KING'S
College
LONDON
Founded 1829

University of London

Background



Moses
Maimonides

*'Treatise on
Asthma'* c.1300

The 'Holy' Seven Psychosomatic Illnesses

Asthma	Rheumatoid Arthritis
Ulcerative Colitis	Essential Hypertension
Neurodermatitis	Thyrotoxicosis
Peptic Ulcer	<i>(After F. Alexander c.1930)</i>

Background

Table 2
Frequency of psychiatric disorders in asthmatic patients ($n=86$)

	Time frame ^a	<i>n</i>	%
Panic disorder/agoraphobia spectrum disorders	Current	35	40.7
Panic disorder with or without agoraphobia	Current	12	13.9
Agoraphobia without panic disorder	Current	23	26.8
Social anxiety disorder	Current	8	9.3
Generalized anxiety disorder	Current	21	24.4
Major depressive episode	Past 2 weeks	29	33.7
Dysthymia	Past 2 years	1	1.1
Manic episode	Lifetime and current	4	4.6
Alcohol abuse	Current	1	1.1
Psychosis	Lifetime and current	1	1.1

^a Current is defined as 'in the past month' for all diagnoses except generalized anxiety disorder, which has a 6-month time frame and alcohol abuse/dependence for which a 12-month time frame is allowed.

Background

Table 2
Prevalence (%) of depressive disorders among persons with asthma versus persons without asthma, and age-adjusted and sex-adjusted odds of association

Country	Major depression			Dysthymia		
	Without asthma (%)	With asthma (%)	OR (CI) (adjusted for age and sex)	Without asthma (%)	With asthma (%)	OR (CI) (adjusted for age and sex)
Colombia	5.7	19.7	3.8 (1.8, 8.3)*	0.9	6.7	7.5 (1.6, 34.7)*
Mexico	4.1	5.0	1.2 (0.4, 3.0)	0.9	0.7	0.7 (0.1, 3.5)
United States	7.9	11.3	1.4 (1.1, 1.7)*	2.1	3.7	1.7 (1.1, 2.6)*
Japan	2.2	2.8	1.2 (0.3, 4.3)	0.8	0.6	0.9 (0.1, 7.1)
Beijing	2.3	4.0	2.5 (0.8, 8.1)	0.3	1.3	2.8 (0.3, 26.9)
Shanghai	1.7	2.2	1.4 (0.2, 7.8)	0.4	0.0	–
New Zealand	6.0	9.5	1.5 (1.2, 1.8)*	1.7	2.6	1.5 (1.0, 2.1)*
Belgium	5.5	6.5	1.2 (0.4, 3.2)	1.4	0.3	0.2 (0.0, 2.2)
France	5.8	9.3	1.5 (0.7, 3.2)	1.5	3.2	2.6 (0.7, 9.9)
Germany	2.9	5.6	2.1 (0.5, 9.4)	0.8	4.3	5.4 (0.8, 37.3)
Italy	3.0	5.9	2.2 (1.1, 4.4)*	1.0	1.6	1.6 (0.4, 5.9)
The Netherlands	5.1	7.2	1.4 (0.6, 3.5)	1.7	2.6	1.6 (0.6, 4.4)
Spain	3.8	8.8	2.7 (1.6, 4.5)*	1.3	2.7	2.5 (1.1, 6.0)*
Ukraine	9.2	25.5	2.7 (1.4, 5.2)*	3.9	16.7	3.6 (1.5, 8.6)*
Lebanon	1.8	3.8	–	0.7	0.0	–
Nigeria	1.1	8.8	–	0.2	0.0	–
Israel	5.9	8.1	1.4 (0.9, 2.1)	1.2	1.4	1.1 (0.5, 2.7)
South Africa	4.6	9.5	2.1 (1.1, 4.0)*	0.1	0.0	–
→ Pooled OR	–	–	1.6 (1.4, 1.8)*	–	–	1.7 (1.4, 2.1)*

OR is not listed and the percentage of those with asthma is shown as 0.0 if fewer than 25 respondents have asthma or if the cross-classification of mental disorder and asthma is null.

* $P < .05$.

Background

Table 2. Mental Disorders (Weighted Percentages) Among 4181 Adults in the Community (Aged 18-65, GHS-MHS) With and Without Asthma*

Mental Disorders (DSM-IV)	Past 4 Weeks						Lifetime							
	No Asthma (n = 4074)		Nonsevere Asthma (n = 52)		Severe Asthma (n = 55)		No Asthma (n = 3945)		Nonsevere Asthma (n = 143)		Severe Asthma (n = 93)			
	Weighted %	OR†	95% CI	Weighted %	OR	95% CI	Weighted %	OR	95% CI	Weighted %	OR	95% CI		
Any affective disorder	6.1	2.42‡	1.03-5.72	13.6	2.03	0.89-4.69	12.5	18.3	1.44	0.94-2.19	23.0	1.21	0.75-1.98	
Unipolar	5.5	2.41	0.97-6.04	12.2	1.72	0.72-4.15	10.0	17.0	1.48	0.96-2.29	18.1	0.97	0.59-1.62	
Bipolar	0.5	2.31	0.30-17.82	1.4	4.75	0.65-34.67	2.5	0.9	1.37	0.41-4.50	4.9	5.64‡	1.95-16.35	
Any anxiety disorder§	8.7	1.56	0.70-3.46	14.1	2.65‡	1.35-5.18	21.0	15.1	1.51‡	1.00-2.32	28.8	2.09‡	1.30-3.36	
Panic disorder	1.1	0.97	0.13-7.26	1.1	4.61‡	1.09-19.40	4.9	3.7	0.88	0.37-2.08	10.0	2.61‡	1.29-5.25	
Social phobia	1.2	NA	NA	NA	3.6	2.81	0.67-11.91	1.9	1.9	0.94	0.29-3.07	6.3	3.28‡	1.42-7.59
Specific phobia	4.5	1.67	0.61-4.58	8.2	4.78‡	2.35-4.05	18.9	7.2	1.51	0.88-2.58	19.7	2.93‡	1.71-5.00	
Agoraphobia without panic	1.0	1.82	0.25-13.50	2.1	1.67	0.22-12.52	1.9	1.5	2.06	0.79-5.33	2.9	1.71	0.56-5.21	
Anxiety disorder NOS	1.3	2.65	0.77-9.18	3.5	1.7	0.28-5.65	1.7	3.3	2.08‡	1.03-4.23	3.0	0.83	0.32-2.18	
Generalized anxiety disorder	1.1	1.85	0.24-14.61	2.0	3.14	0.67-14.70	4.0	1.4	1.21	0.34-4.32	7.6	5.51‡	2.29-13.22	
Panic attacks	1.8	2.39	0.81-7.07	4.4	4.12‡	1.32-12.80	7.5	7.5	1.41	0.83-2.40	20.0	2.84‡	1.66-4.89	
Any substance use disorder	2.8	1.89	0.53-6.76	5.1	3.08	0.84-11.23	6.7	9.8	1.58	0.91-2.75	8.2	0.98	0.43-2.27	
Any somatoform disorder	7.3	2.07	0.91-4.69	14.5	1.1	0.43-2.81	8.7	15.8	1.70‡	1.14-2.53	21.7	1.34	0.78-2.31	
Any of the above (severe)¶	12.2	2.17‡	1.10-4.28	24.1	1.63	0.84-3.18	19.5	21.7	1.58‡	1.07-2.33	32.9	1.64‡	1.03-2.61	

Background

Table 2

Rates and adjusted odds ratios of mental disorders and suicidal ideation in AIM patients with and without asthma (n = 998)

	Asthma N=176 %	No asthma N=822 %	P-value from chi-square test, df=1	AOR* (95% CI)	AOR** (95% CI)
Mental disorders					
Major depression	20.5	18.6	p=.6	1.0 (.7, 1.5)	.6 (.4, 1.1)
Panic attacks	26.1	14.4	p<.0001	1.8† (1.2, 2.7)	1.7† (1.1, 2.6)
Generalized anxiety disorder	19.9	13.7	p=.046	1.4 (.9, 2.2)	1.3 (.8, 2.3)
Alcohol use disorder	8.0	6.4	p=.5	1.5 (.8, 2.9)	1.3 (.7, 2.6)
Drug use disorder	5.1	2.1	p=.03	2.7† (1.1, 6.5)	1.8 (.7, 4.8)
Suicidal ideation	12.6	6.0	p=.003	2.0† (1.2, 3.5)	1.9† (1.03, 3.4)

* AOR=adjusted odds ratio. Adjusted for age, gender, race, marital status, and education; ** CI=confidence interval. Adjusted for age, gender, race, marital status, education, comorbid mental disorders and suicidal ideation. † p<.05.

Renee RD *et al*; Gen Hosp Psych 2003

Background

Table 3 Multivariate associations between antidepressant prescribing volume and six predictor variables^a

Predictor variable	Adjusted regression coefficient B	(95% CI)	Standardised adjusted regression coefficient, β
Index of Multiple Deprivation score	13.92	12.75 to 15.10	0.24***
Proportion of patients from a Black ethnic group	-34.44	-37.15 to -31.73	-0.24***
Asthma ^b	118.49	107.11 to 129.67	0.20***
Proportion of patients from an Asian ethnic background	-12.66	-13.90 to -11.42	-0.19***
Epilepsy ^b	755.45	668.52 to 842.36	0.17***
COPD ^b	183.94	159.65 to 208.22	0.16***

COPD, chronic obstructive pulmonary disease.
 a. This model explains 43.5% of the variation. Model containing all the predictors from the univariate analysis explains 49.0% of the variation in the volume of antidepressants prescribed.
 b. Unadjusted prevalence.
 *** $P < 0.001$.

Walters P, Ashworth M and Tylee A
 BJPsych 2008;**193**.1-5

Aims

To determine:

- a) the incidence of depression in primary care patients with asthma
- b) the incidence rate ratio (IRR) of depression in this population compared to depression in the general primary care population without asthma.

Hypotheses

We hypothesised that

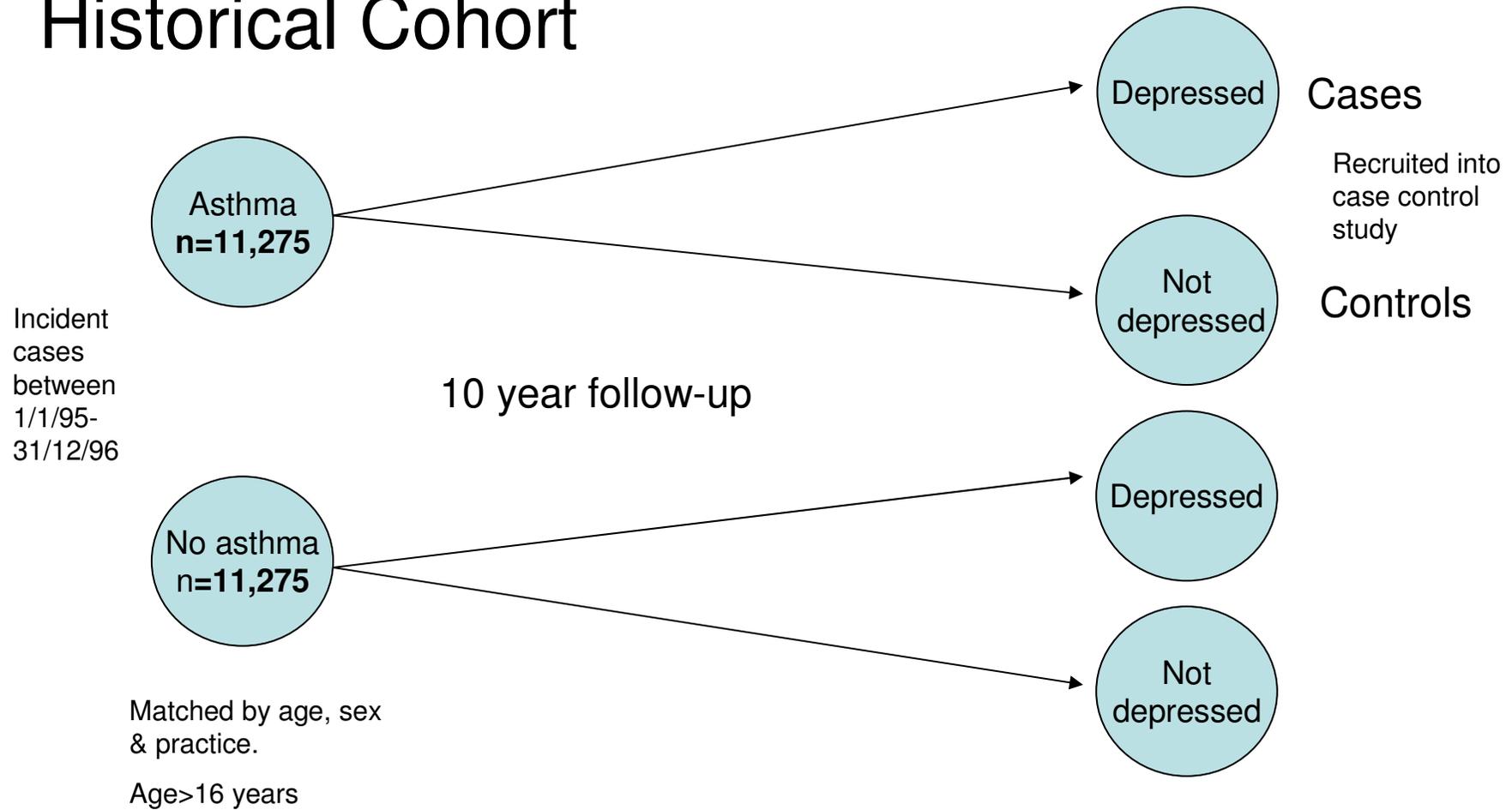
- primary care patients with asthma would have an increased incidence of depression compared with primary care patients without asthma.
- primary care patients with asthma and depression would have a higher age and sex standardized mortality rate compared with primary care patients with asthma but no depression.

Method

- A historical cohort study and nested case control study using data derived from the General Practice Research Database.

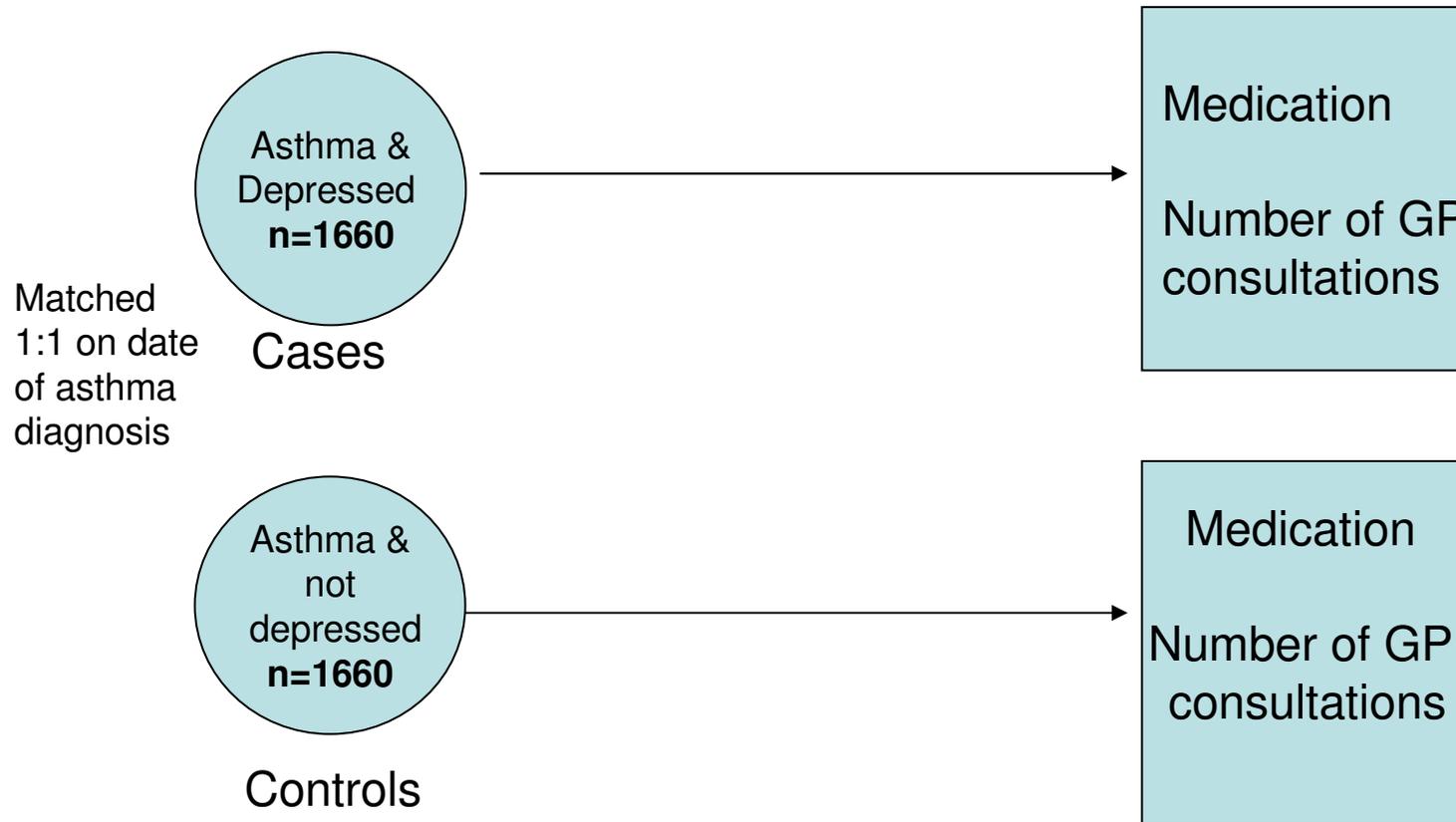
Method

Historical Cohort



Method

Nested Case-Control Study



Results-cohort study

	Asthma	No Asthma	Total
n	11275	11275	22550
Person years of follow-up	78096	98229	
Number of new cases of depression over study period	1752	1353	3105
IR per 1000 pyrs	22.4	13.8	
Age-, Sex-, Practice-adjusted Incident Rate Ratio	1.63 (95% CI 1.52-1.75)		
IRR after adjusting for chronic illnesses and smoking	1.58 (95% CI 1.47-1.70)		

Results- Case-control

	Asthma Depression	Asthma	<i>p-value</i>
Mean (sd) age in years	46.1 (18.7)	49.6 (18.5)	p<0.01
GP visits: Mean (sd)	8.3 (7.1)	5.3 (5.7)	p<0.01
Any anti-asthma medication in year before study (%)	51.8	48.2	p<0.01
β2-Agonists (%)	52.4	47.6	p=0.29
Inhaled corticosteroids (%)	48.8	51.2	p=0.35
Corticosteroids (%)	57.4	42.6	p<0.01
Crude OR for depression in women compared to men	2.09 (95% CI 1.93-2.24)		

Pearson's correlation coefficient (r) for asthma severity and number of GP visits = 0.3

Age- and Sex-Standardised Mortality Ratio = 1.87 (95%CI 1.54-2.27)

Results- Case-control

Adjusted Odds ratios (OR) for depression in primary care patients with asthma

	Adjusted OR	<i>p</i> -value	95% confidence interval
<i>GP visits in year prior to study inclusion</i> (cases n=1355, controls n=1647):			
<5 visits	1		
5-9 visits	1.91*	<0.001	1.57-2.31
10-19 visits	3.35*	<0.001	2.62-4.28
≥ 20 visits	4.70*	<0.001	3.32-6.65
Per visit	1.09*	<0.001	1.07-1.11
<i>Asthma severity</i> (cases n=1660, controls n=1660):			
No medication	1		
β2-Agonists	0.83**	0.192	0.64-1.09
Inhaled corticosteroids	0.81**	0.056	0.66-1.01
Oral corticosteroids	0.88**	0.372	0.67-1.16

* Adjusted for age, sex and severity (type of treatment in the year prior to inclusion in the study)

** Adjusted for age, sex and number of GP visits in year prior to inclusion in study

Limitations

- Limitations of the GPRD (e.g. coding)
 - No studies have examined the validity of GPRD diagnosis of depression
- Sensitivity analyses suggest that effects of misclassification on our estimates are minimal.
- Severity of asthma was not measured directly
- Residual confounding by socio-economic status could be a problem in the case-control study

Discussion

- Statistically significant association between a diagnosis of asthma and depression in primary care population.
- Important as asthma one of the commonest chronic illnesses in primary care.
- The reason for the association is unclear.
- Depression does not appear to be associated with our proxy measure for asthma severity

Discussion Continued

- Corticosteroid use does not appear to be the cause of the increased rate of depression
- Frequent attendance at GP practices is associated with a diagnosis of depression (?extra consultations for depression)
- This is unlikely to be due to a diagnostic bias as the correlation between asthma proxy severity and GP consultations is low ($r = 0.3$)

**Institute of
Psychiatry**

at The Maudsley

KING'S
College
LONDON
Founded 1829

University of London

Depression in Primary Care Patients with coronary heart disease (UPBEAT-UK)

Section of Primary Care Mental Health
Institute of Psychiatry

Depression in Primary Care Patients with coronary heart disease (UPBEAT-UK)

Professor Andre Tylee Principal Investigator

Dr Paul Walters Programme Coordinator

Professor Anthony Mann, Dr Paul McCrone, Dr Joanna Murray, Dr Diana Rose Dr Morven Leese, Dr June Brown, Dr John Chambers, Prof John Weinman, Prof Gill Rowlands, Dr Mark Ashworth

Dr Elizabeth Barley, Rosemary Simmonds, Alison Smith, Zoe Fortune, Anita Mehay, Julie Smith, Rachel Phillips

Funded by:

- NIHR 5 year Programme Grant
- NIHR Research Methods Fellowship



Depression and heart disease

Whooley et al JAMA 2008;300;20;2379-2388

- Depression is a risk factor for;
 - Development of cardiovascular disease in healthy patients
 - Recurrent events in patients with cardiovascular disease
 - Adverse outcomes after coronary bypass graft surgery

Depression predicts cardiac events in patients with coronary artery disease

Carney RM, Rich MW, Freedland KE et al Psychosomatic Medicine 1988; 50;6;627-633

- 52 patients at cardiac catheterisation
- 9 had MDD prior to catheterisation
- At 1 year, MDD was the best predictor of MI, angiography, coronary artery bypass grafting and death (adjusted for CAD severity, LVEF and smoking)

Depression post MI predicts death

Frasure-Smith N, Lesperance F and Talajic M JAMA 1993; 270;(15);1819-1825

Frasure Smith N, Lesperance F and Talajic M Circulation 1995; 91; 999-1005

- Depression post MI was a significant predictor of death at 6 months;
 - HR **5.74** (95%CI 4.61-6.87 p = 0.0006)
 - HR (adjusted for LV dysfunction and previous MI) **4.29** (95% CI 3.14-5.44 p = 0.013)
- Depression post MI was a significant predictor of death at 18 months
 - OR (adjusted for previous MI, Killip Class, premature ventricular contractions >10/hr) **6.64** (95% CI 1.76-25.09 p = 0.0026)
 - If Depression + premature ventricular contraction >10/hr...OR **29.1** (95% CI 6.97-122.07 p = 0.00001)
 - ??arrhythmic mechanism

Candidate mechanisms

Whooley et al JAMA 2008;300;20;2379-2388

- Smoking, poor diet (e.g. low omega-3 fatty acids) and lack of exercise or low physical activity
- Poor adherence to medication and antidepressant toxicity
- Worse underlying cardiac disease severity in studies
- Lower heart rate variability and greater catecholamine levels
- Enhanced HPA axis activity
- Increased serotonin and platelet activation
- Inflammatory processes (assoc with CRP, IL-1, IL-6)

Possible mechanisms

- Poor compliance with lifestyle changes and medication especially physical inactivity (Heart and Soul Study)*
 - HR 1.50 (95% CI 1.16-1.95 p = 0.02)
 - HR 1.31 (95%CI 1.00-1.71 p = 0.04)(adjusted for co morbidity, disease severity, depression symptoms
 - HR 1.24 (95% CI 0.94-1.63 p = 0.12)(adjusted for above plus potential biological mediators e.g. CRP)
 - HR 1.05 (95%CI 0.79-1.40 p = 0.75) (adjusted for above plus potential behavioural mediators including physical inactivity).
- *Whooley MA et al JAMA 2008; **300**;20;2379-2388.

UPBEAT NIHR Programme

Study 1. Cohort/case control

- Prevalence, incidence and risk factors for depression in patients on GP CHD registers
- Course, prognosis and current management of CHD/depression
- Effect of co-morbid depression on mortality, symptom severity, quality of life, disability, pain, service use, service costs and lost employment costs

UPBEAT- sub-studies

- **Study 2.** CHD patients' perspectives on distress, depression, service needs and treatment options
- **Study 3.** GP and practice nurse views on distress, depression, service needs and treatment options
- **Study 4.** RCT of intervention for patients with CHD/depression in primary care
- Extra study. Inflammatory factors and DNA

UPBEAT-Progress

- **Cohort study:** On target to recruit 800 patients into cohort study by end 2009.
- **Qualitative study of patients:** patient interviews completed and analysed.
- **Qualitative study of primary care professionals:** interviews with GPs and practice nurses completed and analysed.

Demographics

	<i>n</i>	<i>Mean</i>	<i>SD</i>	<i>Range</i>
<i>Age (yrs)</i>	555	70	11.2	27.5-98.2
<i>Gender</i>	555	Male (%) 380 (68.5)	Female (%) 175 (31.5)	
<i>Ethnicity</i>	n	%		
<i>White</i>	466	84		
<i>Black Caribbean</i>	17	3		
<i>Black African</i>	9	2		
<i>Indian</i>	29	5		
<i>Pakistani</i>	7	1		
<i>Other Asian</i>	7	1		
<i>Other</i>	20	3.6		

Rose Angina Questionnaire

	<i>n</i>	<i>Yes (%)</i>	<i>No (%)</i>
<i>Q1 Pain or discomfort in chest ever</i>	554	248 (45)	306 (55)
<i>Q3 Pain on walking</i>	248	76 (31)	170 (69)
<i>Q4. Pain on hurrying</i>	248	138 (56)	102 (41)

Depression history

	<i>N (%)</i>	<i>Yes N (%)</i>	<i>No N (%)</i>	<i>Mean (sd)</i>
<i>History of depression</i>	549	135 (24)	414 (75)	
<i>How many episodes?</i>				
<i>1</i>	69 (50)			
<i>2</i>	27 (20)			
<i>3</i>	11 (8)			
<i>>3</i>	24 (18)			
<i>Age at first episode (yrs)</i>				48 (20)
<i>Antidepressant treatment?</i>	124	107 (86)	15 (12)	
<i>Talking therapy?</i>	124	55(44)	67 (55)	
<i>Current treatment</i>	553	49 (9)	504 (91)	
<i>Alcohol</i>	553	394 (71)	158 (29)	
<i>Units:</i>				
<i>1-10</i>	264 (67)			
<i>11-20</i>	68 (17)			
<i>21-30</i>	40 (10)			
<i>>30</i>	22 (6)			
<i>Recreational drugs</i>	553	9 (1.6)	542 (98)	

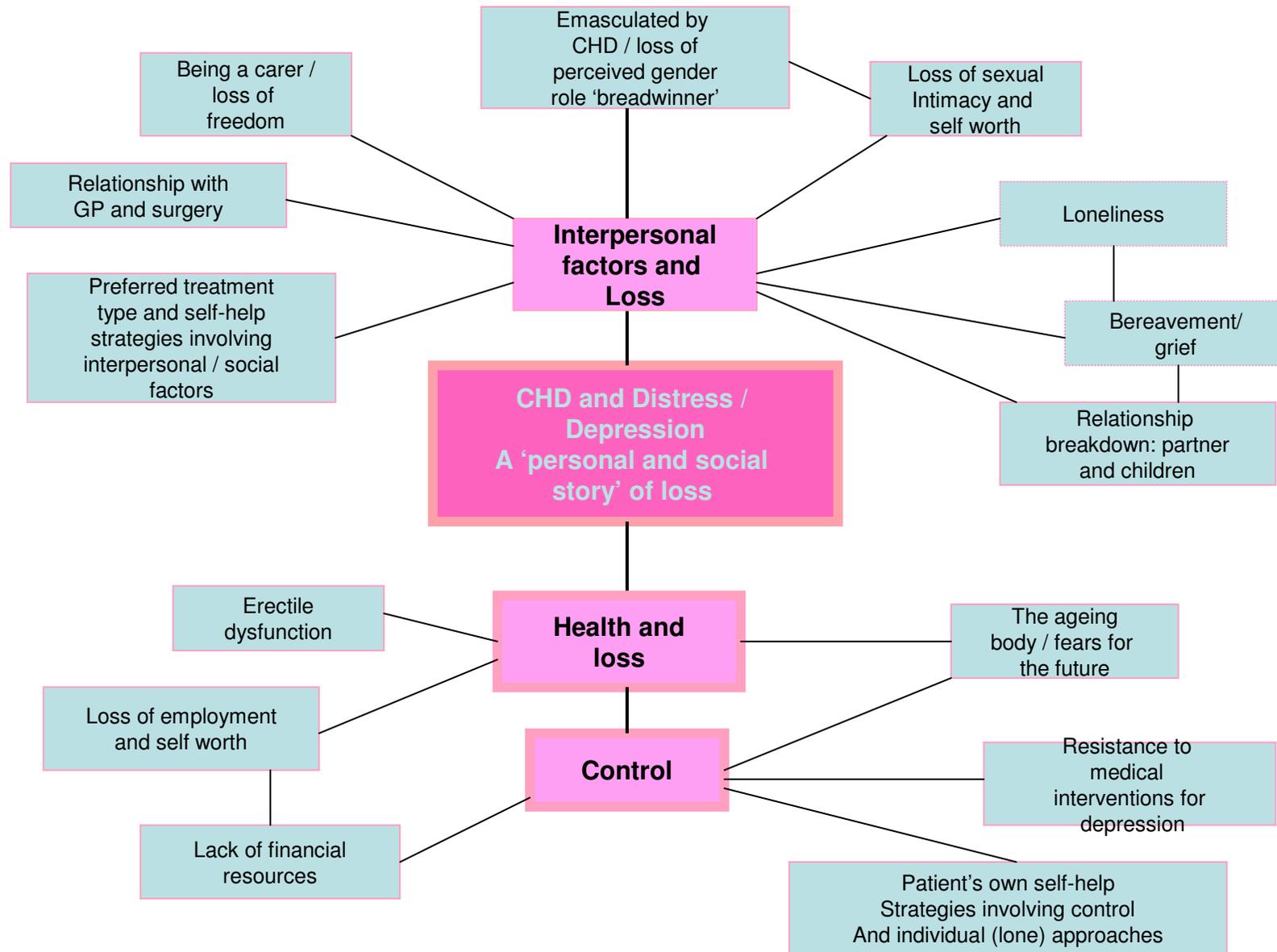
HADS and PHQ-9 data

	<i>n</i>	<i>Mean (sd)</i>	<i>Range</i>	<i>95% CI</i>
HADS Scores				
<i>HADS Depression score total</i>	550	3.5(3.6)	0-19	3.2-3.8
<i>HADS Anxiety score total</i>	550	5.2 (4.4)	0-18	4.8-5.5
		Non-case n(%)	Case n(%)	
<i>HADS-depression categorical (cut off>8)</i>	550	492 (89.5)	58 (10.6)	
<i>HADS-anxiety categorical (cut off>8)</i>	550	424 (77.0)	126 (22.9)	
PHQ-9 Scores				
	n	Mean (sd)	Range	95% CI
<i>PHQ total score</i>	551	4.9 (5.5)	0-27	4.5-5.4
		Non-case n(%)	Case n(%)	
<i>PHQ categorical (score>9)</i>	551	447 (81.1)	104 (18.9)	

Patients' Perceptions of Depression and Coronary Heart Disease – A Qualitative Study

- Although there is a 'striking and consistent' relationship between heart disease and depression it is unclear how the nature of the association is perceived by *patients themselves*.
- 30 semi-structured interviews with cohort study participants – all with CHD and depression.
- Patient interviews underpinned by a theme of 'loss' including *interpersonal and health/control factors*.
- Heterogeneous group, differing needs. CHD was not the main or only cause of depression.
- Patients preferred interpersonal and group/exercise approaches.
- A flexible, individualized, collaborative, 'mentoring' approach to treatment intervention is recommended.

Themes: Patients' perceptions of CHD and depression



GPs' & PNs' Views and Experience of Depression in Coronary Heart Disease

- **Background:** Depressed patients have an increased mortality and morbidity from CHD. The views of primary care staff are needed to inform future interventions.
- **Method:** In-depth qualitative interviews with 22 GPs & PNs
- **Main Findings:** Uncertainty exists as to how best to manage depression in CHD as GPs and PNs are unsure how to address the psychosocial issues associated with this condition. Nurses expressed lack of time and skills.

UPBEAT plans for pilot trial

- Pilot feasibility study to identify and meet needs of this unknown heterogeneous group vs. TAU
- Blend of “Personalised Care Plans” for chronic physical illness (DH 2009), our qualitative findings (e.g. multiple losses) and recovery based methods
- Initial “collaborative” assessment then case management for up to 12 wks (e.g. sign posting (e.g. IAPT, cardiac rehab etc), encouraging to meet own goals etc)
- Depression is primary outcome
- Cardiac outcome, HRQoL etc secondary outcomes

Conclusion

- Depression in people (mainly men) with heart disease may be quite different and require different innovative approaches to management that is more needs based and personalised
- The feasibility trial will provide insight into what could be a possible intervention for a definitive trial.

Grazie mille!