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Can we now explain medically unexplained symptoms?

Francis Creed

University of Manchester, UK

Hackett Award Lecture

APM Las Vegas

13th Nov 2009

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APM 56th Annual Meeting

Disclosure: Francis Creed, MD

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Note: Portions of the grid that are not needed can be grayed out. A good example might be when less than four companies are involved.

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Collaborators:

Psychiatrists

- Else Guthrie
- Nav Kapur
- Arthur Barsky
- Wayne Katon

Psychologists

- Judy Jackson
- Maggie Fiddler
- Adrian Wells

Physicians

- David Thompson
- Nick Read
- Lawrence Cotter
- David Neary
- Tony Lembo

Statisticians

- Barbara Tomenson
- Andrew Pickles

Health economist

- Stephen Palmer

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Medically unexplained symptoms

Kroenke & Price 1993, Nimnuan and Wessely, 2000

- Joint pains
- Back pain
- Headache
- Fatigue
- Chest pain
- Arm/leg pain
- Abdominal pain
- Dizziness

- Gastroenterology - Irritable Bowel Syndrome
- Rheumatology - Fibromyalgia
- Neurology - Headache, Chronic Fatigue

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Medically unexplained symptoms

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- Neurology - Headache, Chronic Fatigue

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Medically unexplained symptoms

- How common are they?
- Primary care: 15-19%
- Medical out-patients: 35-52%

Burton C. British Journal of General Practice 2003;
Nimnuan Journal of Psychosomatic Research 2001
Hamilton J Journal of the Royal College of Physicians 1996.
Jackson J Journal of Psychosomatic Research 2006.
Kooiman CG Psychosomatic Medicine 2000

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Medically unexplained symptoms in medical out-patient clinics

	No of pts	% unex	Clinics
Nimnuan 2001	550	52%	Gynaecology, Neurology Cardiology, Gastroenterology
Van Hemert 1993	191	52%	General medical
Hamilton 1996	324	35%	Neurology, Cardiology, Gastroenterology
Fiddler 2004	295	39%	
Kooiman 2004	695	39-50%	General Medicine

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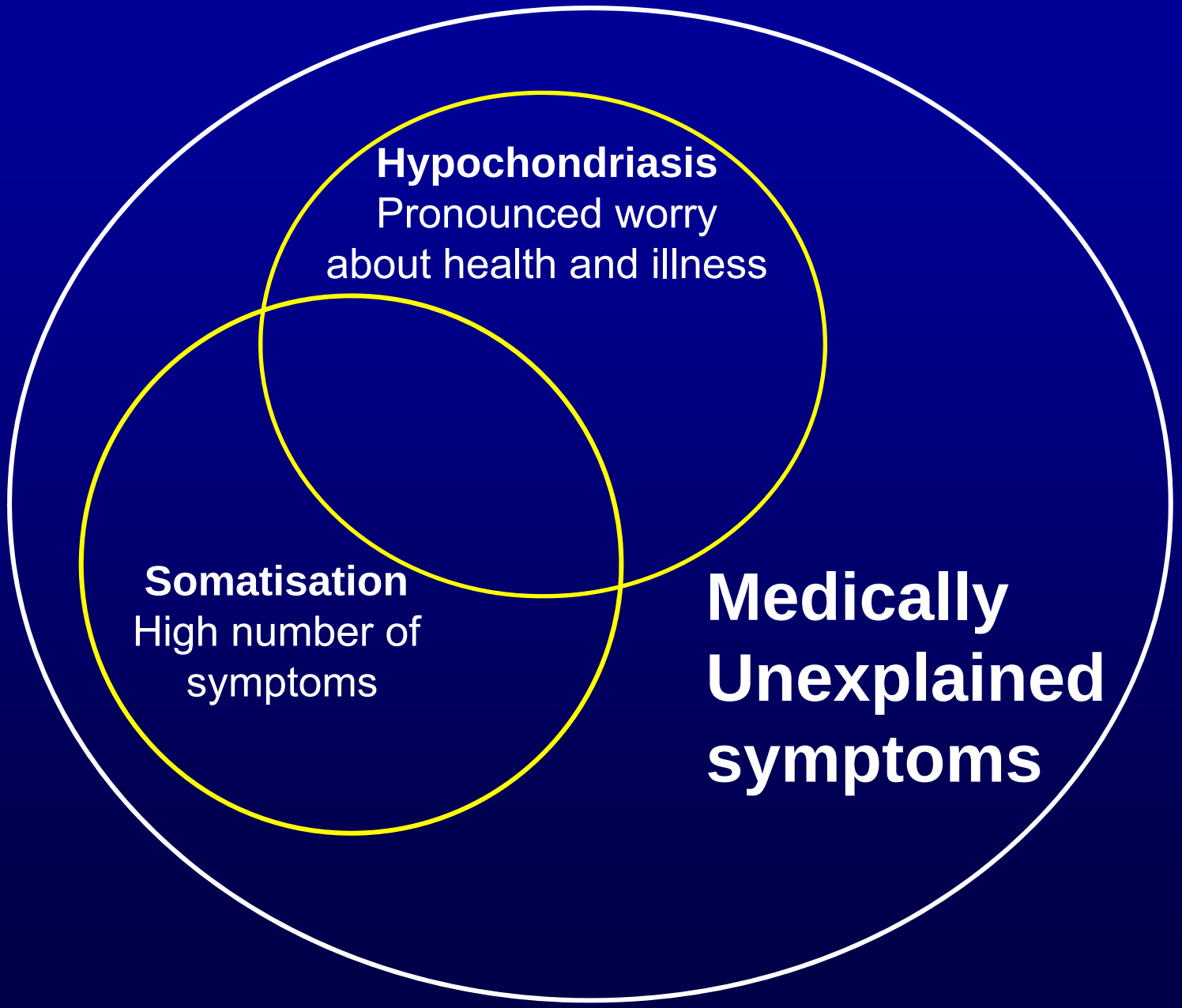

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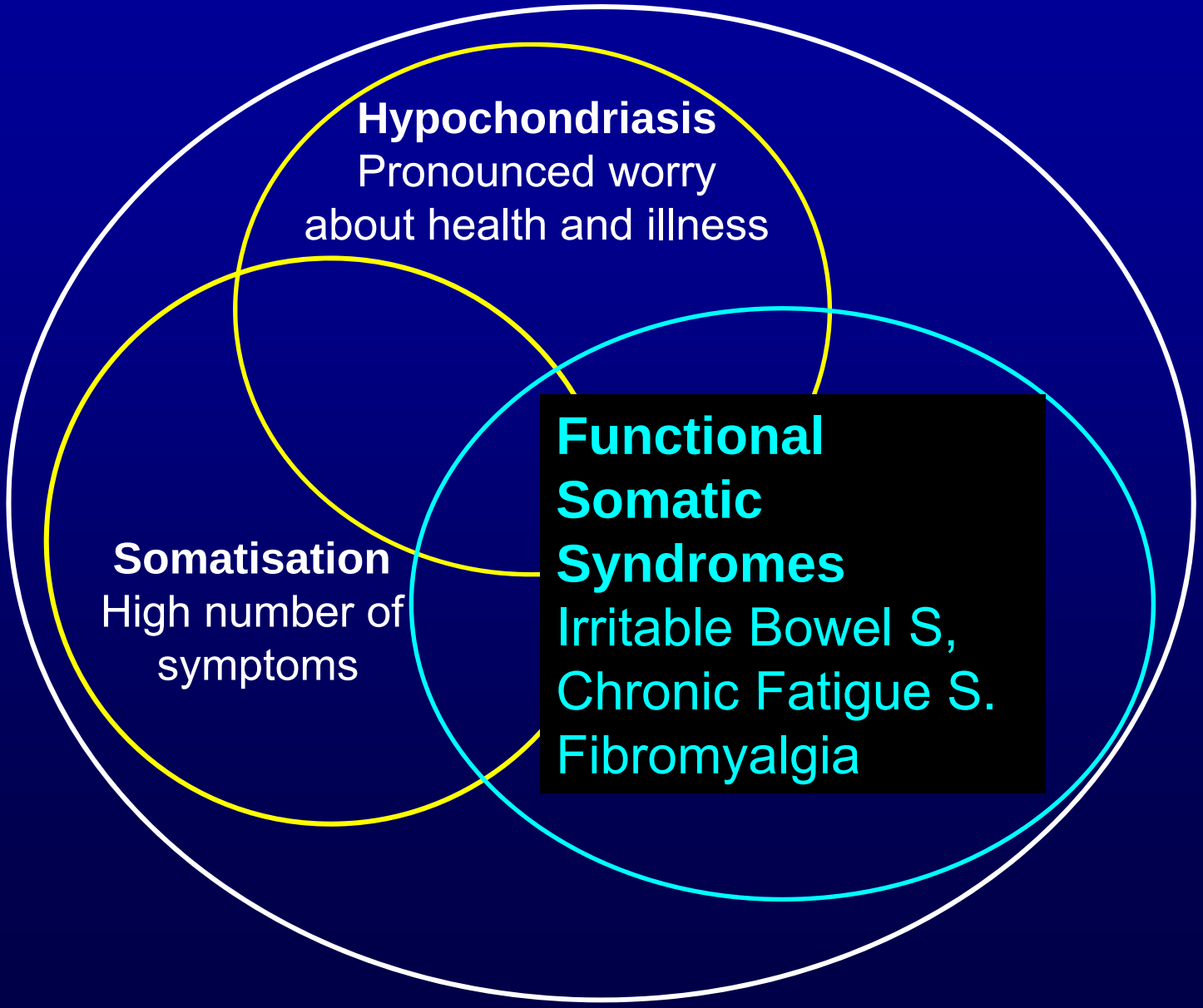
Medically Unexplained symptoms



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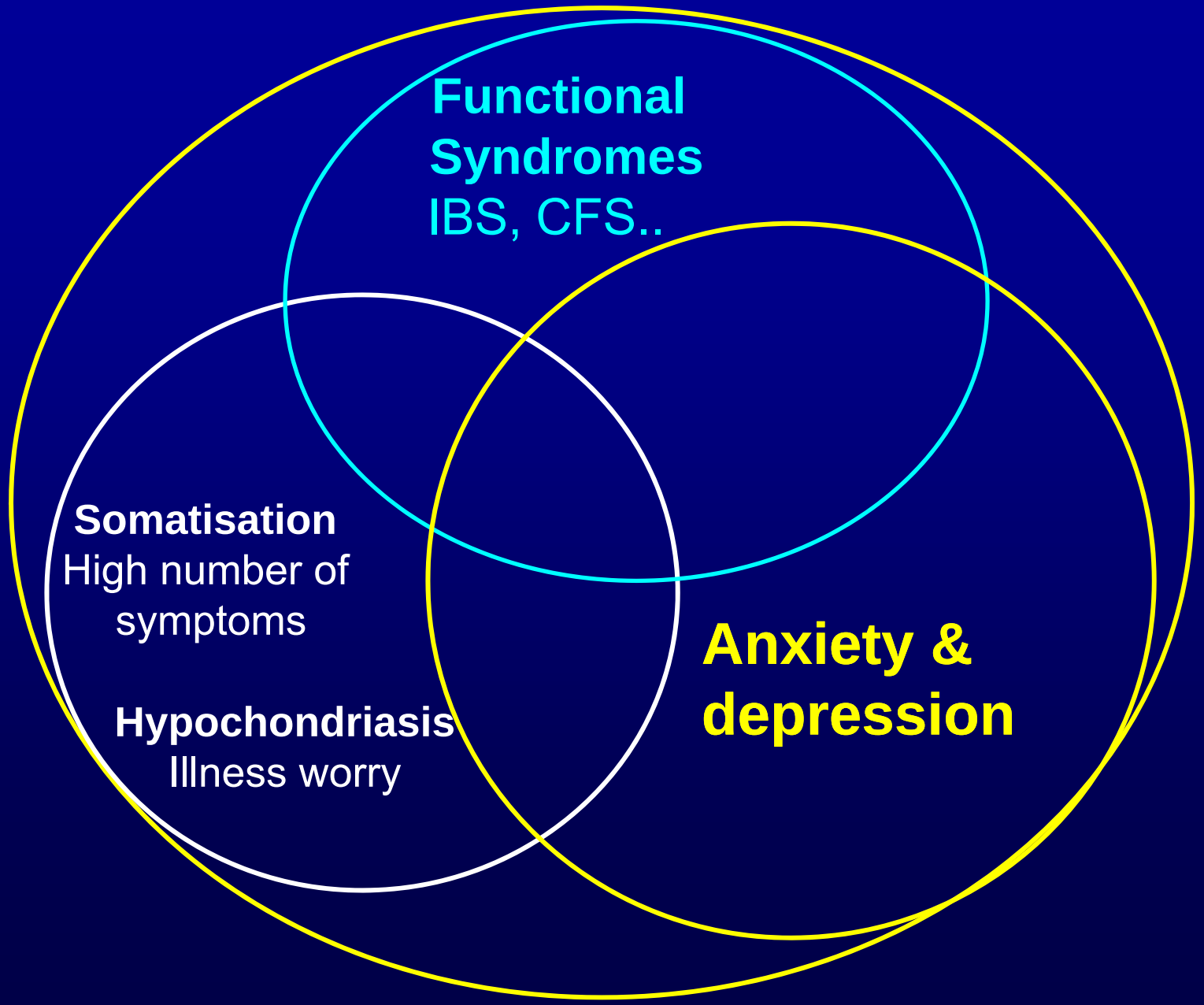
Medically Unexplained symptoms



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ICD diagnosis: "Signs, symptoms & ill-defined conditions" (ICD codes 780-789)

- UK NHS : most costly diagnostic category of out-patients
- 4th most expensive category in 1^0 care
- Netherlands: 5th most expensive category
- USA: 5th most frequent reason for clinic visits (60 million per annum)
- Cherry et al . National Ambulatory Medical Care Survey: 2005 CDC National Center for Health Statistics. 2007.

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Medically unexplained symptoms

- Common in primary care and in medical out-patients
- Associated with high costs

= Major problem in medicine !

Generally not well managed

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Medically unexplained symptoms
100 consecutive medical out-patients

- Psychotropic medication 7%
- Lifestyle advice 8%
- Specialist nurse 1%
- Symptomatic medication 26%
- Further review 14%
- No action/no recommendation 44%

Mangwana et al INT'L. J. PSYCH IN MED. 2009 39; 33-44

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Practice point

- Don’t let internists/primary care doctors think that all patients with MUS should see a psychiatrist - you will never go home at night!
- Do spend time helping internists/primary care doctors to develop their skills in managing these patients

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MUS a major problem in medicine

- Why such little progress in explaining?
- DSM definition of Somatisation disorder
- Dualism - separating mind & body

- The way ahead
- A Psychosomatic perspective
- A New Classification?

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MUS a major problem in medicine

- Why such little progress in explaining?
- DSM definition of Somatisation disorder
- 3 problems:
- Wrong threshold
- “MUS” difficult to measure
- “MUS” reinforces dualism

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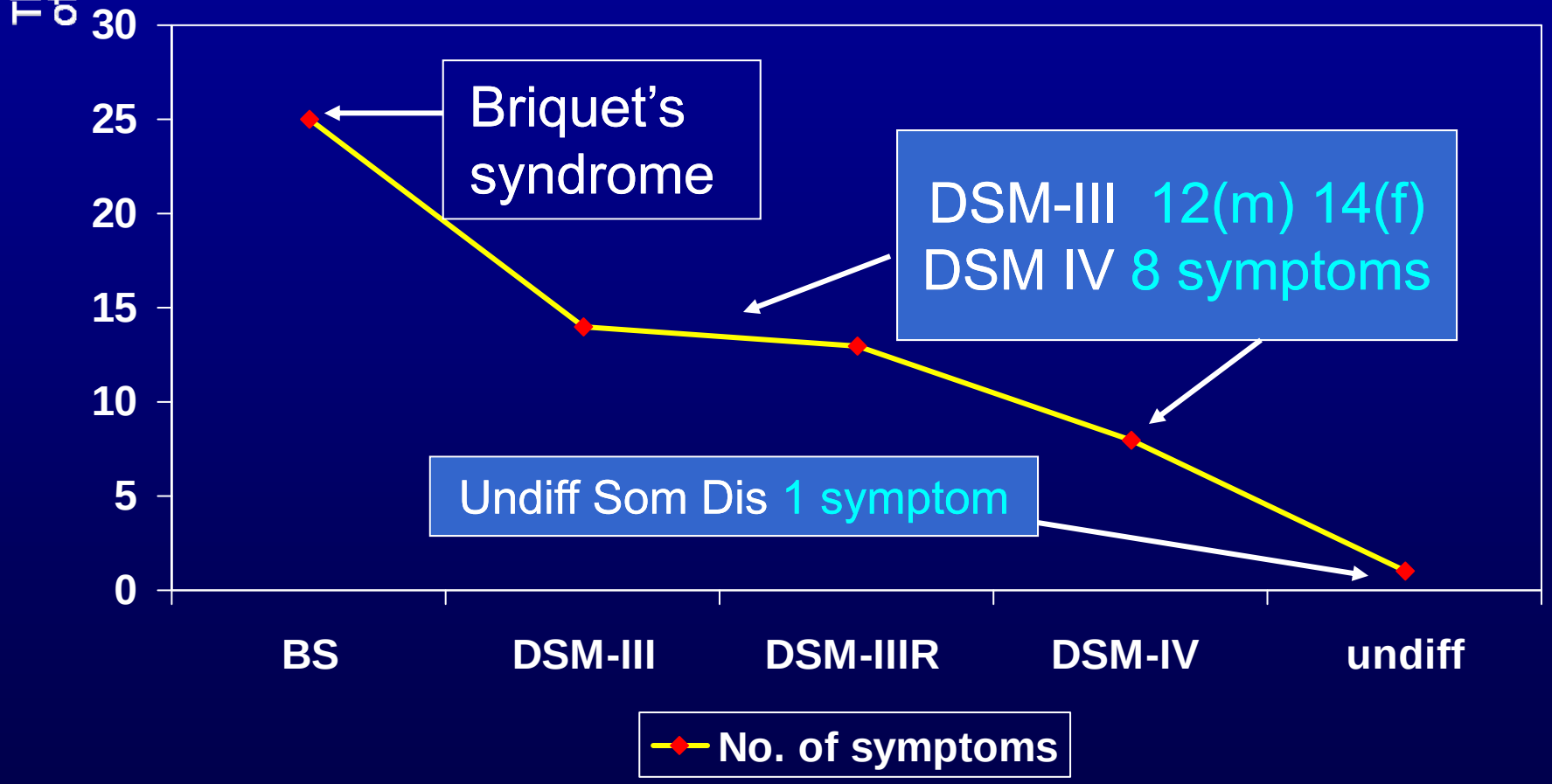
No. of bodily symptoms required for diagnosis



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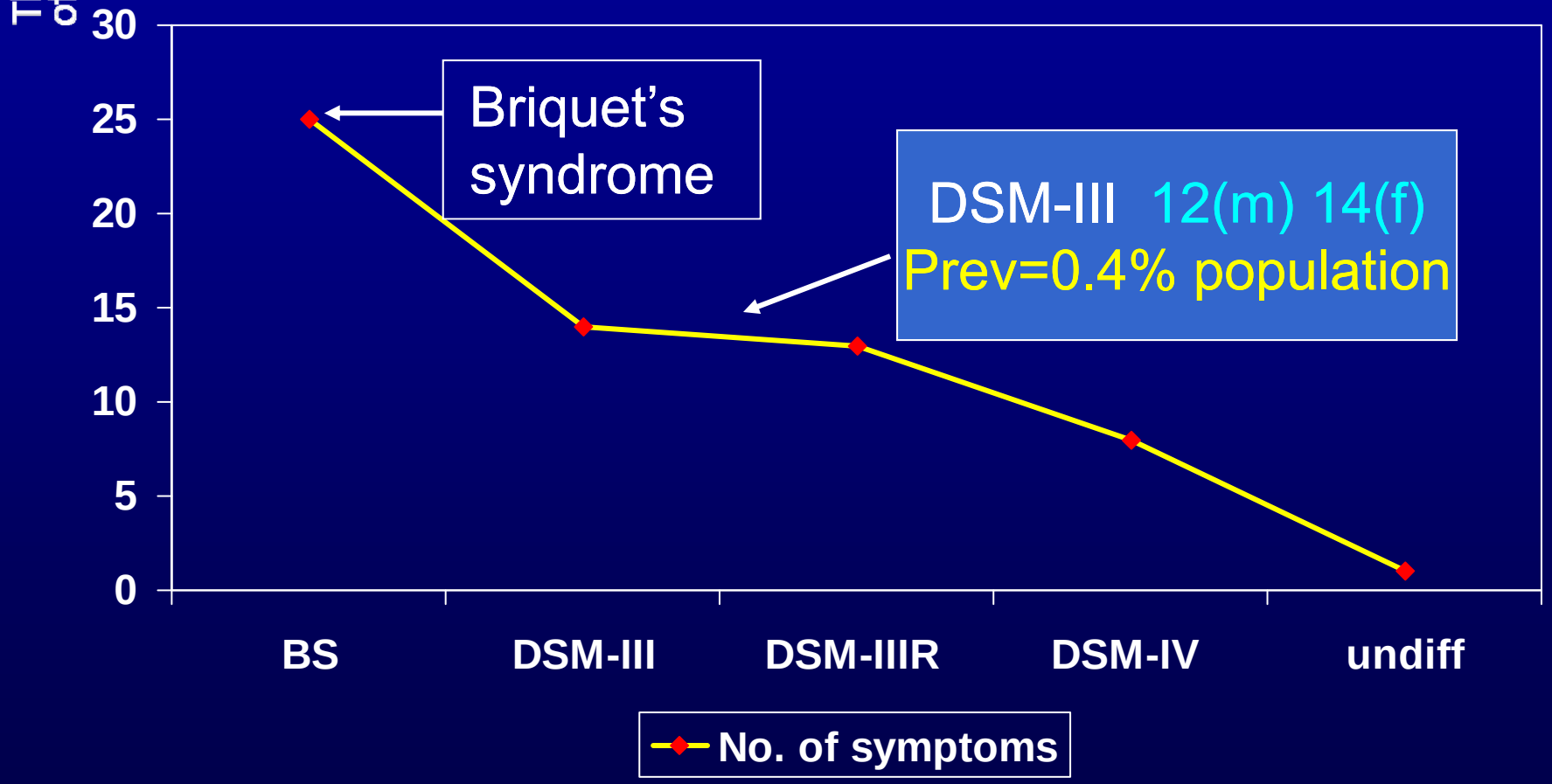
No. of bodily symptoms required for diagnosis



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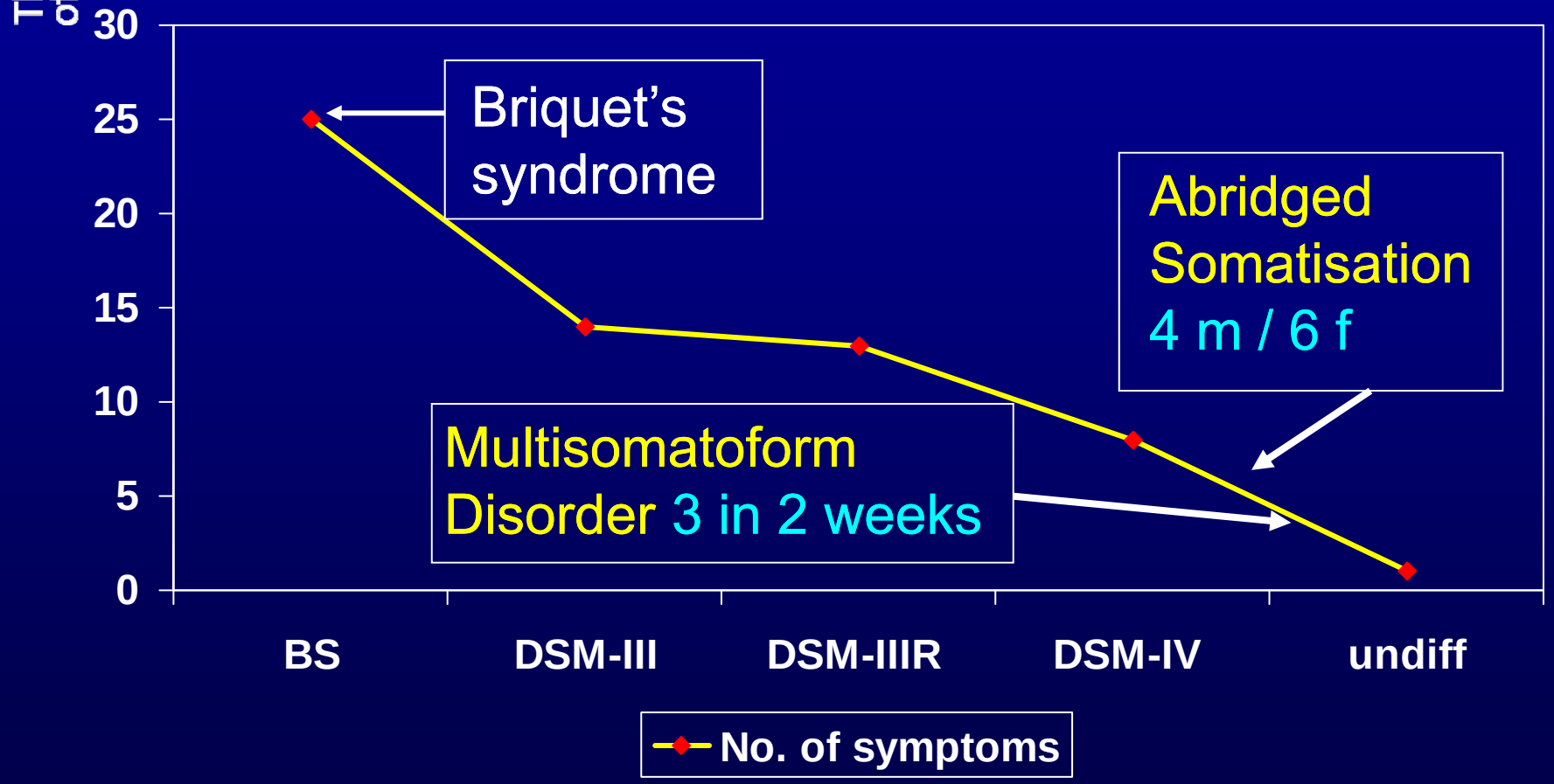

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Prevalence of these disorder in primary care

Abridged somatisation (4m/6f)	6%
Multisomatoform disorder	24%
DSM IV somatization disorder	<1%
DSM IV Undifferentiated somatoform disorder	79%

Lynch DJ et al Prim Care Companion J Clin Psychiatry 1999

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206 high-utilising MUS patients:

Smith et al Psychosom Med. 2005

- Of 206 high-utilising MUS patients:
- 4.4% any DSM-IV somatoform diagnosis
- (+ 18.9% - abridged somatisation disorder)

- 60.2% - anxiety or depression diagnosis without DSM-IV somatoform diagnosis

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119 distressed high-utilising patients:

Katon et al Gen Hosp Psych 1990

- Of 119 distressed high-utilising MUS patients
  - mean of 8.7 medically unexplained symptoms :
- 20.2% - DSM-III-R Somatisation disorder
- 73% - Abridged (4/6) criteria of somatisation


What's taken you so long, Francis?


Abridged!

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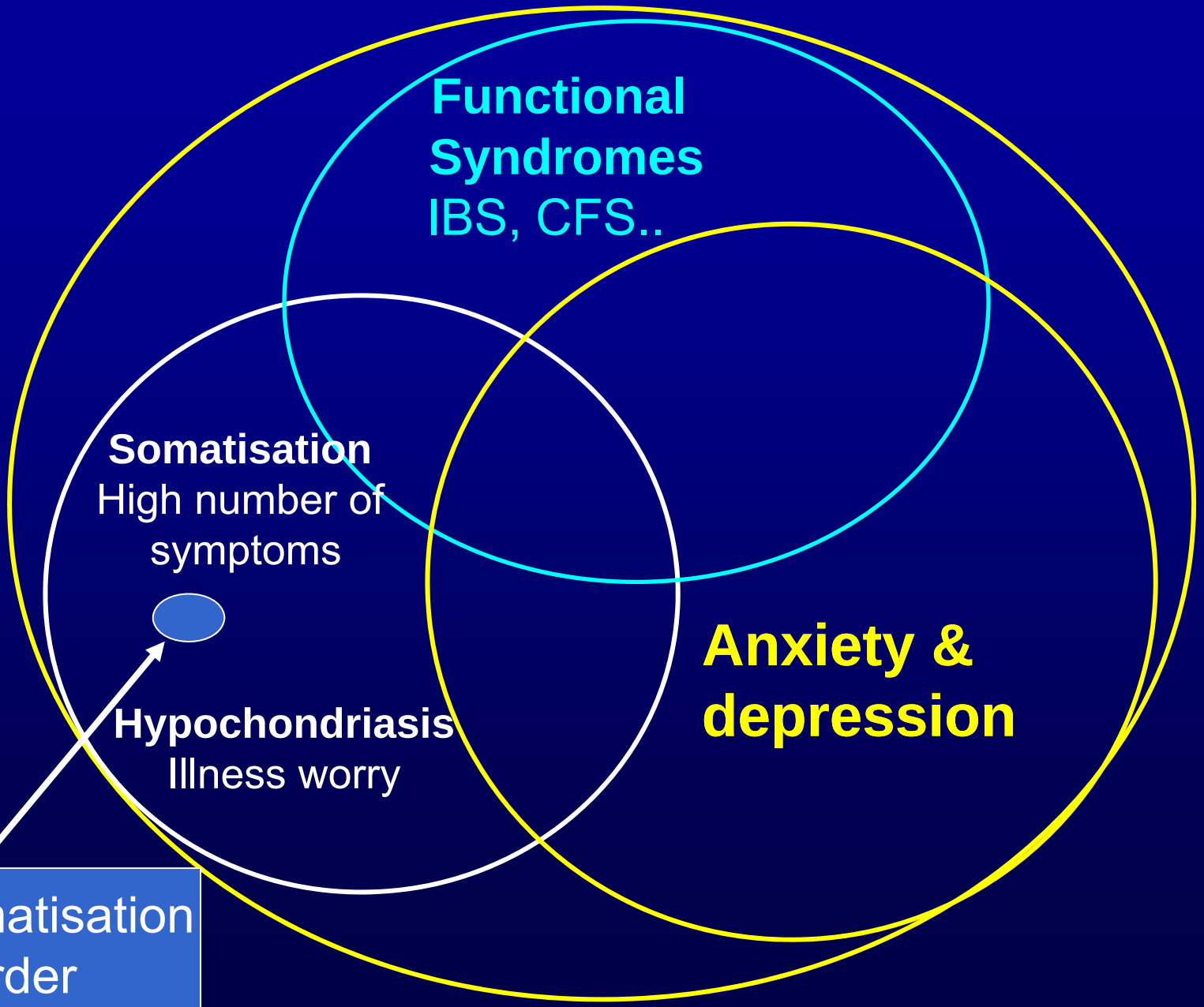
Medically Unexplained symptoms



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Practice point

- How do we diagnose patients with multiple bodily symptoms?
- Many have depression and/or anxiety but this diagnosis may not do justice to their treatment needs

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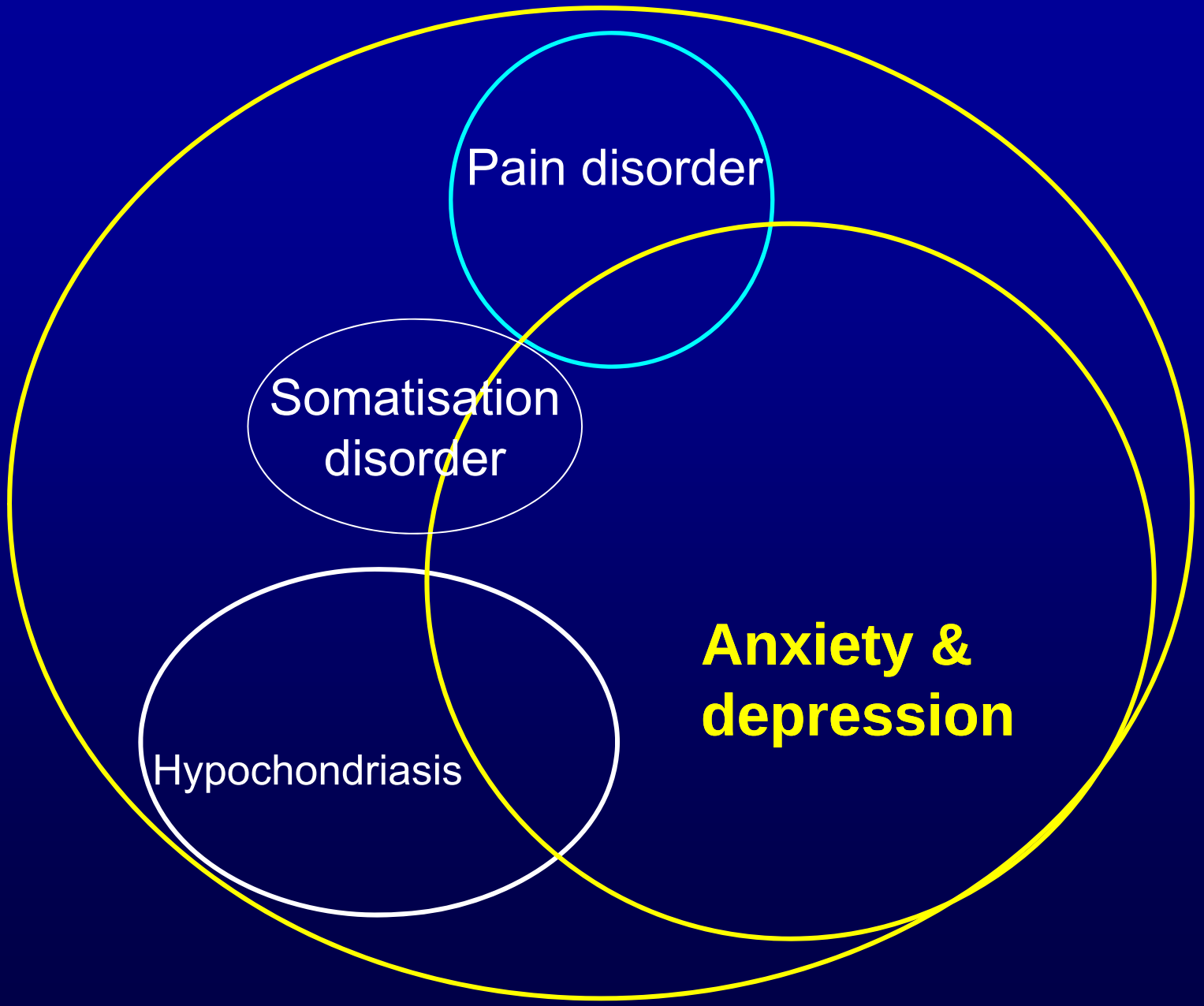
DSM Somatoform disorders



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DSM-IV Definition of somatisation disorder

- "Multiple physical complaints ……:
- cannot be fully explained by known medical condition (after full investigation)

Difficult to measure:
Been to Dr?
Not caused by
medical illness

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Somatoform disorders

- Not included in National Surveys of mental health

* USA - National Comorbidity Survey. Kessler RC et al 1994
* USA - National Comorbidity Survey replication. Kessler 2005
* UK - National Psychiatric Morbidity survey Jenkins R 1997.
* Australia - National Mental Health Survey. Andrews G. 2001
* Netherlands – NEMESIS. Bijl SPPE 1998
* World Mental Health Surveys: Kessler. JAMA 2004

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Somatoform disorders

- Psychiatrists and health service planners tend to neglect these disorders

Somatization … a forgotten public health agenda?
Saxena S In Somatoform disorders. 2005

Creed F. World Psychiatry Oct 2006

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Somatoform disorders

German group that has included somatoform disorders

"…… astonishing considering that these disorders are the third most frequent in the general population"

Baumeister SPPE 2007.

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MUS a major problem in medicine

- Why such little progress in understanding?
- Definition of Somatisation disorder

Rare in primary Care/population
Difficult to measure
Omitted from epidemiological research

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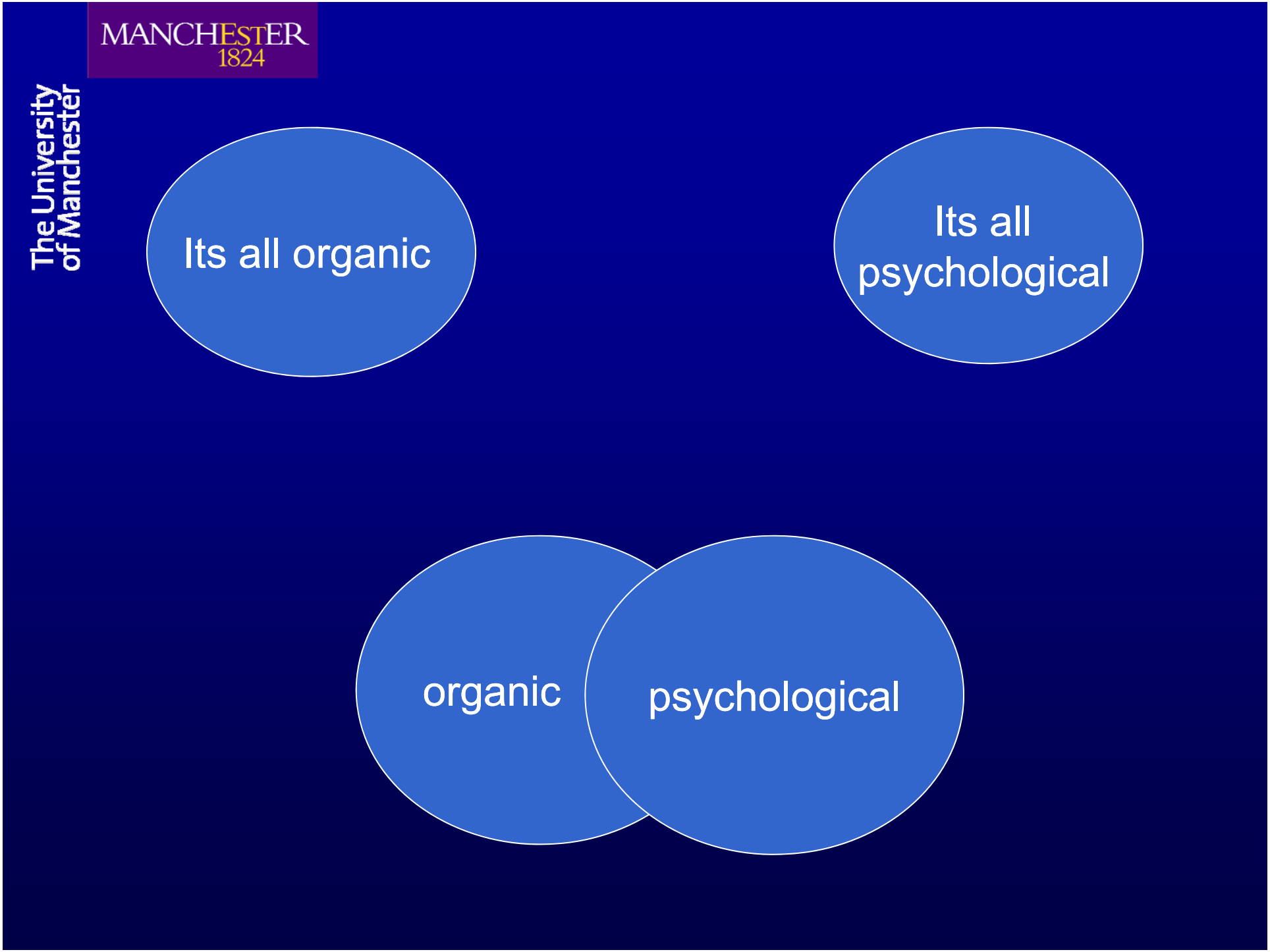
MUS a major problem in medicine

- Why such little progress in explaining?
- Definition of Somatisation disorder
- Dualism - separating mind & body



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~~Its all organic~~

Its all psychological

Medically unexplained??

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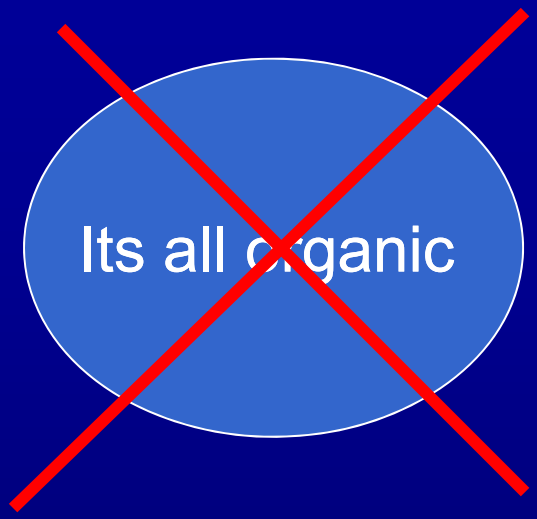
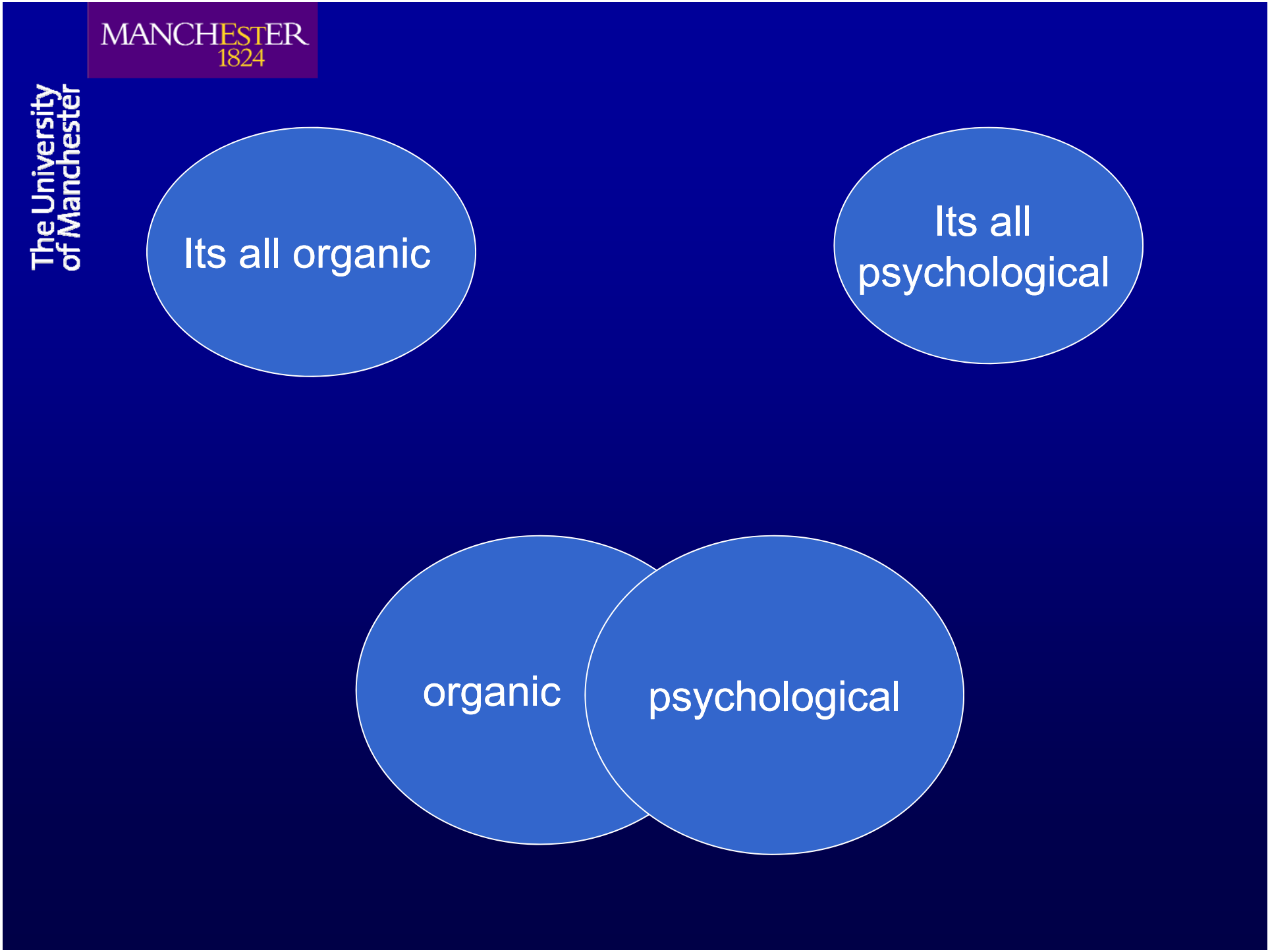


Medically unexplained??

Patient - post laparotomy for abdominal pain, weight loss & diarrhoea:

"Well, Mrs S. there is absolutely nothing wrong with you – its all psychological"



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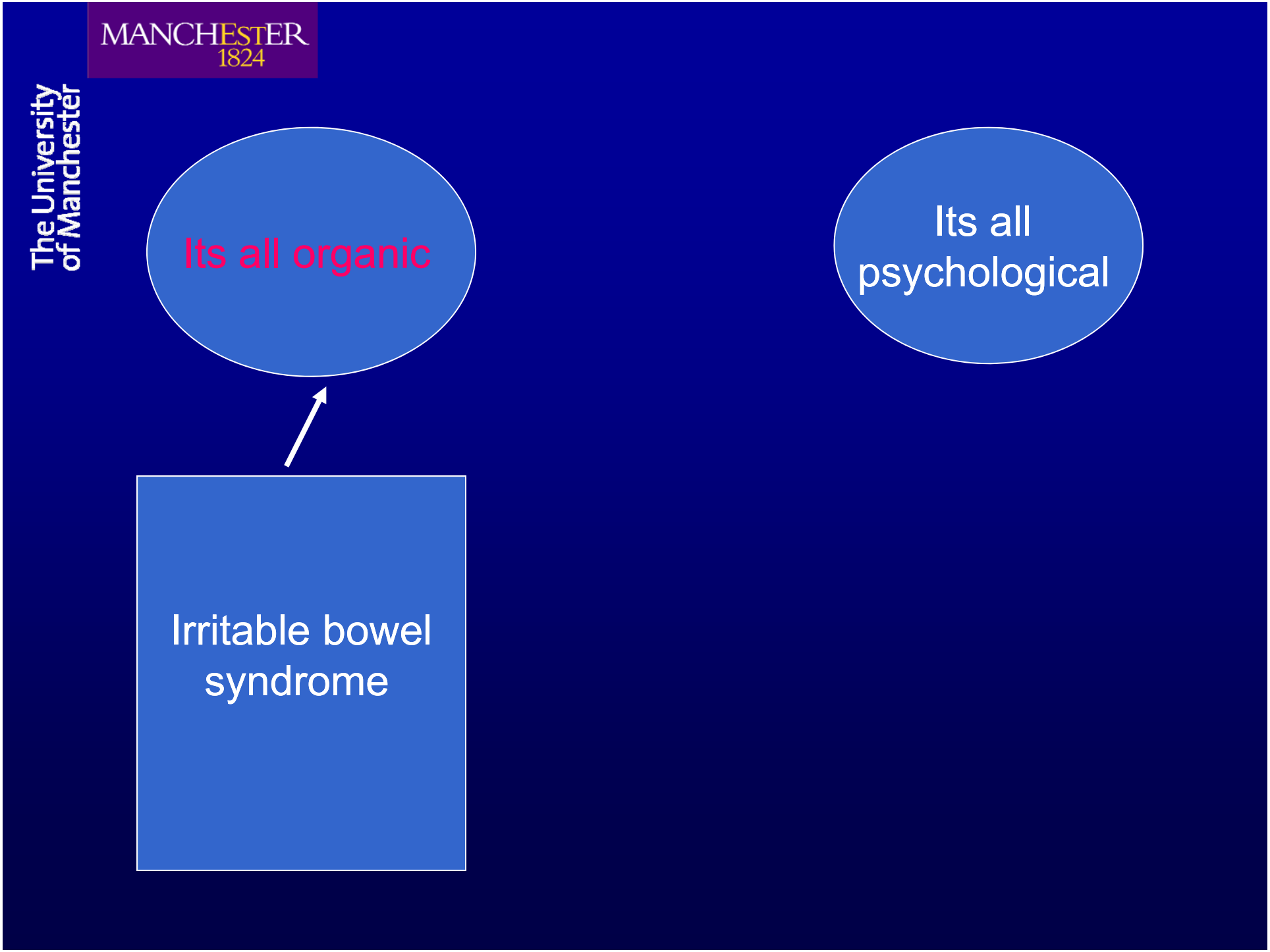
The term: "Medically unexplained symptoms"

- Negative definition - defines group by what it is not
- Reinforces the "either/ or" notion - that symptoms are either due to organic disease or something else.

- Creed et al: Is there a better term than "Medically unexplained symptoms"? J Psychosom Res in press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Its all organic
Its all psychological
Irritable bowel syndrome

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Its all Organic!

- Irritable Bowel Syndrome: a little understood organic bowel disease?
  Talley & Spiller Lancet 2002

- "IBS… in the past relegated to the realm of psychosomatic and unimportant….
- ..colonic flora might be abnormal .."
- Inflammation … could contribute to diarrhoea…

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Its all organic

Its all psychological

Evidence for pure organic aetiology is weak
Links to GI infection
GI inflammation

Psychological factors not limited to treatment seeking
Abnormal processing of pain

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Its all organic

Its all psychiatric

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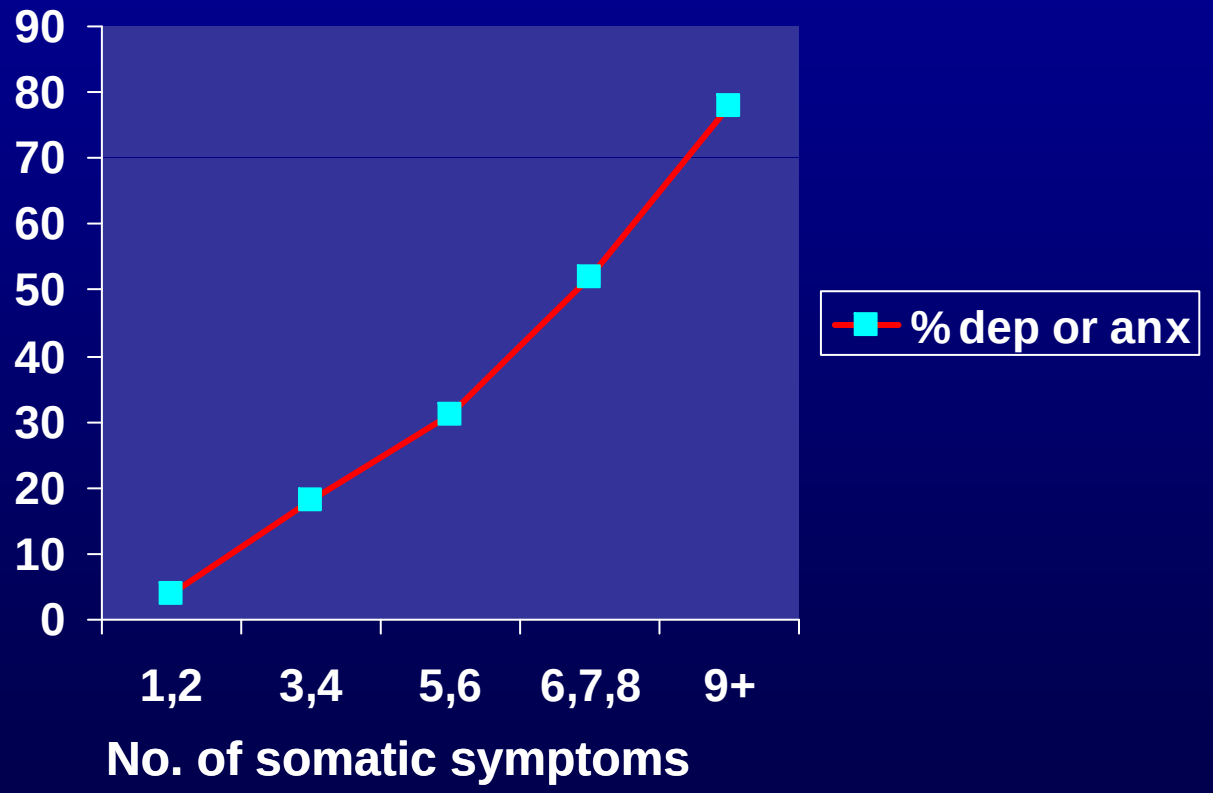
Number of somatic symptoms & % with anxiety/depressive disorder



Kroenke et al Am J Med 1997

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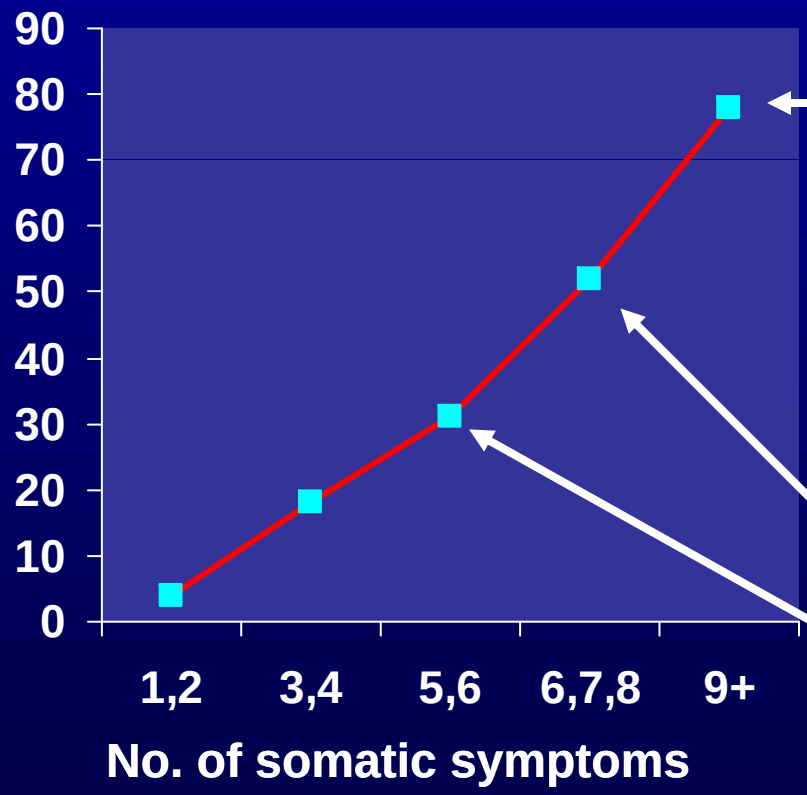
Number of somatic symptoms & % with anxiety/depressive disorder



Patients with 9+ bodily symptoms – 78% have anx/depr.

% anx/dep
6-8 sympts = 52%
4-5 sympts = 32%

Kroenke et al Am J Med 1997

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Association of Functional Syndromes with Depression and Anxiety

- Meta-analysis of 244 studies:
  - IBS, CFS, Fibromyalgia
- → Syndromes clear association with depression and anxiety

• Effect size was small to moderate – unexplained symptoms often arise without anxiety or depression

Henningsen et al Psychosom Med 2002

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Post-viral fatigue

Wessely et al lancet 1995

- Follow up study of primary care patients

  →

- No association between infection and later chronic fatigue.

- "common infections play little part in the aetiology of chronic fatigue syndrome"

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Post-infective chronic fatigue

Hickie et al BMJ 2006

- Follow-up study of patients with Epstein-Barr and other viral infections

- → 11% developed chronic fatigue syndrome
- CFS was predicted by severity of viral infection not psychological factors

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Post-infective chronic fatigue

Hickie et al BMJ 2006

- Post-infective fatigue syndrome is a valid illness model for investigating one pathophysiological pathway to chronic fatigue syndrome.

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Its all organic

not
Its / all
psychiatric

Psychiatric disorder
only in some patients
with MUS

What other factors?

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MRC 1946 birth cohort study Multiple Symptoms aged 36 years

Hotopf et al, Am J Psych 1999

- Poor parental health aged 15 years associated with multiple bodily symptoms aged 36 years (adjusted for current psychiatric disorder)

Psychiatric disorder is also a predictor….

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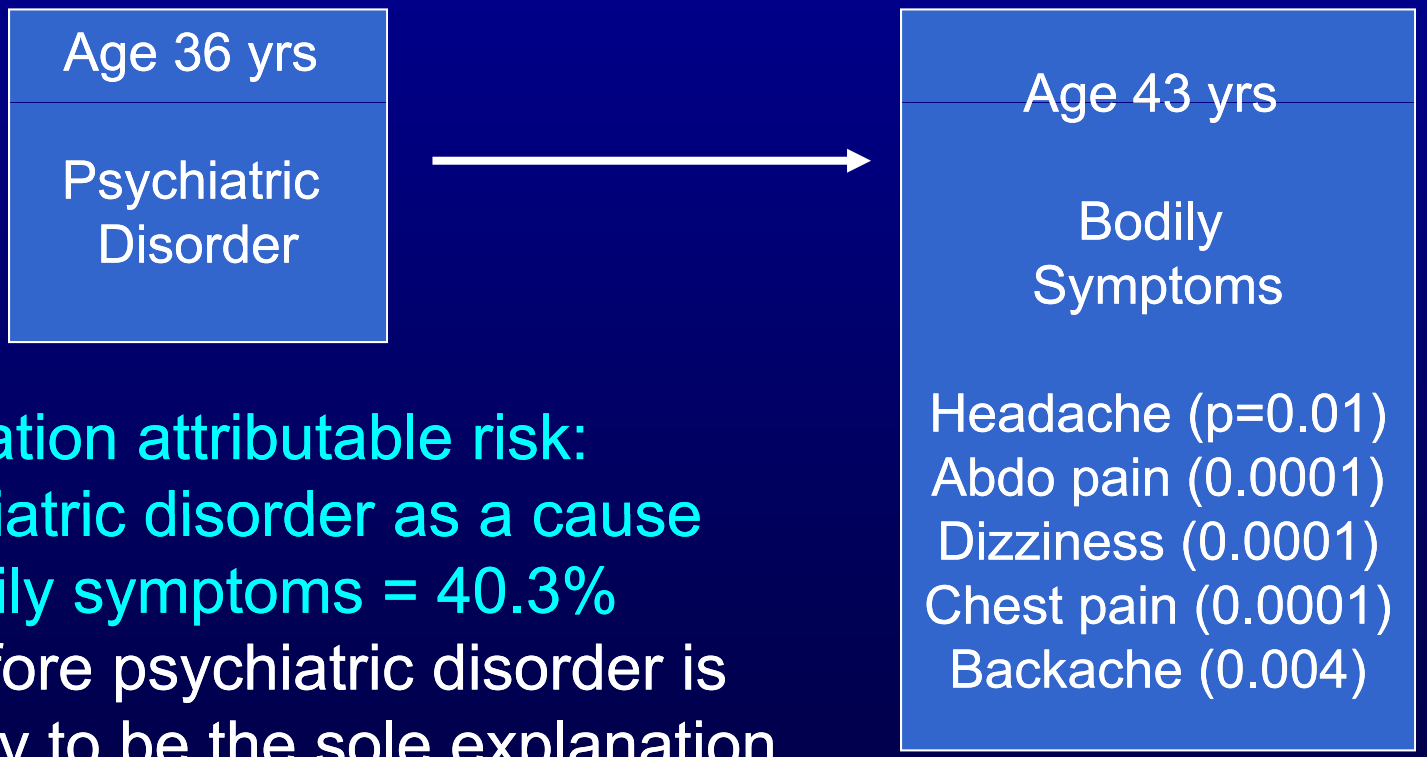
Psychiatric disorder and Multiple Symptoms

Hotopf et al, Am J Psych 1999



Population attributable risk:
Psychiatric disorder as a cause of bodily symptoms = 40.3%
Therefore psychiatric disorder is unlikely to be the sole explanation for most cases

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Psychiatric disorder and Multiple Symptoms

Hotopf et al, Am J Psych 1999

Age 36 yrs	→	Age 43 yrs
Psychiatric Disorder		Bodily Symptoms Headache (p=0.01) Abdo pain (0.0001) Dizziness (0.0001) Chest pain (0.0001) Backache (0.004) Fatigue

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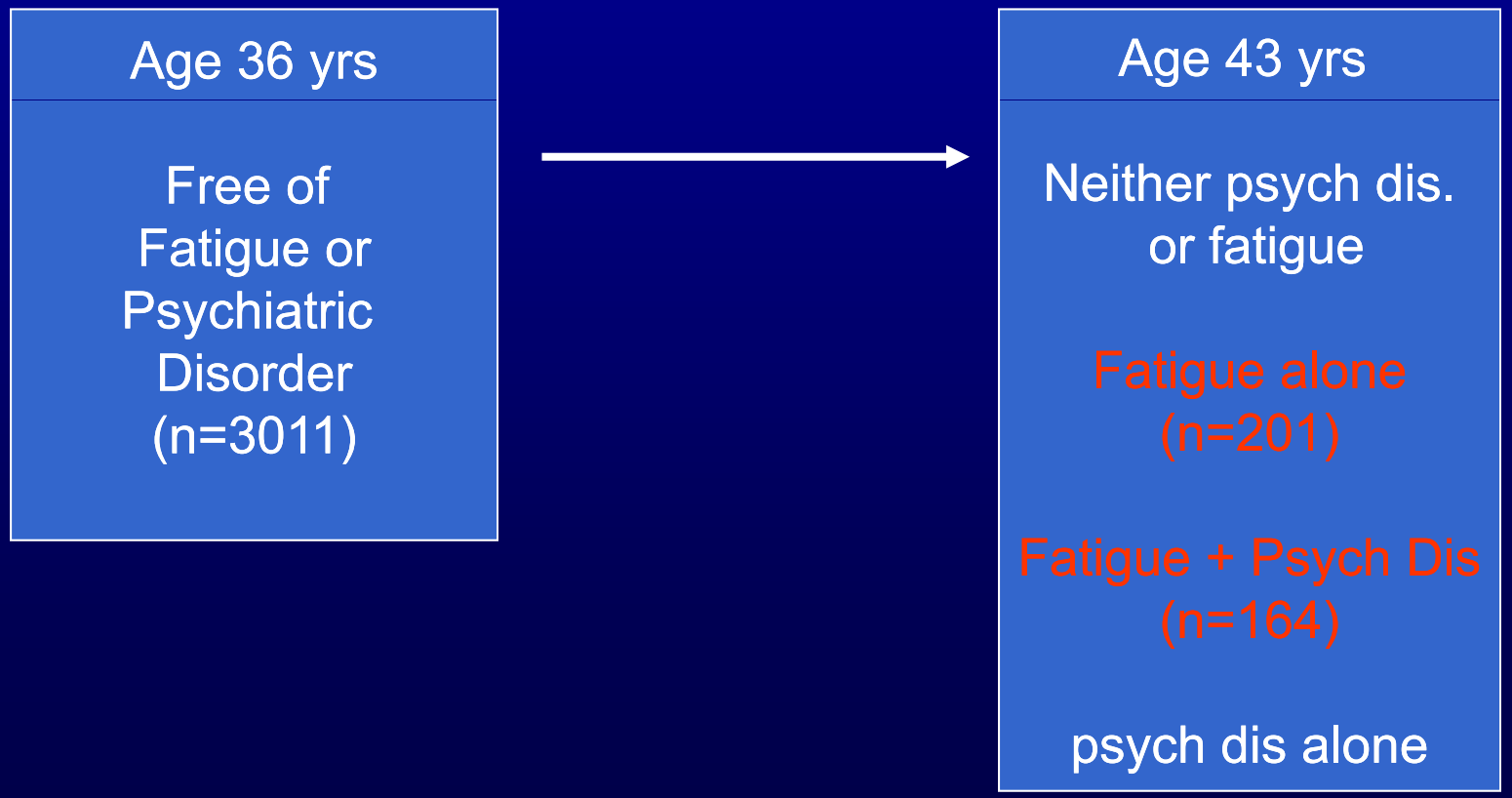
Psychiatric disorder and Multiple Symptoms

Harvey & Wessely. J Psychosom Res 2009



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Psychiatric disorder and Multiple Symptoms

Harvey & Wessely. J Psychosom Res 2009

Age 36 yrs

"energetic" child
Overweight 36 yrs
neuroticism

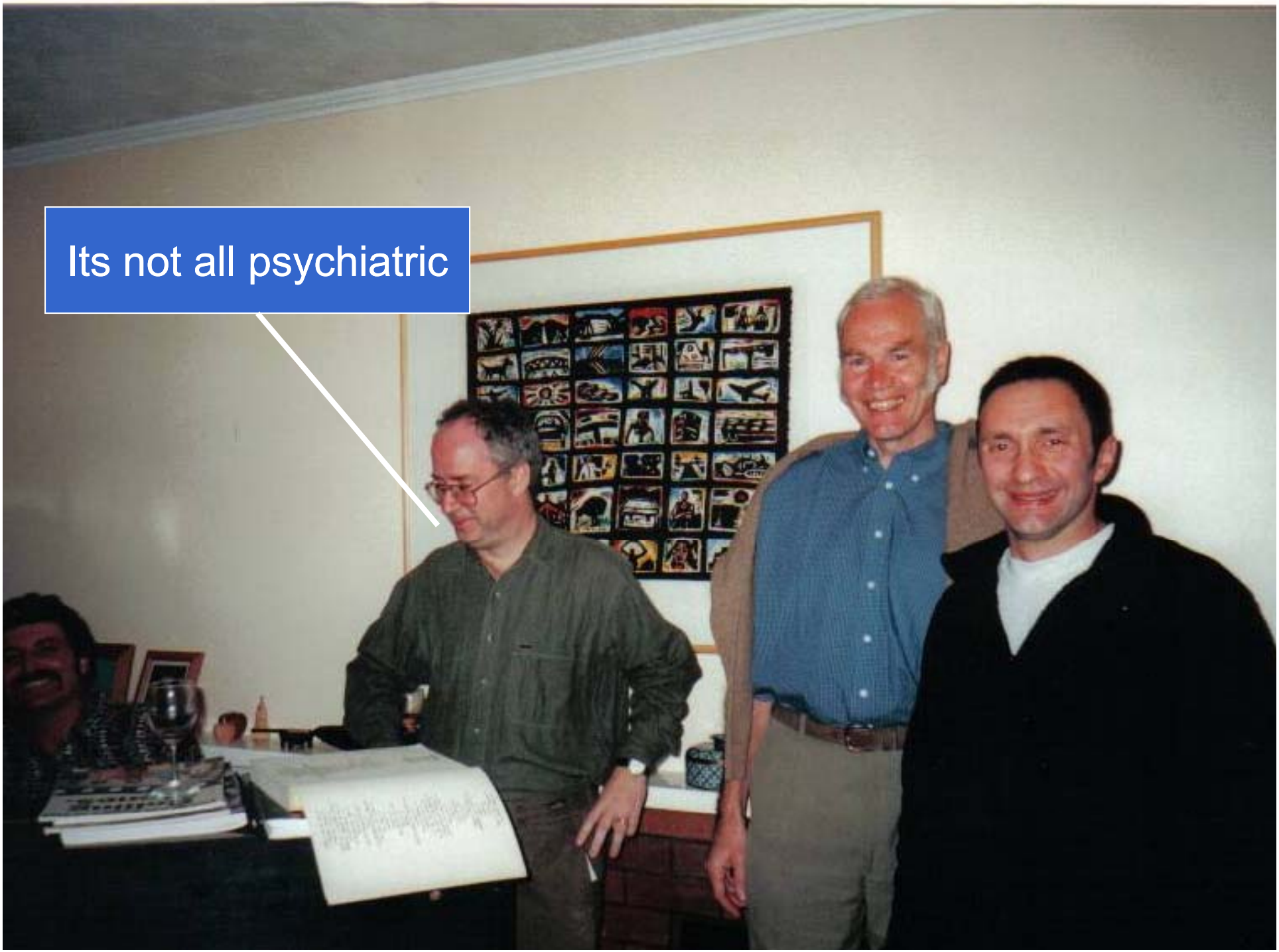
FH Psych dis.
-ve life events
neuroticism

Age 43 yrs

Compared:

Fatigue alone
(n=201)

Fatigue + Psych Dis
(n=164)


Its not all psychiatric

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Practice point

- Do not get caught in a mind v body argument with patients.
- I disallow “its all in the mind” and point out that modern research shows that we cannot separate mind and body.
- We need models to explain this to patients, e.g. heart rate when faced with danger, pain worse with depression, tense muscles etc…

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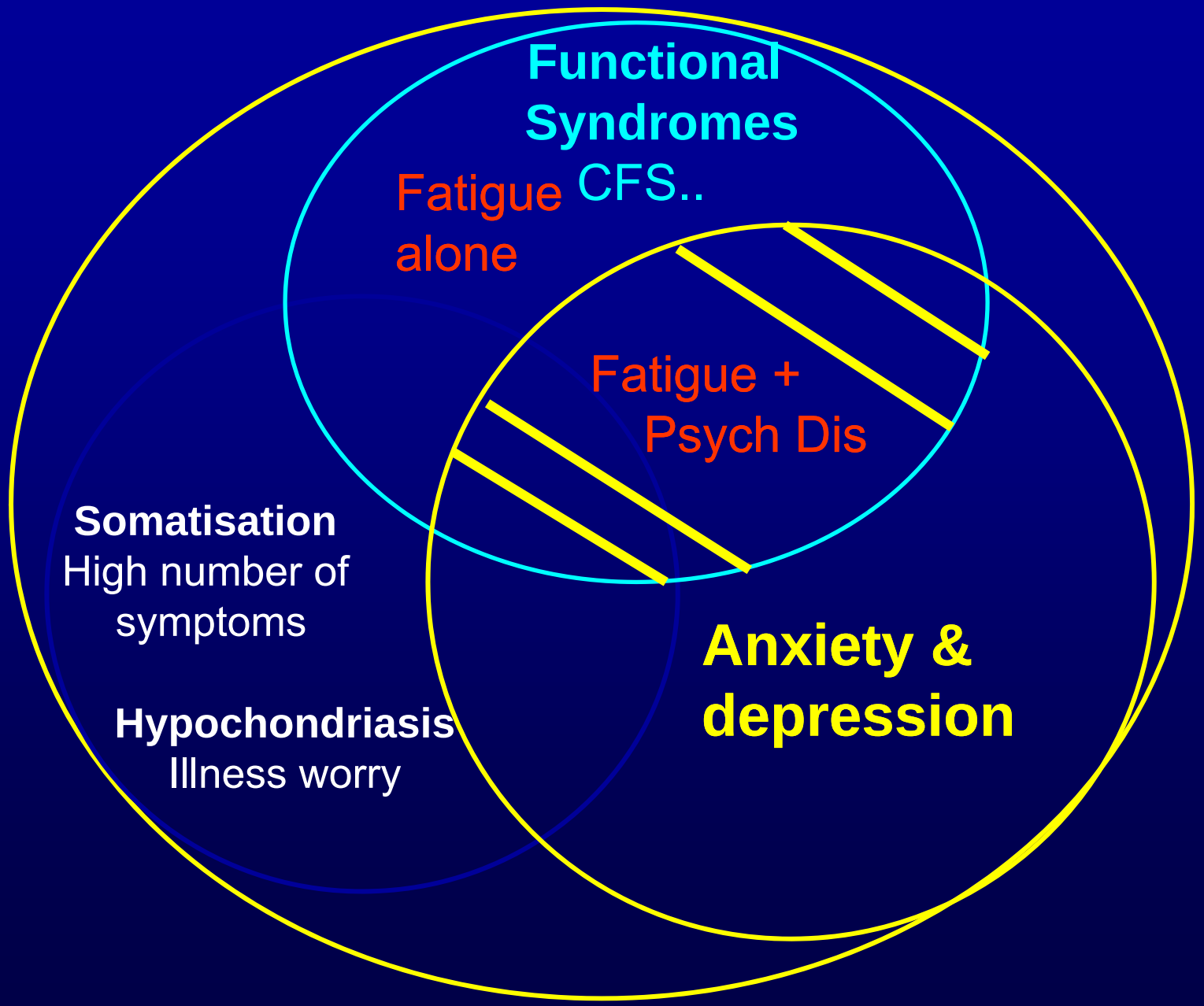
Medically Unexplained symptoms



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Its not all Psychiatric

Psychiatric disorder is only partial explanation:
Illness in parent while a child
Other factors
Improvement from Psychological therapy?

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CBT for somatization and symptom syndromes : Systematic Review

Kroenke Psychotherapy & Psychosomatics 2000; 69: 205-215.

- 29 RCTs (back, chest pain, CFS, IBS etc)
- CBT → overall improvement compared to controls: for Bodily symptoms & functional status

- Beneficial effects of CBT seem to occur independent of improvement in psychological distress

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Changes in cognitions 6 months after 1st consultation (105/110)

Van Dulmen Psychol Med 1997

- Improvement in abdominal complaints associated with:
- less anxiety ($p<0.01$)
- less fear of cancer ($p=0.02$) and
- greater attribution to stress ($p=0.04$)
- Catastrophised less ($p=0.002$)

Health Anxiety & Attribution Poor coping

- Outcome not related to number of consultations or investigations

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Irritable bowel syndrome Cognitive Behaviour Therapy

- CBT → Improved global well being with little change in pain
- "the pain is still there but I manage it better" (better coping)

Drossman et al Gastroenterology 2003; 125:19-31

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Chronic Fatigue Syndrome

Prins et al Lancet 2006

Intensive CBT → improvement

The positive effect of CBT for CFS is related to changes in
illness related cognitions and self-efficacy

After prolonged rest…. exercise is painful ….
…therefore exercise is damaging
I know that this illness will never improve…
There is nothing I can do to improve my state of health

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Its all organic

not
Its / all
psychological

Psychiatric disorder
only partial explanation
of bodily symptoms
* Illness in parent during
childhood
* Benefit from
Psychological therapy
suggests cognitive factors

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Practice point

- Always ask patients “what do you think causes these symptoms?”
- Explore fears of serious illness and the relationship to:

a) previous (viral) illness

b) stress

- Simple explanation my be very helpful to patients……..keeping a diary of symptom severity may also help.

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Practice point

- Do not aim to “cure” or greatly reduce pain or fatigue if they are chronic – aim to increase functioning and decrease healthcare use.
- Explain the deleterious effects of avoidance (exercise in CFS/fibromyalgia; food avoidance in IBS)

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Antidepressant therapy for unexplained symptoms and syndromes. Systematic Review

O'Malley et al J Fam Pract 1999; 48: 980-990.

- 94 RCTs (headache, fibromyalgia, IBS etc)
- 48 studies → meta-analysis response of unexplained physical symptoms – antidepressants superior to placebo: pooled OR = 3.4 (95%CI: 2.6-4.5)

- Beneficial effects of antidepressant seemed to occur independent of improvement in psychological distress

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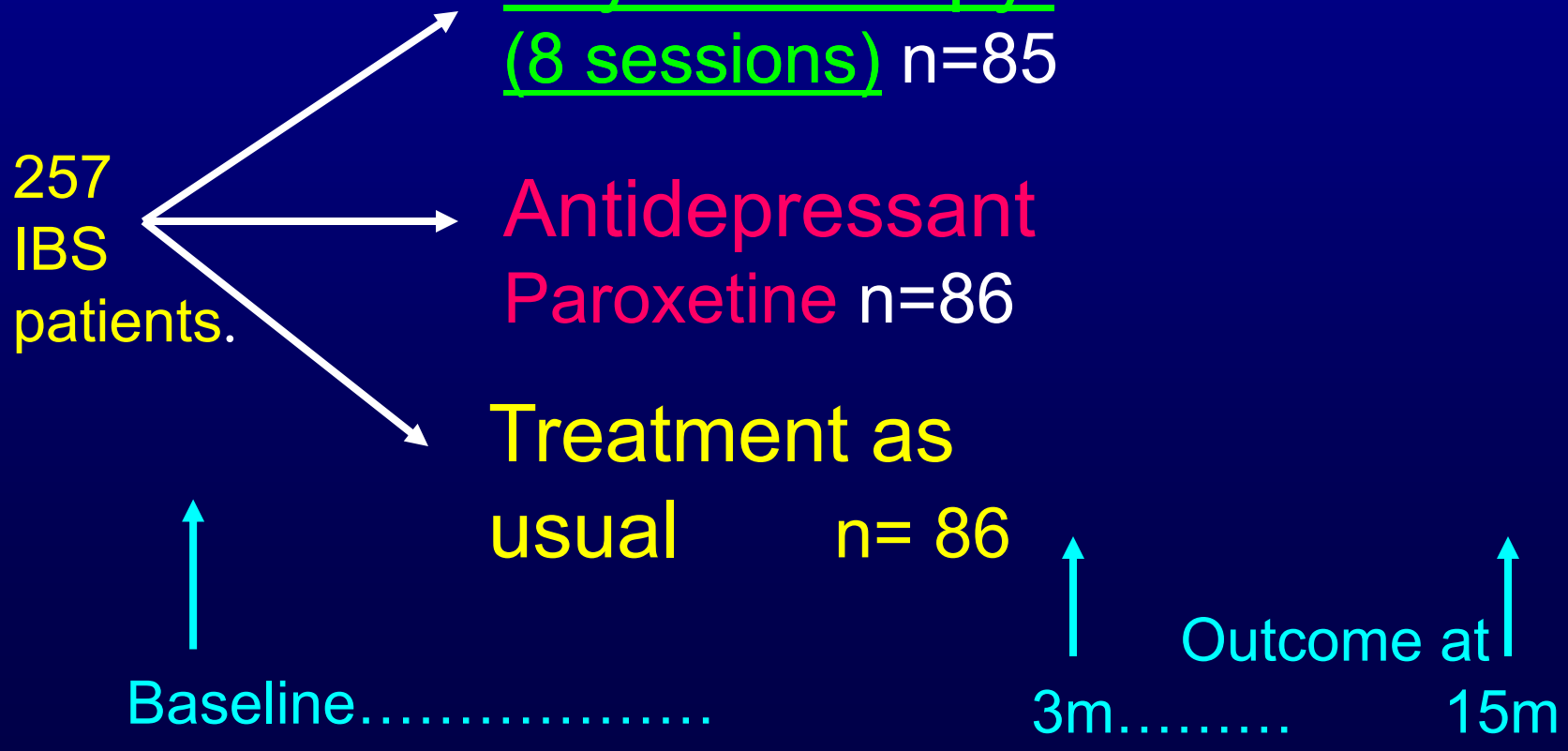
Randomised Controlled Trial

Creed et al *Gastroenterology 2003 124: 303-317*



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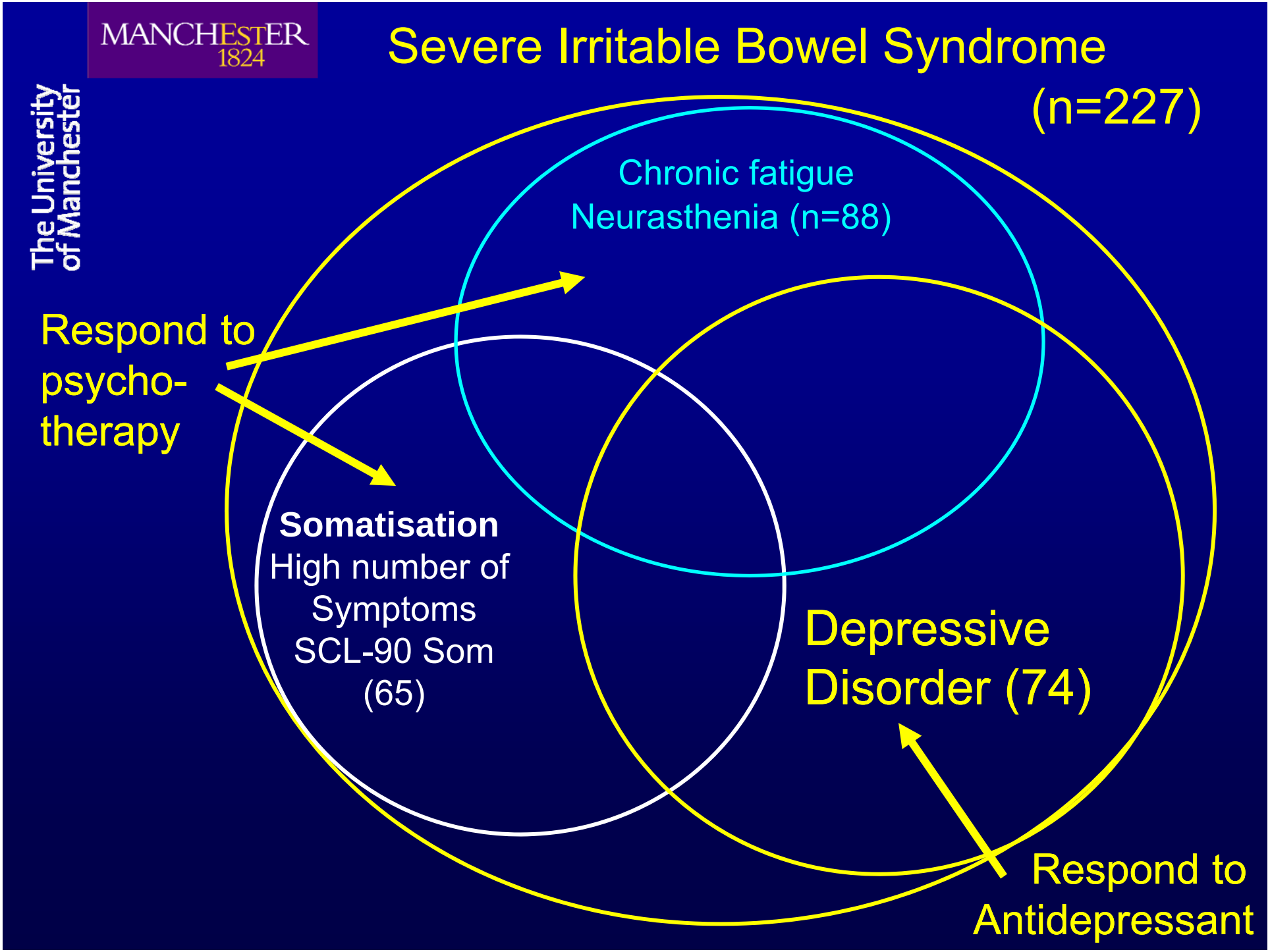
Overall result

Creed et al *Gastroenterology 2003 124: 303-317*

- In the long-term:
- Antidepressant and psychotherapy →

- Significant improvement in:
- Health status at no additional costs

- But this result cannot be explained simply by improved abdominal pain and depression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Severe Irritable Bowel Syndrome (n=227)
Chronic fatigue Neurasthenia (n=88)
Respond to psycho-therapy
Somatisation
High number of Symptoms
SCL-90 Som (65)
Depressive Disorder (74)
Respond to Antidepressant

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Practice point

- In patients with Irritable bowel syndrome + depressive disorder:
- If depressive disorder is adequately treated → reduced pain and improved quality of life.
- So must treat depression energetically
- SSRI > psychotherapy in reduction of depression at 3 months

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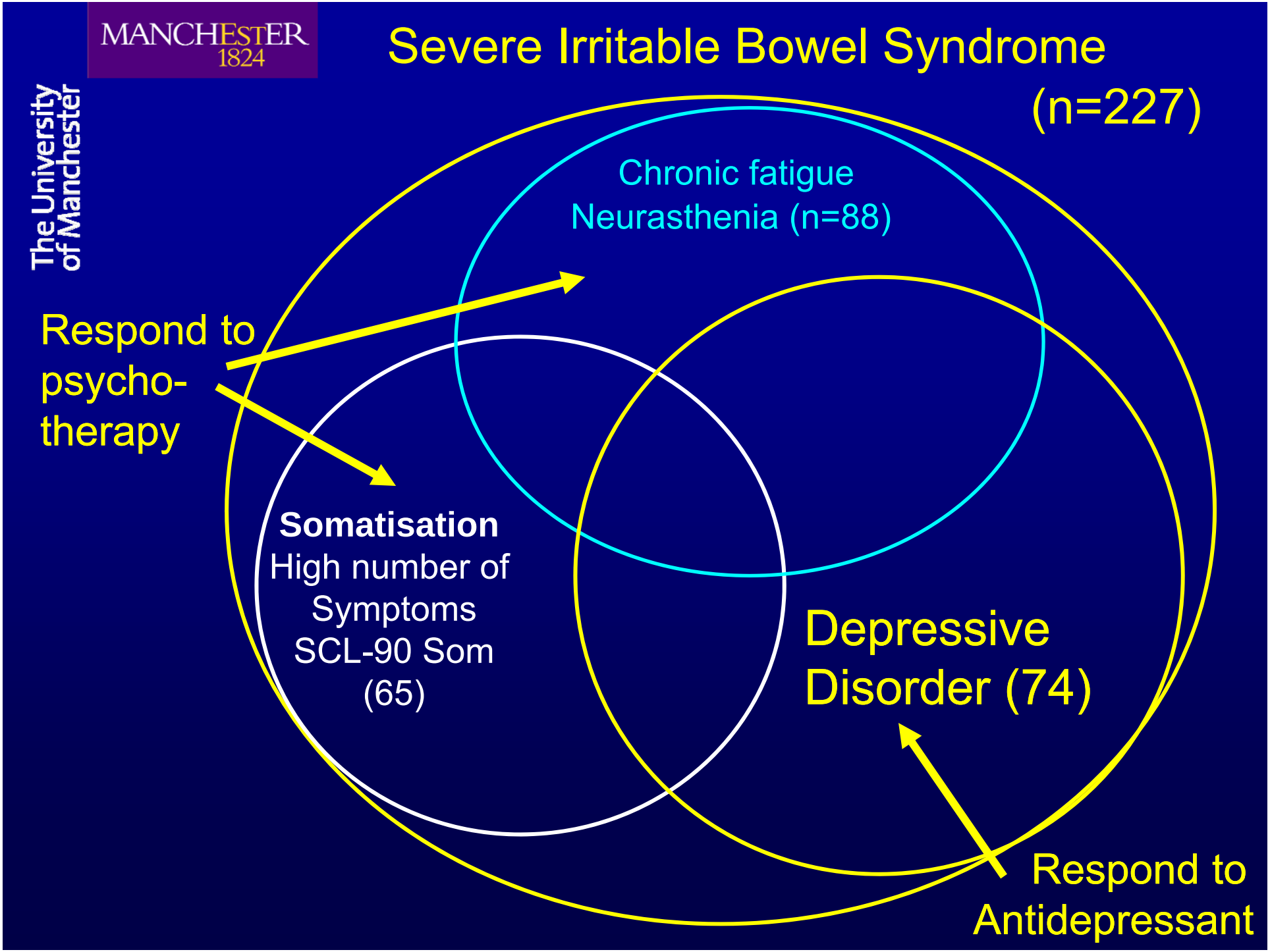
Psychiatric diagnosis (n=257)

- 29% depressive disorder]
- 12% panic disorder] 41.6%
- 14% gen. anxiety disorder]
- 9% hypochondriasis
- 12% severe 23% touch sex abuse
- 25% top quartile somatisation
- 35% neurasthenia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- 12% severe 23% touch sex abuse – mediated by
- 25% top quartile somatisation
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Conclusion re history of sexual abuse

- Patients with a reported history of sexual abuse do particularly well with psychotherapy (NB small numbers)
- Change mediated by somatisation

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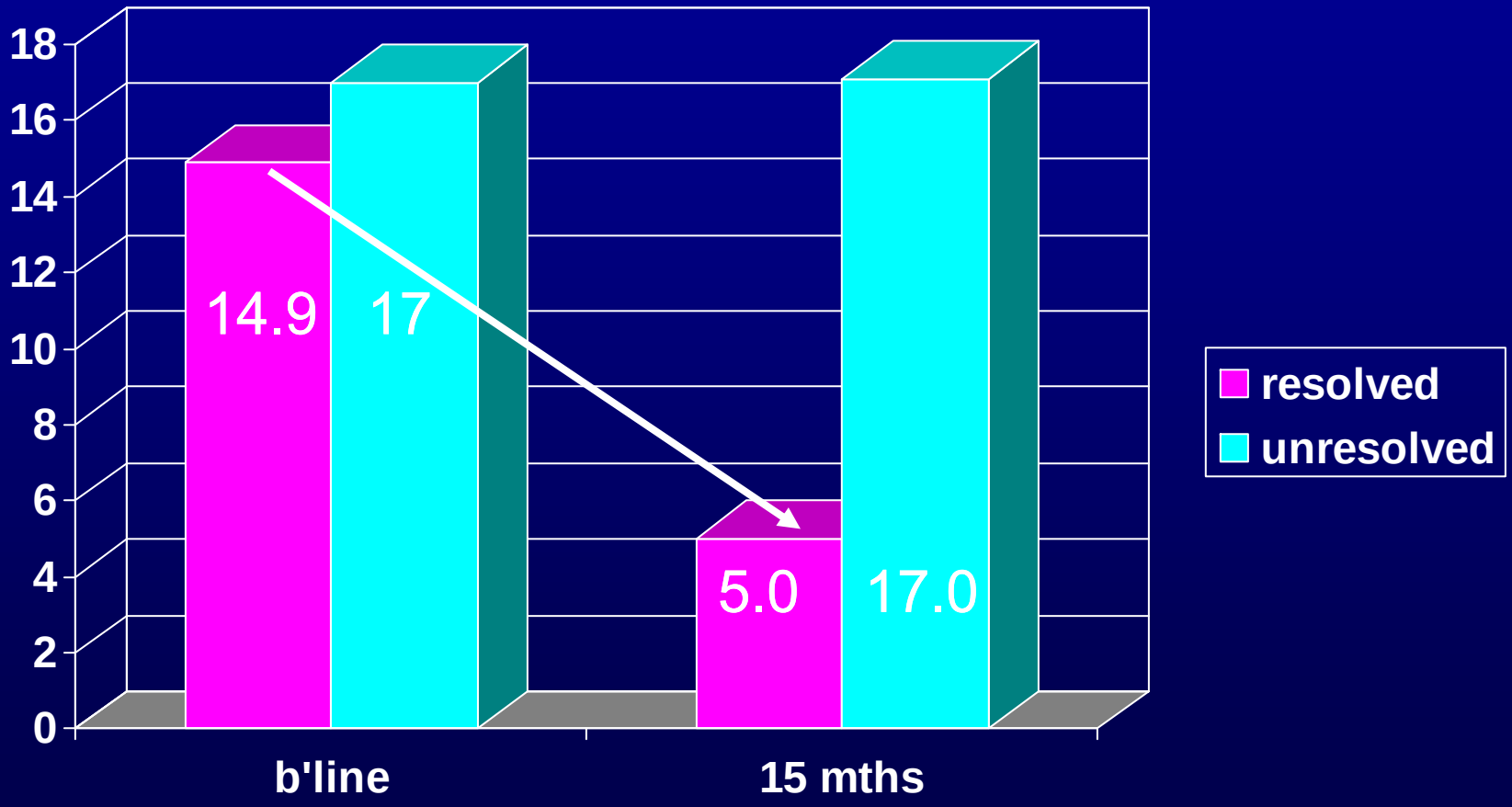
Depressive disorder (29%): 35 resolved 47 unresolved – change on Hamilton Rating Scale



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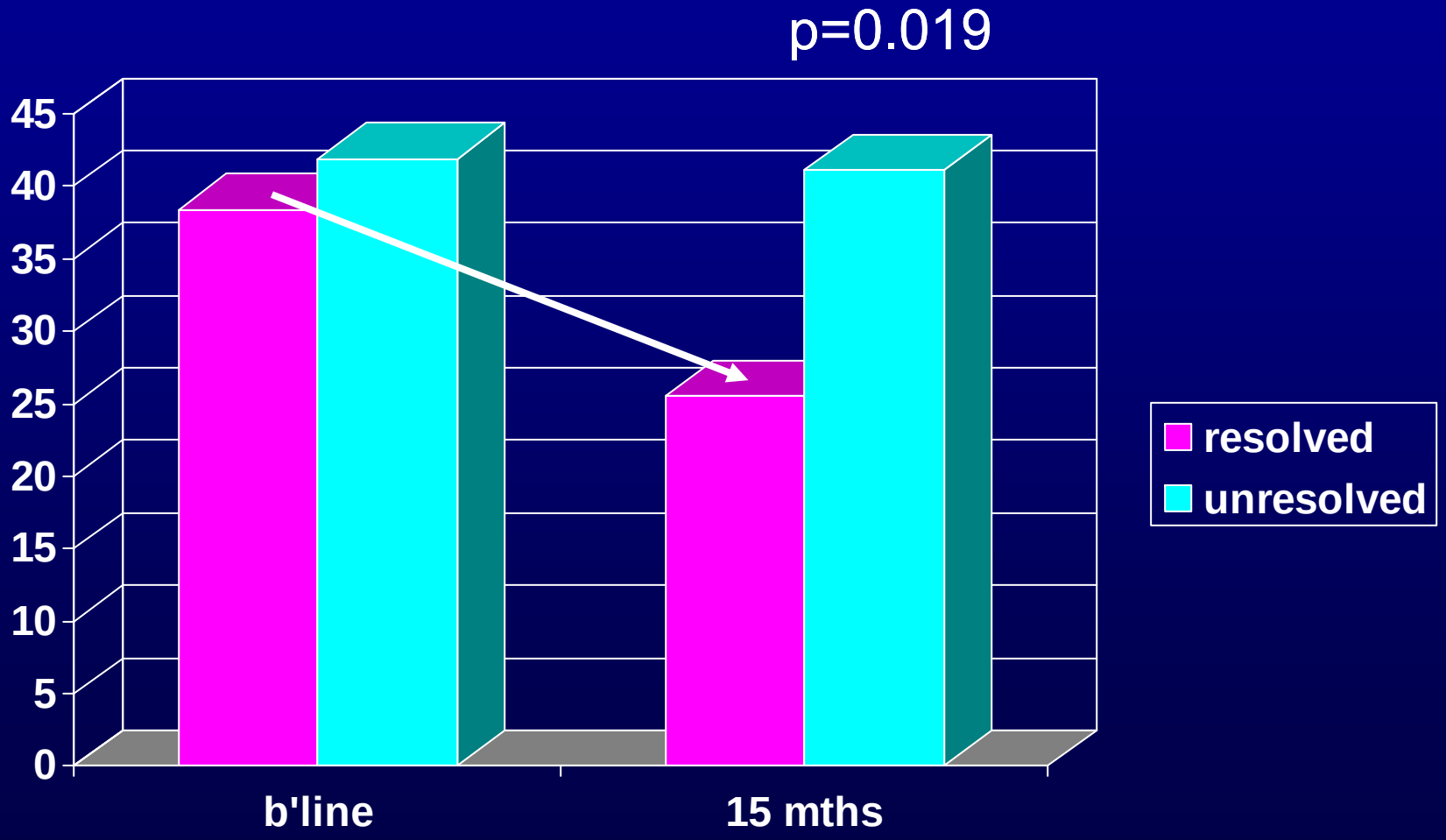
Depressive disorder - resolved v unresolved: Abdominal pain VAS



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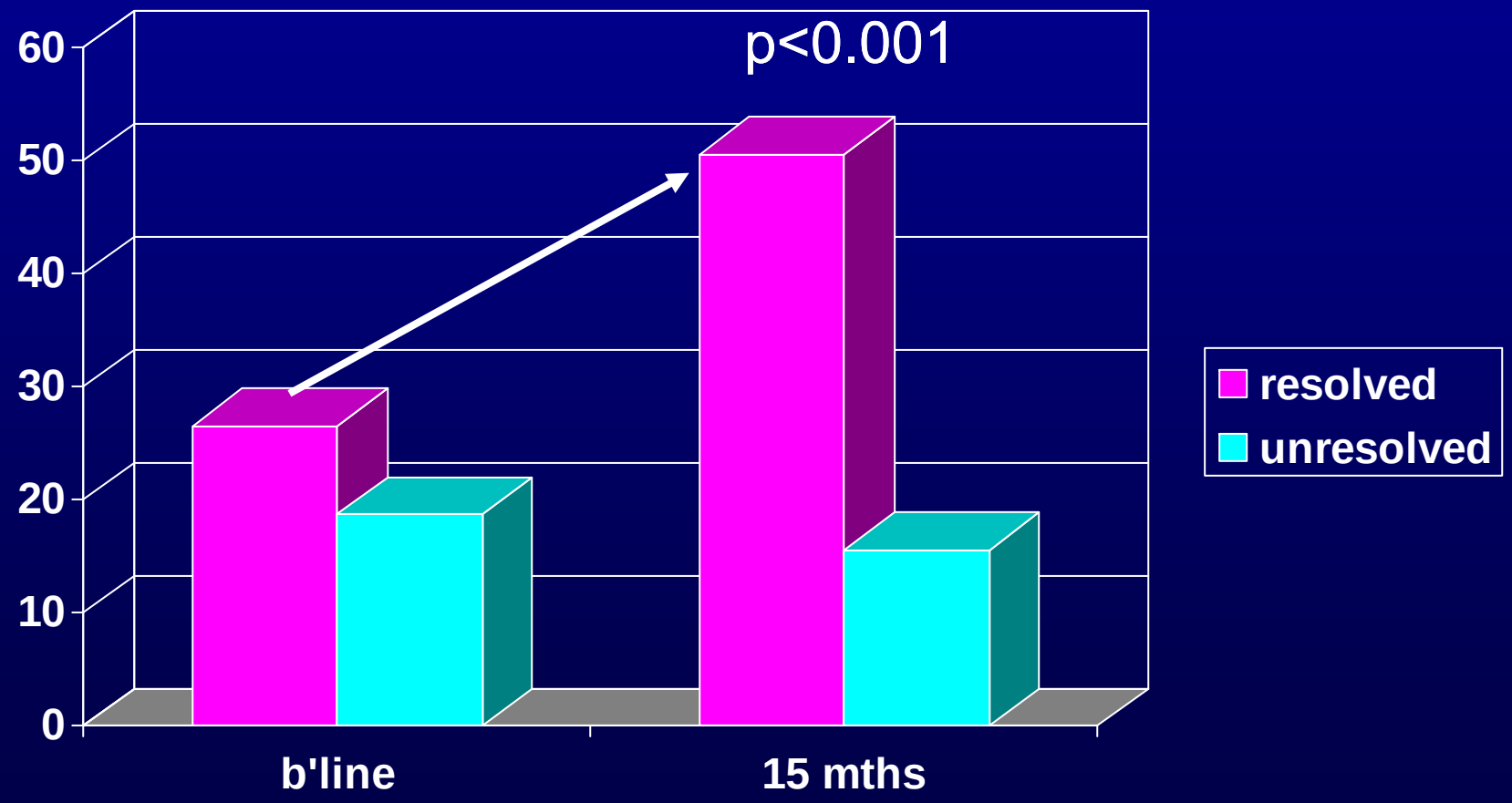
Depressive disorder - resolved v unresolved: SF36 role limitation score



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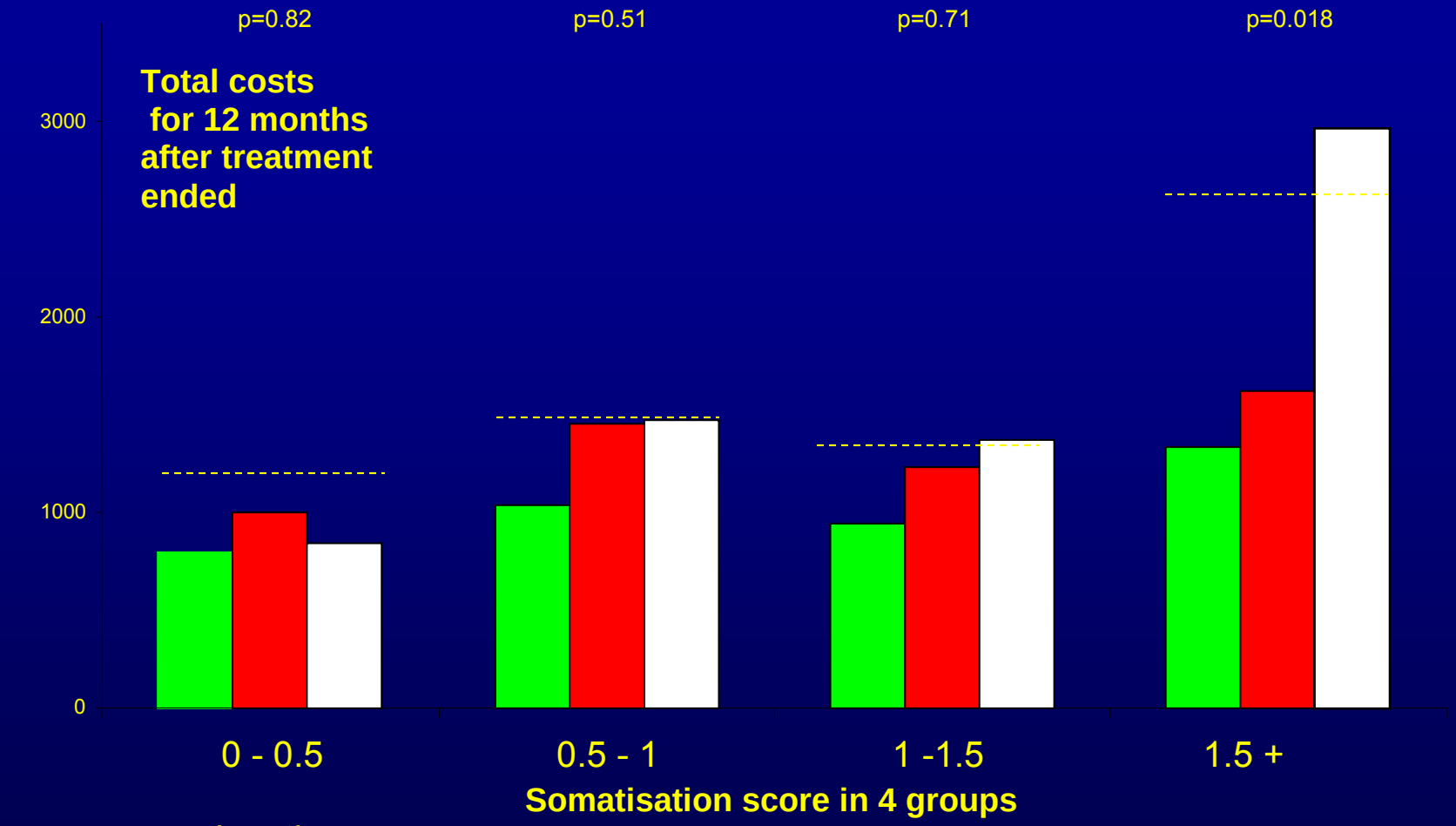
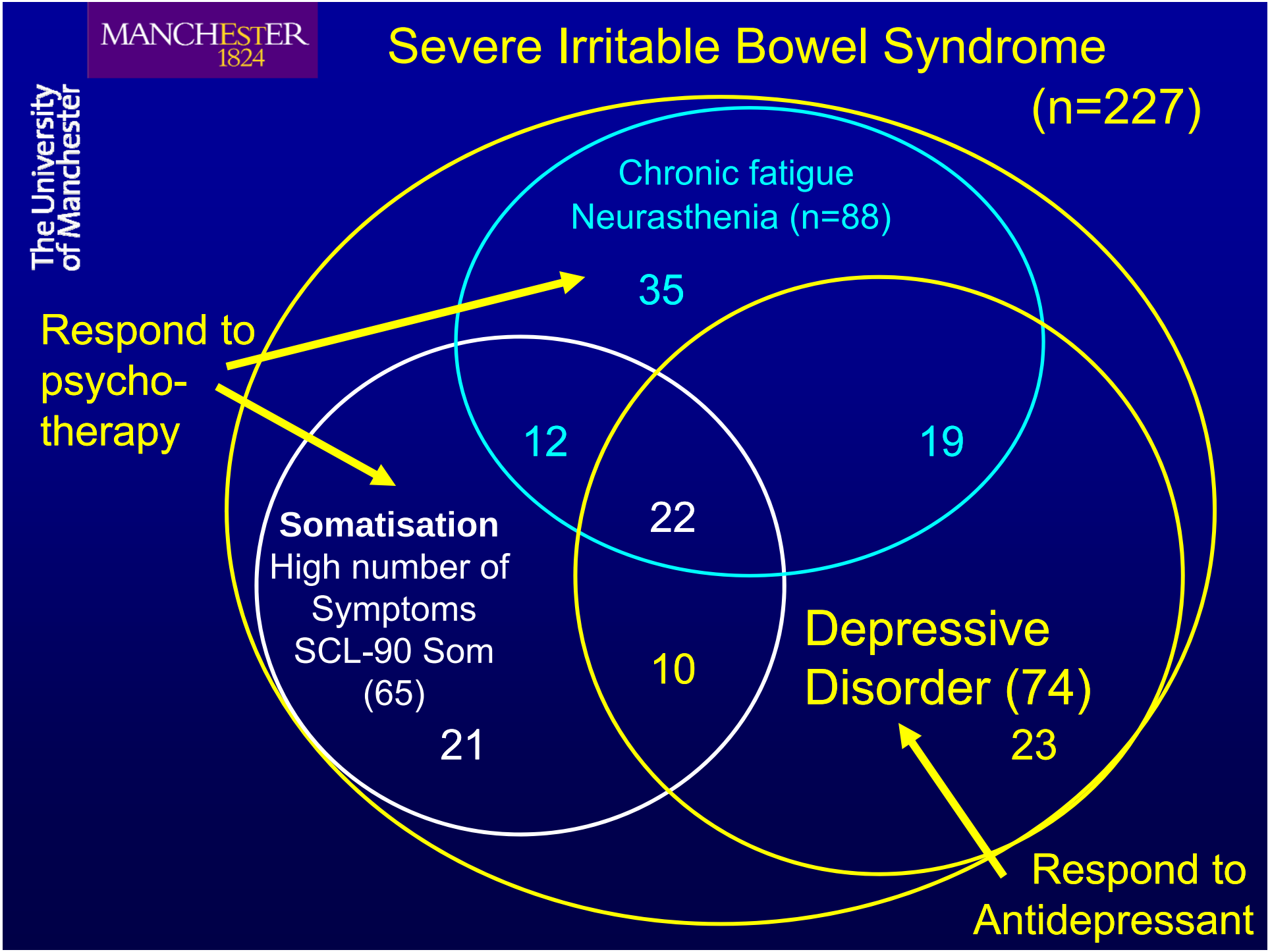
Total costs for 12 months after treatment *



* adj for age, sex, education, depression, panic and GAD abuse history, baseline SF-36 PCS

Psychotherapy Antidepressant Rx as usual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Severe Irritable Bowel Syndrome
(n=227)
Chronic fatigue
Neurasthenia (n=88)
35
Respond to psycho-therapy
12
19
22
Somatisation
High number of Symptoms
SCL-90 Som (65)
21
10
Depressive Disorder (74)
23
Respond to Antidepressant

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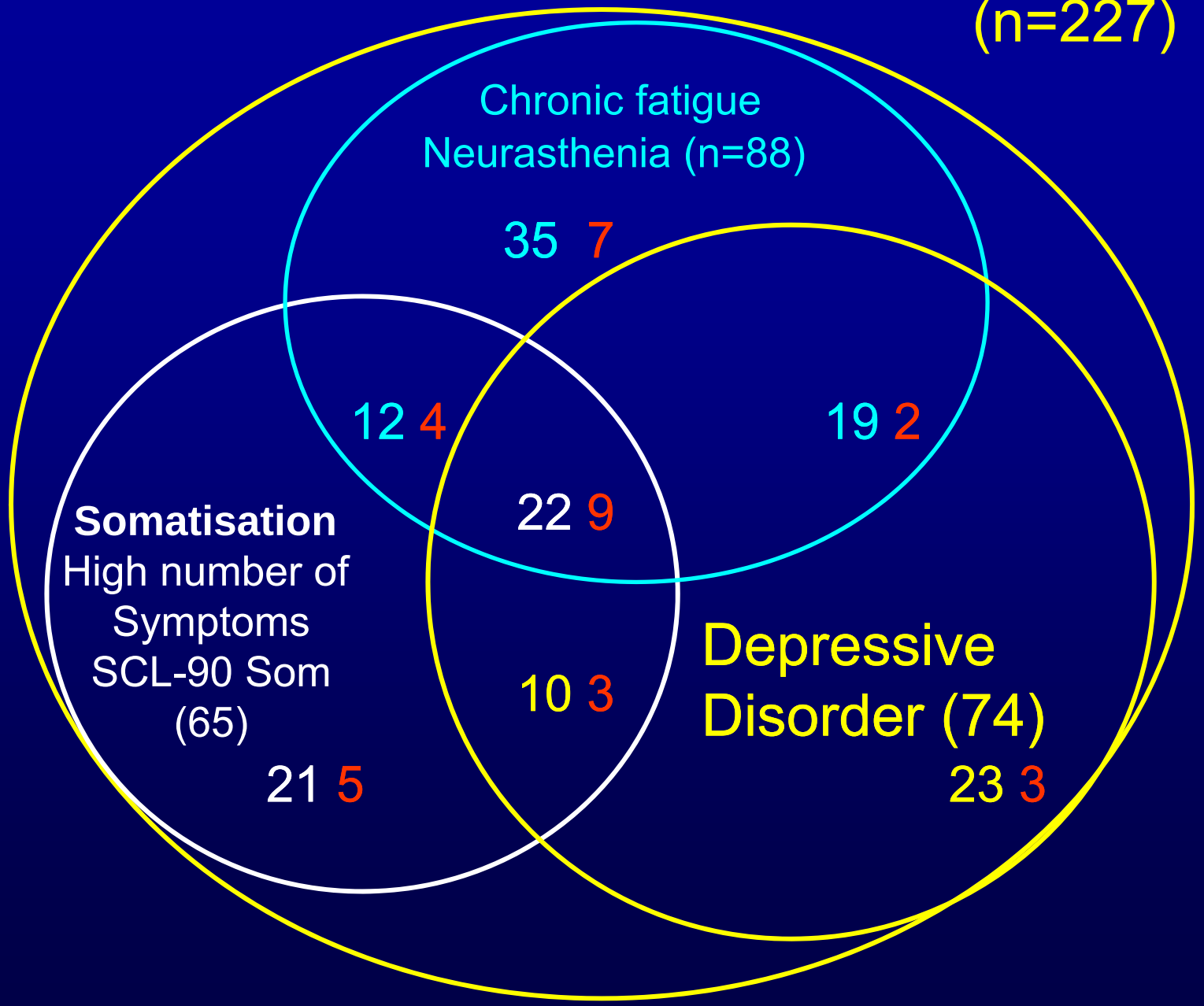
Severe Irritable Bowel Syndrome (n=227)



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Practice point

- Unexplained symptoms/syndromes respond to antidepressants
- And / or CBT.

- If one doesn't work try the other or combination

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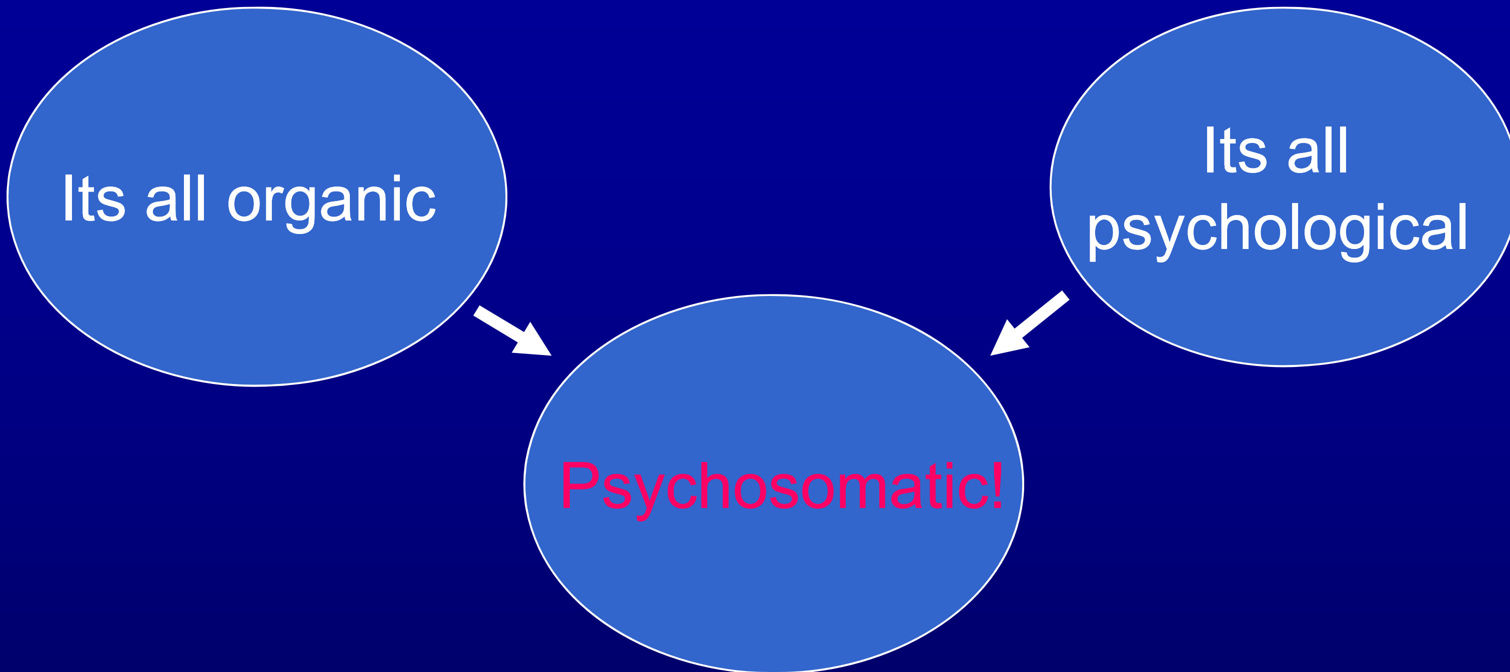
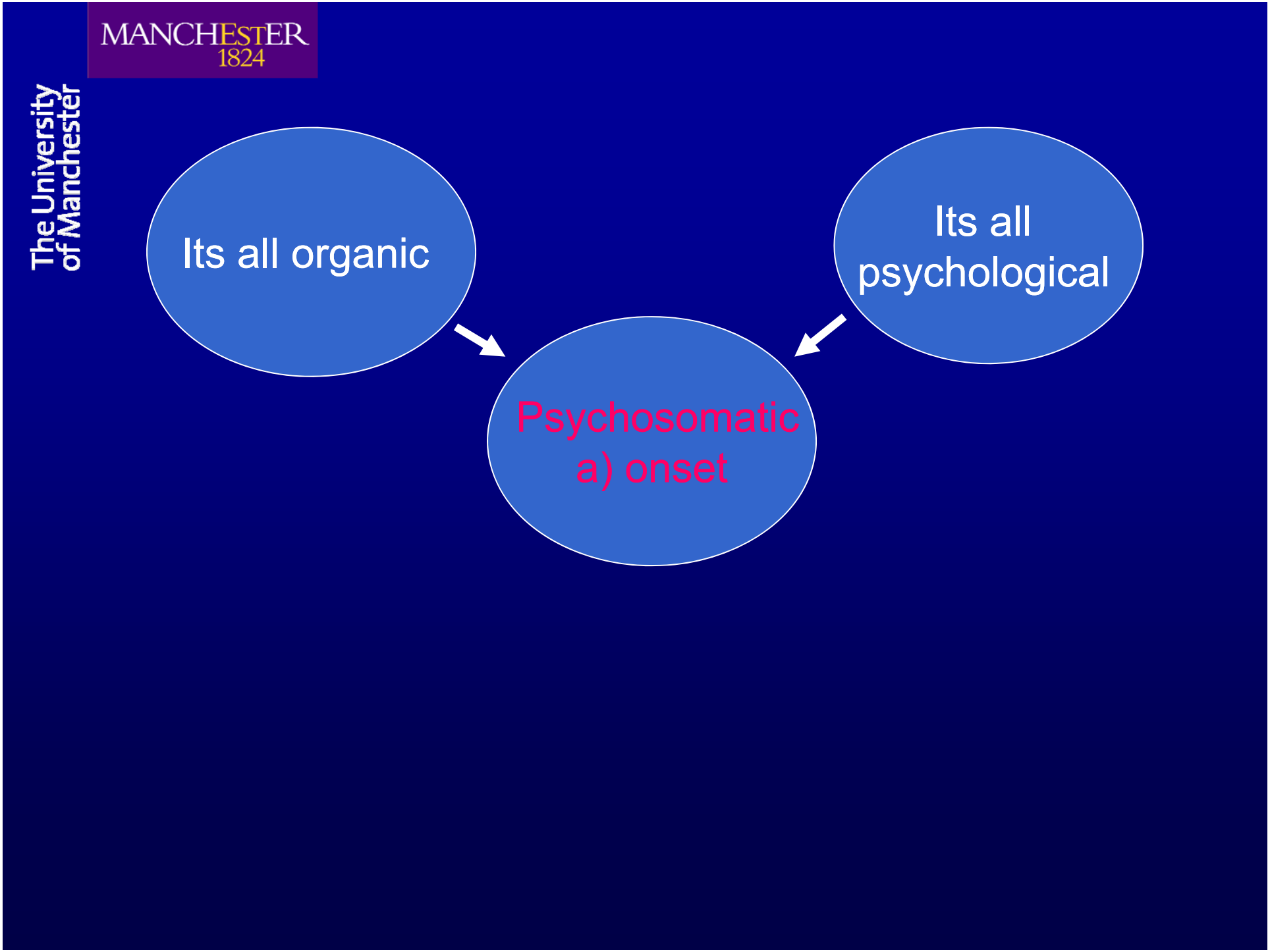
MUS a major problem in medicine

- Why such little progress in explaining?
- Definition of Somatisation disorder
- Dualism - separating mind & body
- The way ahead
- A Psychosomatic perspective
- A New Classification?


Its all organic
Its all psychological
Psychosomatic!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Its all organic
Its all psychological
Psychosomatic
a) onset

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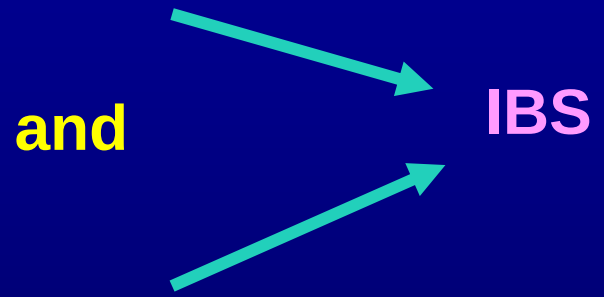
Aetiological model of IBS

- Inflammation – post infective



- Psychological factors

- Data suggest an interaction between infection and psychosocial factors

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Correlates of new onset post-infective IBS

EC cells:
1-sd increase 3.8-fold
(95% CI, 1.3–7.5)

OR=3.8

HADS anxiety & depression
1-sd increase 3.2- fold
(95% CI, 1.8–8.2)

OR=3.2

Post-infective IBS

Dunlop et al. Gastroenterology 2003; 125: 1651-9

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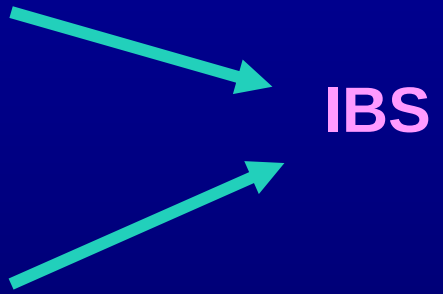
Aetiological model of IBS

- Inflammation – post infective

  specific?

- Psychiatric symptoms



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Specificity hypothesis

Moss Morris 2006

Acute illness		6 months
Campylobacter		11% IBS
gastroenteritis	→	5% Chronic fatigue
Infectious		8% IBS
mononucleosis.	→	8% CF

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Infection and anxiety predict IBS/CF

Moss Morris 2006

	3 months	6 months
Infection with Campylobacter	3.3 (1.6 – 6.4)	2.4 (1.2 – 4.9)
IBS		
Anxiety	2.4 (1.4 – 3.9)	1.8 (1.05 – 3.2)
Infectious Mononucleosis	2.6 (1.0 – 7.1)	1.3 (0.5 – 3.2)
CFS		
Anxiety	2.6 (1.5 – 6.9)	2.6 (1.2 – 5.3)

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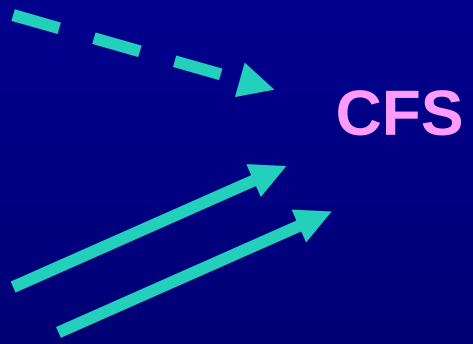
Aetiological model of CFS

Post infective (IM)



- Psychological factors

Associated with persistence also?

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Population-based study of functional somatic syndromes (n=632)

- Predictors of persistent CWP:
- SSI (numerous somatic symptoms)

- Predictors of persistent chronic fatigue: childhood abuse, Neuroticism, depression & SSI (number of somatic symptoms).

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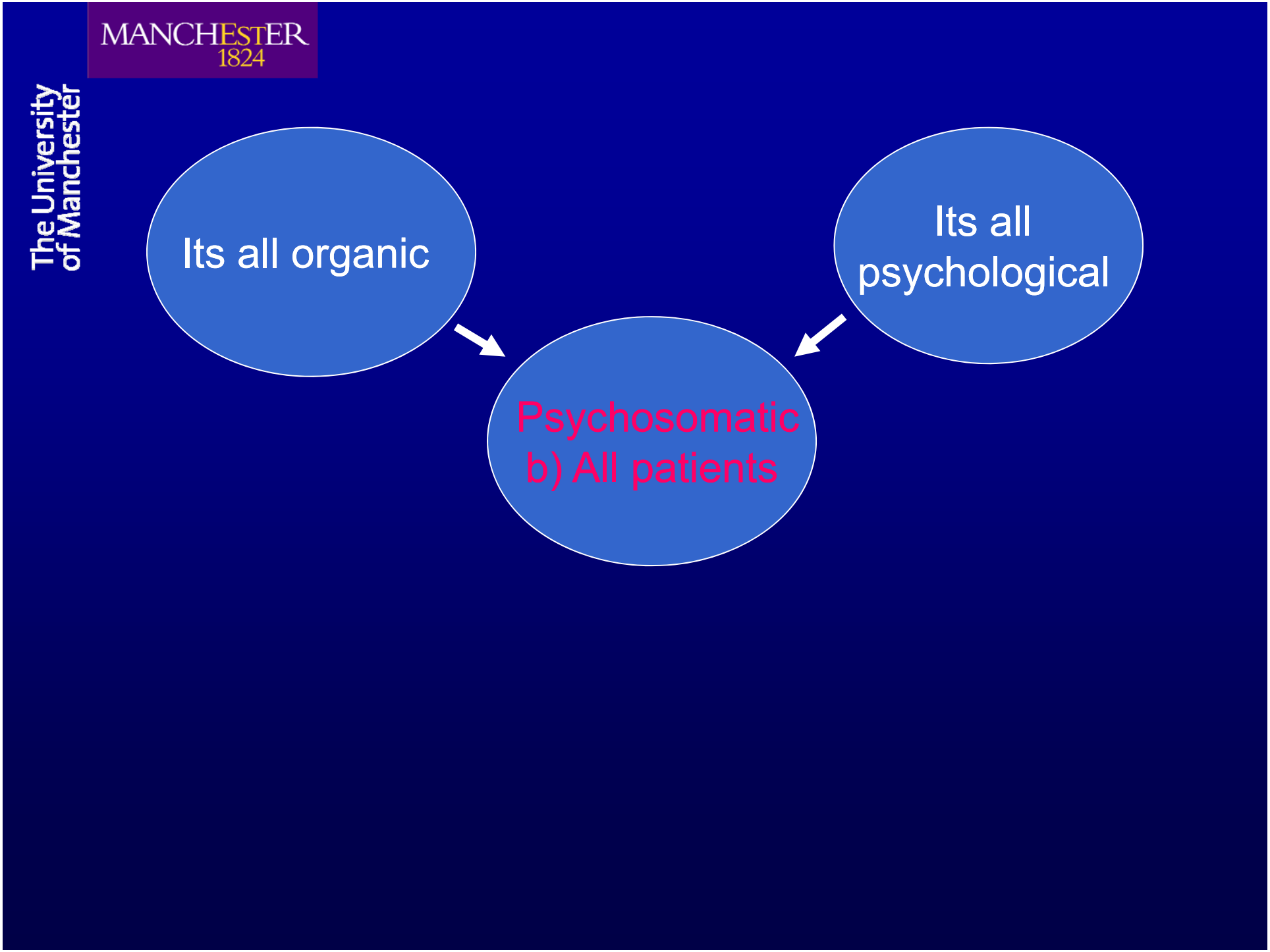
Post-infective IBS & CFS? Psychosomatic model - onset

- But only c. 14% of IBS patients have post-infective IBS.
- Same in Chronic fatigue syndrome?

- One pathophysiological pathway to chronic fatigue syndrome.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Its all organic
Its all psychological
Psychosomatic
b) All patients

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- Include all patients?
- …with Medically Unexplained symptoms
- and
- … with symptoms are explained by organic disease?

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Medical out-patients: Neurology, Cardiology & Gastroenterology

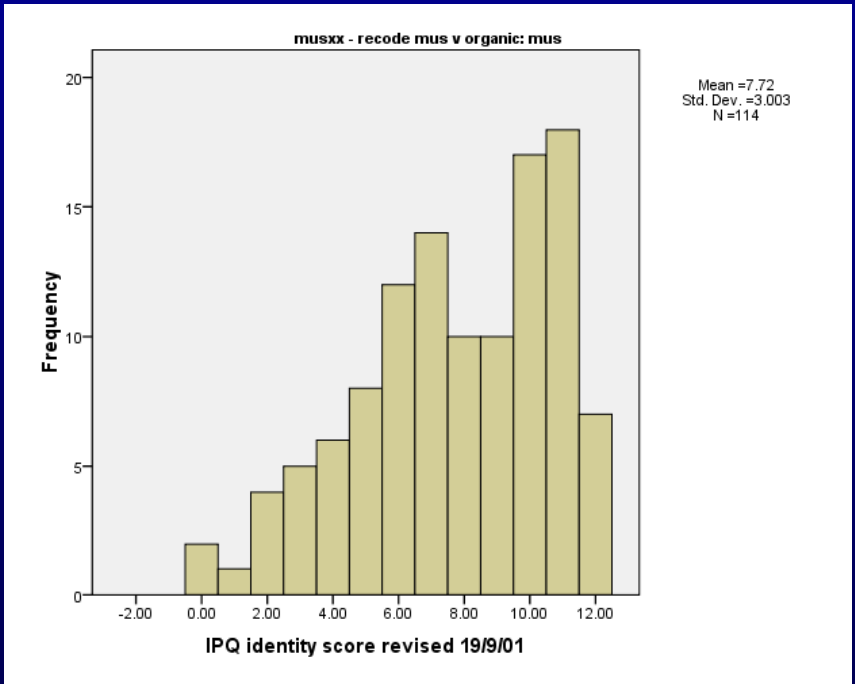
Fiddler et al Gen Hosp Psych 2004
Jackson et al J Psychosom Res. 2006

- 181 - organic - Multiple Sclerosis, stroke, ischaemic Heart Disease, inflammatory bowel disease
- 114 - MUS - headaches, neck/ limb pain, fatigue, parasthesiae, chest pain, breathlessness, irritable bowel syndrome, functional dyspepsia

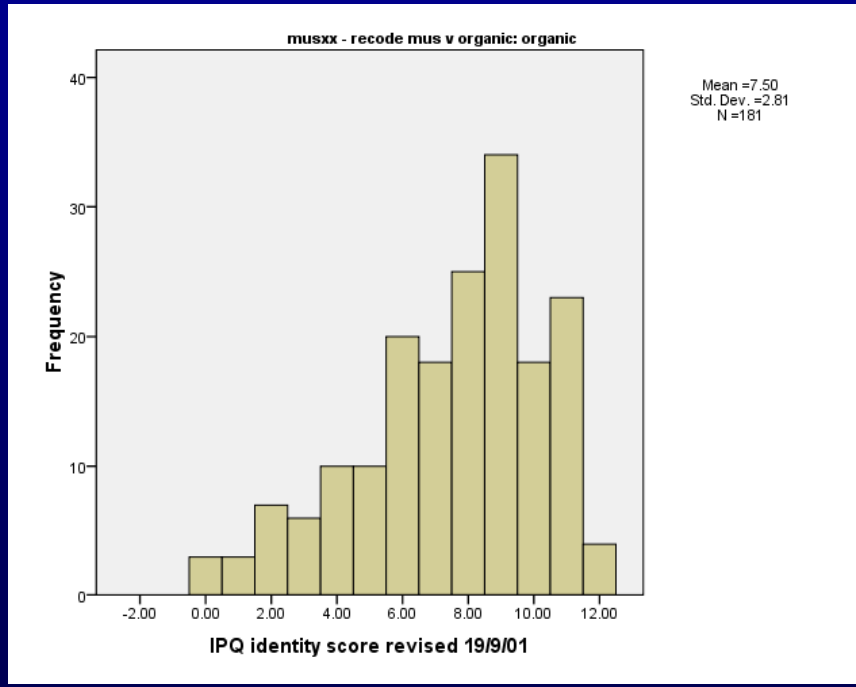
Number of bodily symptoms by patient diagnostic group

Fiddler et al Gen Hosp Psych 2004

medically unexplained (n=114)



expl. by organic disease (n=181)



Means (sd) 7.7 (3.0) 7.5 (2.8)

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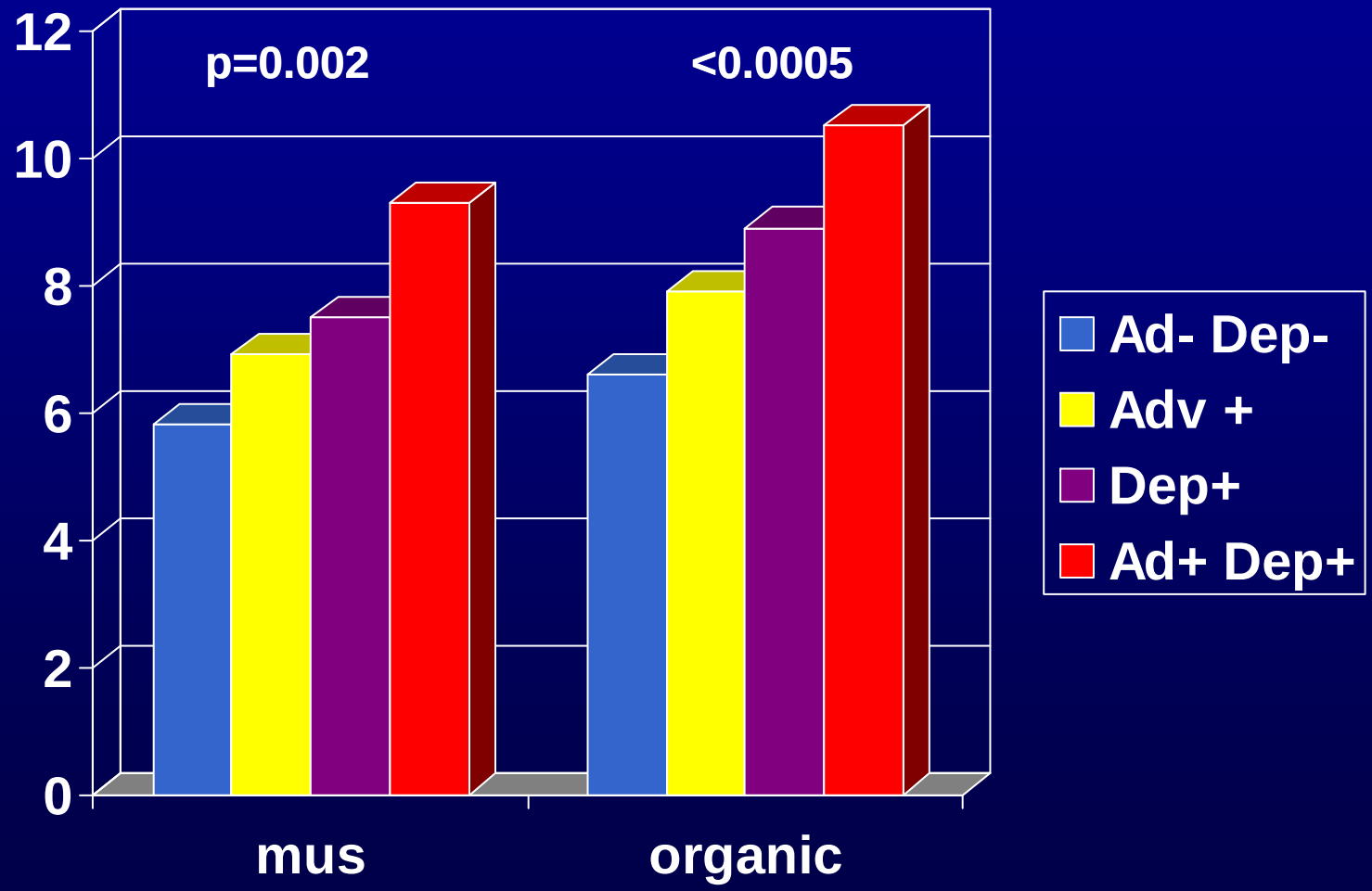
Number of bodily symptoms - childhood adversity and anx/dep as risk factors

Fiddler et al Gen Hosp Psych 2004



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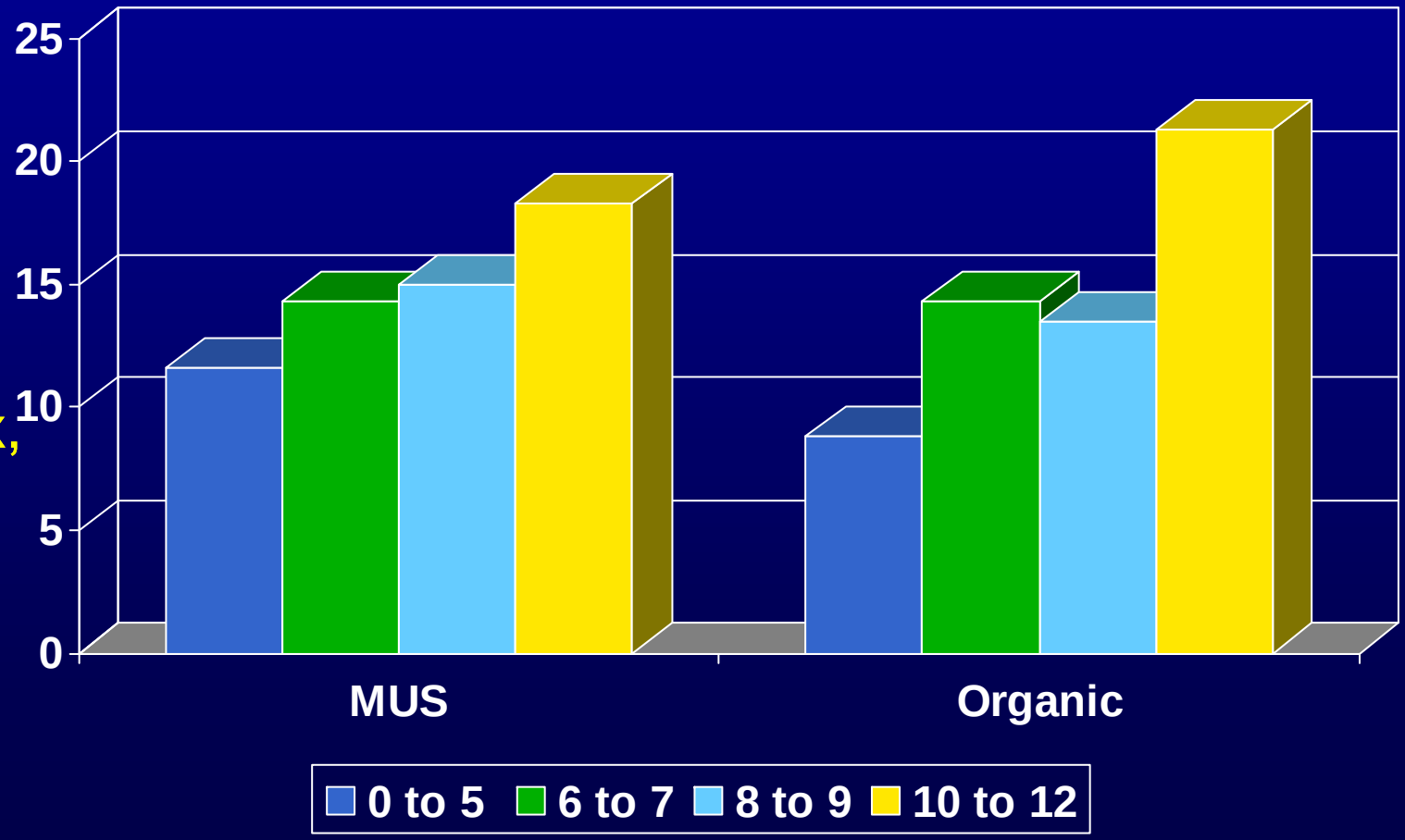
Dr visits increases with number of bodily symptoms

No. dr Visits Adjust. for Age, sex, Anx & depn



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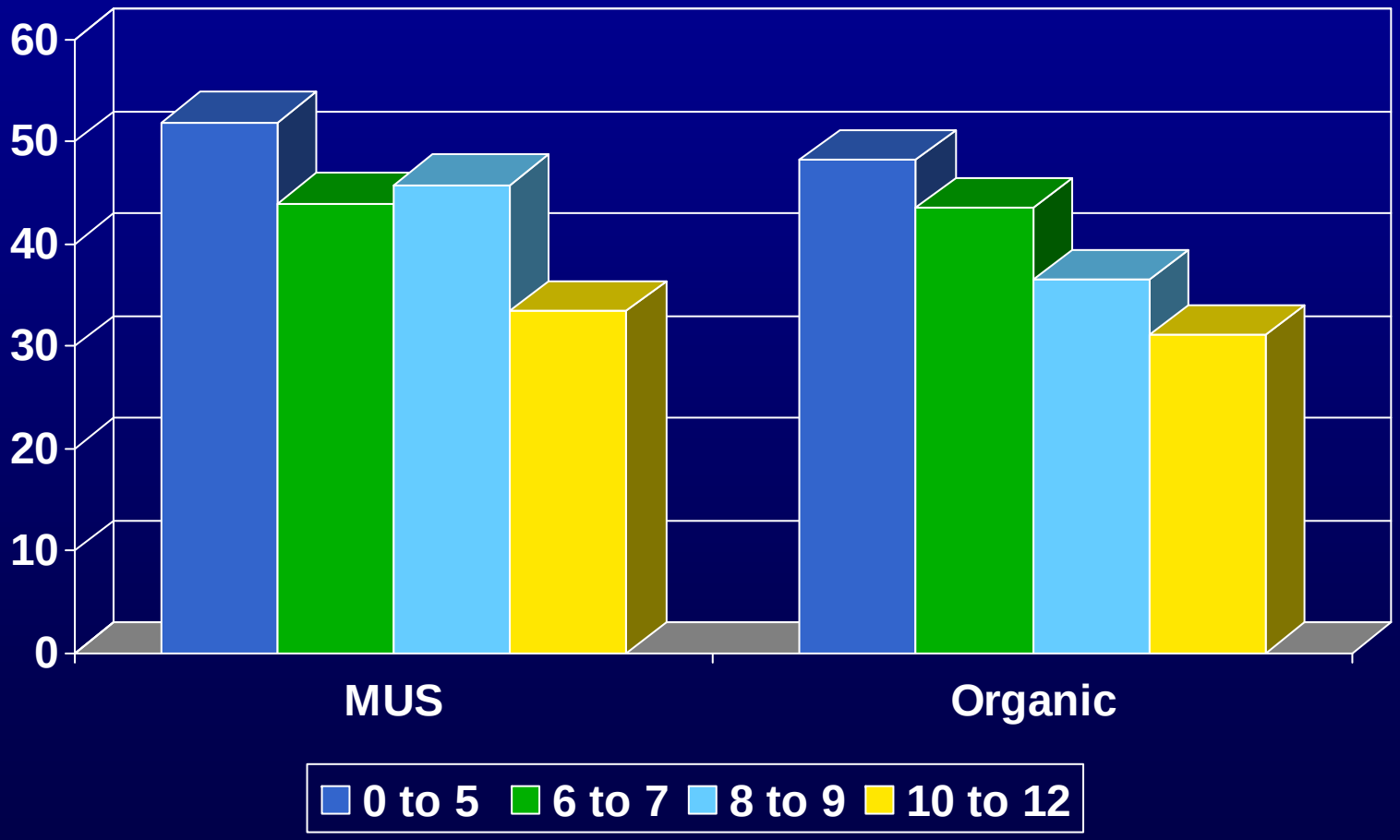
Health status impaired with many bodily symptoms

SF36 PCS Adjust. for Age, sex, Anx & depn



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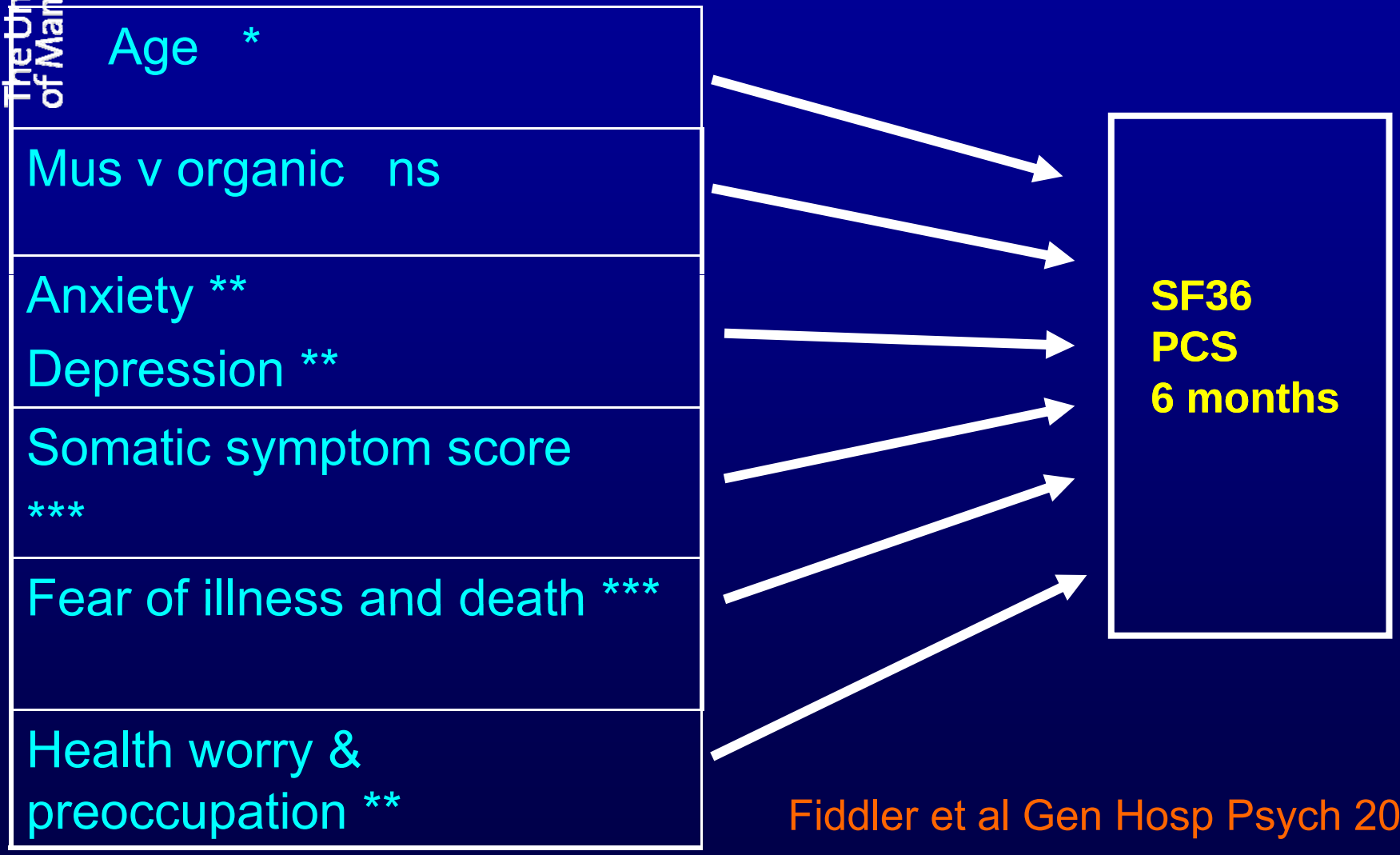
Predictors of health status



Fiddler et al Gen Hosp Psych 2004

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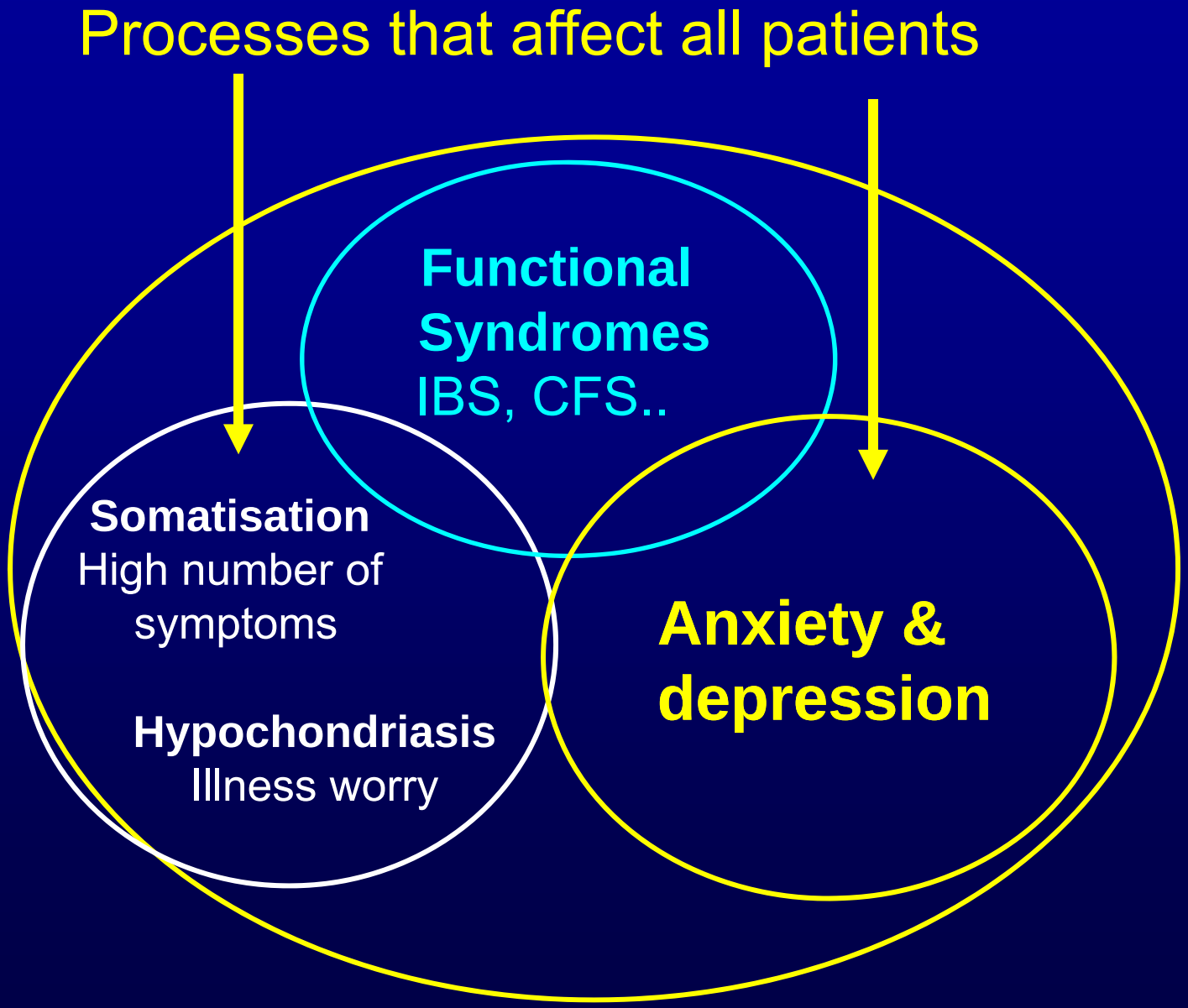
~~Medically Unexplained symptoms~~



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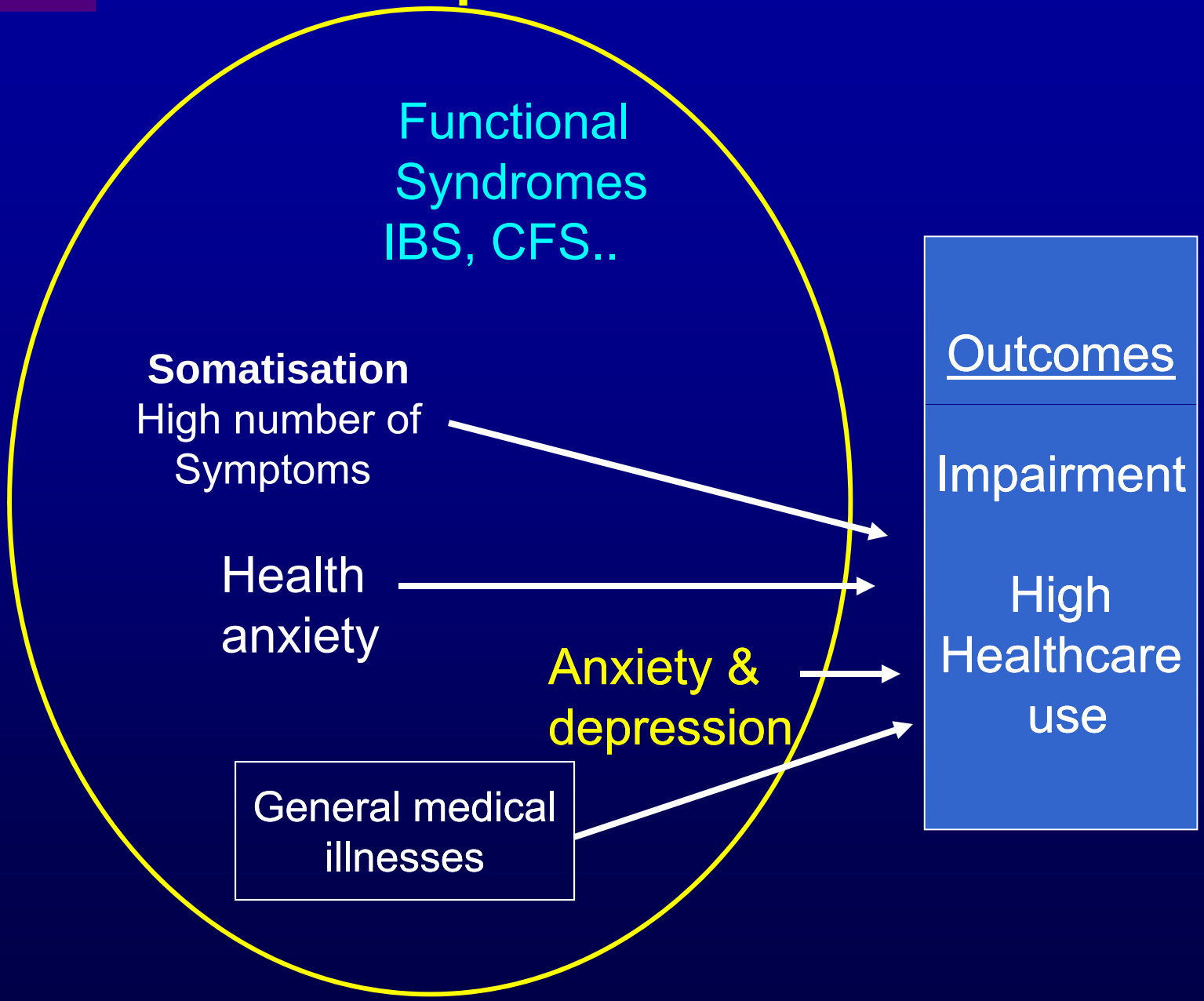
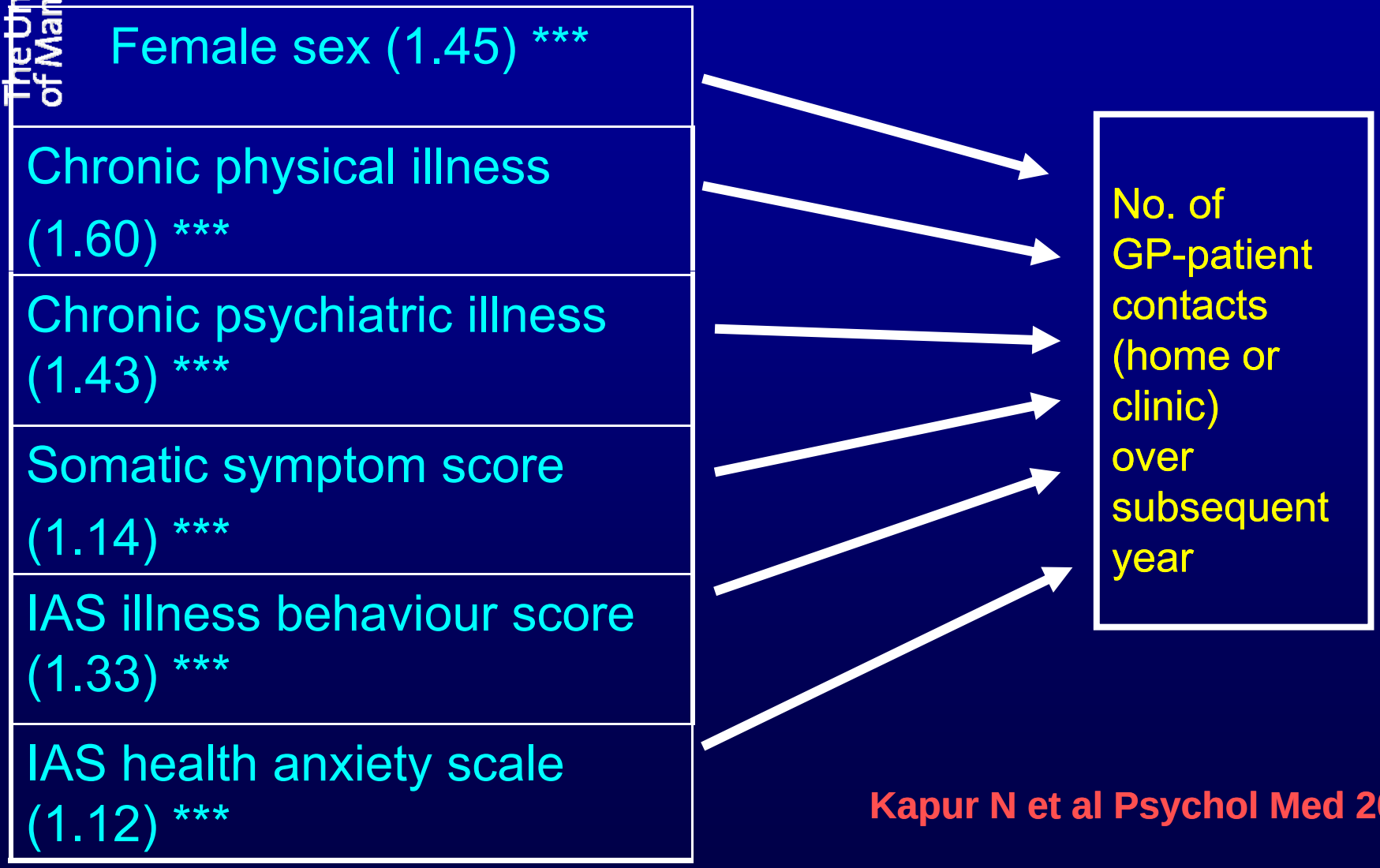
All patients



Predictors of frequency of consultation at primary care (n=738)



Kapur N et al Psychol Med 2004

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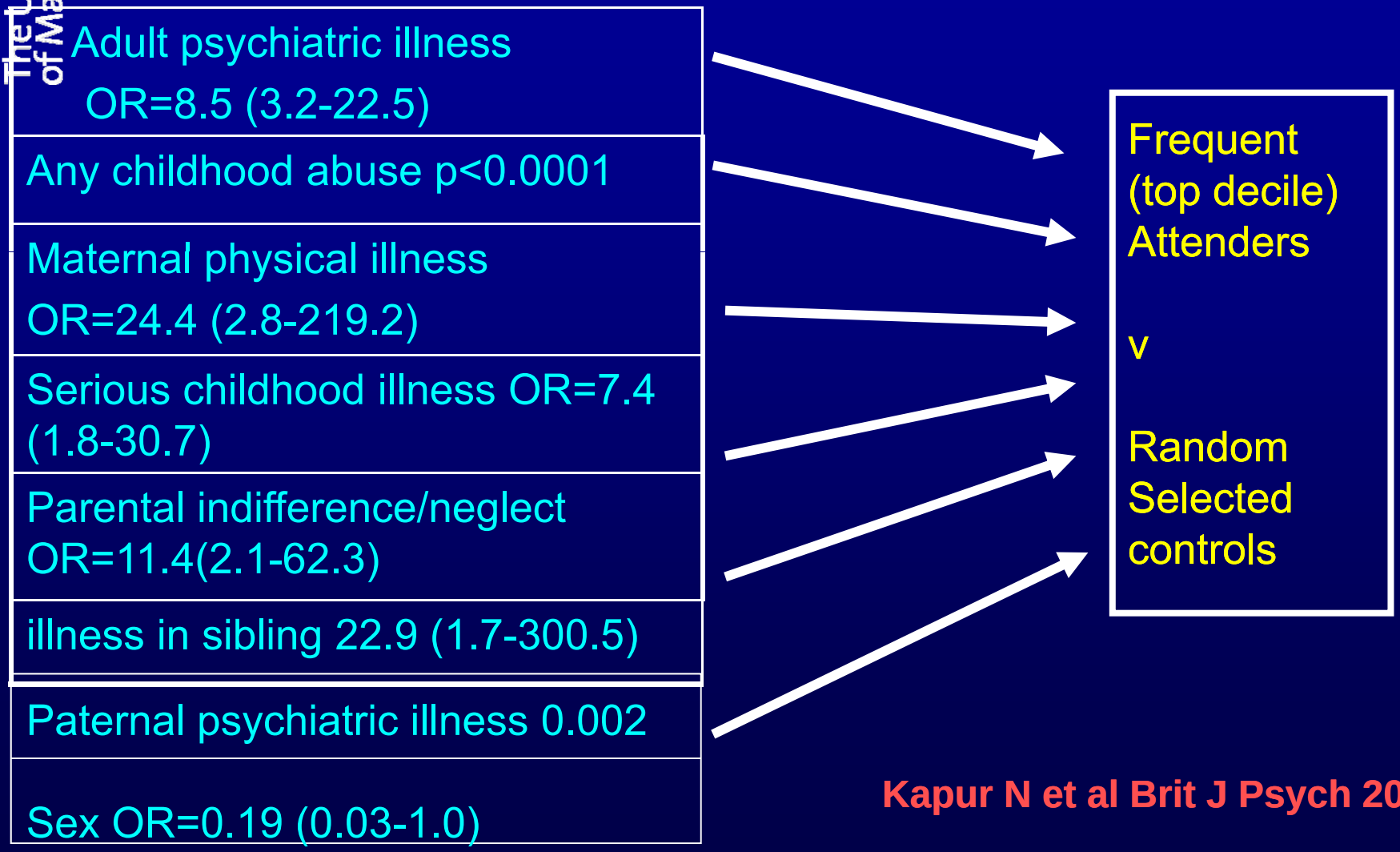
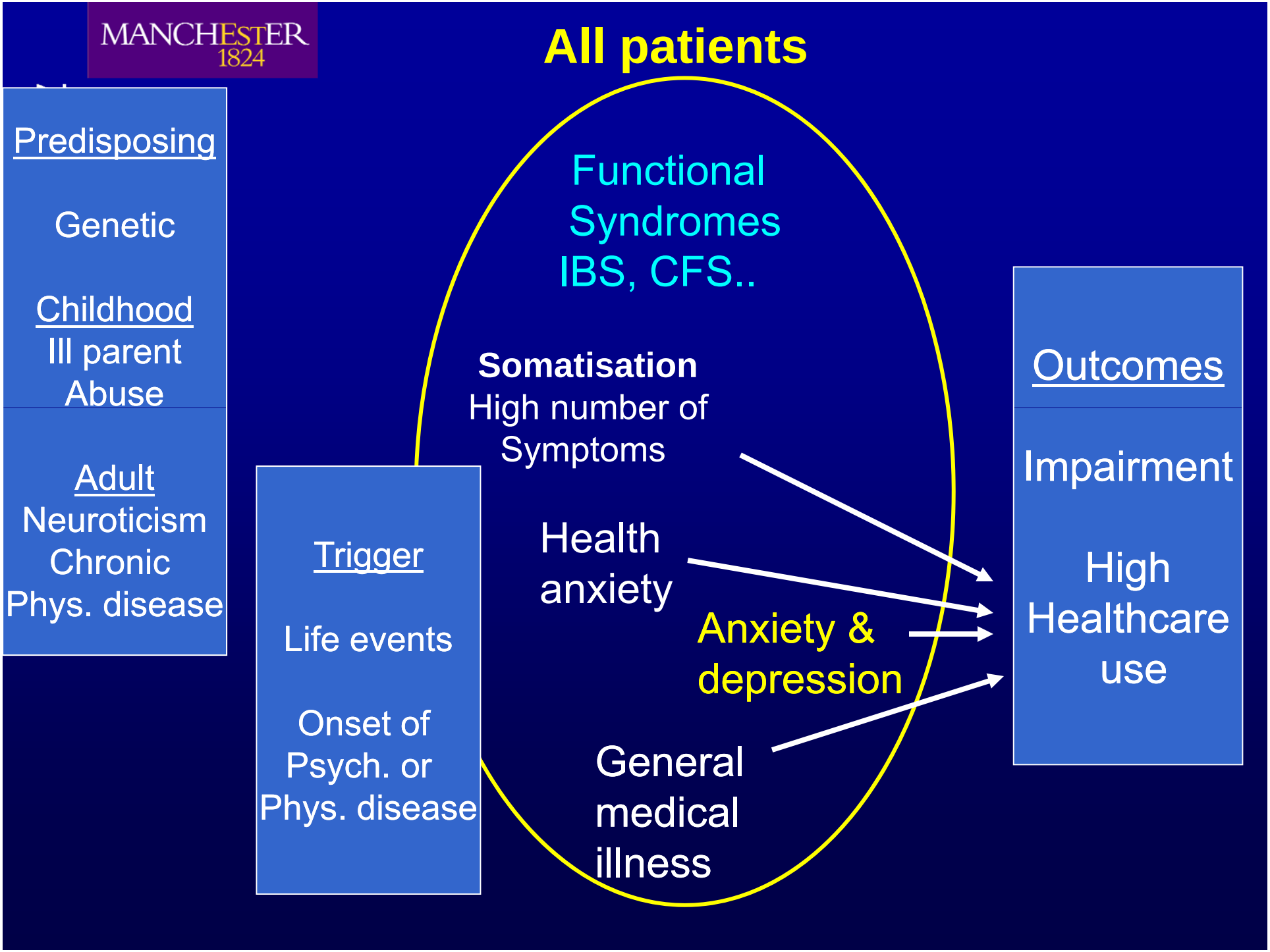
Childhood experiences and consultations at primary care



Kapur N et al Brit J Psych 2004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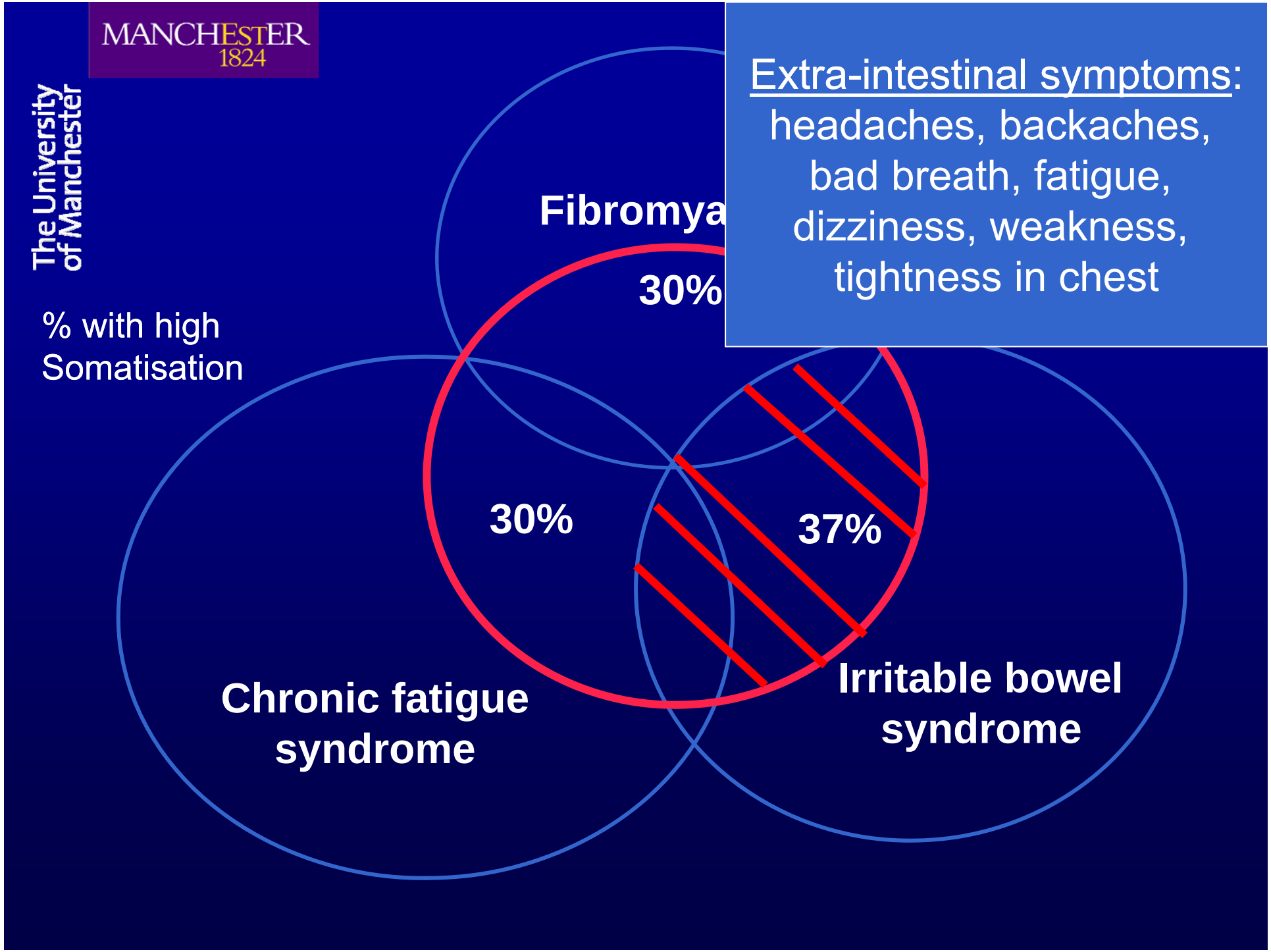
All patients
Predisposing
Genetic
Childhood
Ill parent
Abuse
Adult
Neuroticism
Chronic
Phys. disease
Trigger
Life events
Onset of
Psych. or
Phys. disease
Functional
Syndromes
IBS, CFS..
Somatisation
High number of
Symptoms
Health
anxiety
Anxiety &
depression
General
medical
illness
Outcomes
Impairment
High
Healthcare
use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% with high Somatisation
Extra-intestinal symptoms: headaches, backaches, bad breath, fatigue, dizziness, weakness, tightness in chest
Fibromya
30%
30%
37%
Chronic fatigue syndrome
Irritable bowel syndrome

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Correlates of Extra-intestinal symptoms

- 3,048 participants (twins), 371 (12.2 %) fulfilled Rome II criteria for IBS;

- Logistic regression → EIS
- Age, sex, BMI
- MDD, GAD, Panic disorder, Neuroticism (all $p<0.0005$)
- Fatigue, muscular pains, GERD, dyspepsia, IBS (all $p<0.0005$)

Lembo et al Am J Gastro 2009

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Extra-intestinal symptoms in IBS Twin study

N= 3,048	Monozygotic	Dizygotic
Age	ns	ns
gender	ns	ns
Co-twin has EIS ≥ 12	**6.82 (4.4 – 10.4)**	**2.71 (1.7 – 4.4)**
Neuroticism	1.14 (1.1 – 1.2)	1.27 (1.2 – 1.4)
Psych. Dis.	4.17 (2.3 – 7.6)	3.15 (1.8 – 5.6)
IBS	2.82 (1.7 – 4.6)	1.95 (1.1 – 3.3)

Lembo et al Am J Gastro 2009

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Genetics

Gillespie et al Psychol Med 2000

- Most genetic and environmental variance of somatic distress is shared with depression and phobic anxiety but
- "33% of genetic variance in somatic distress due to a specific gene action unrelated to depression or phobic anxiety"
- and
- "74% of individual environmental influences on somatic distress also unrelated to depression or phobic anxiety"

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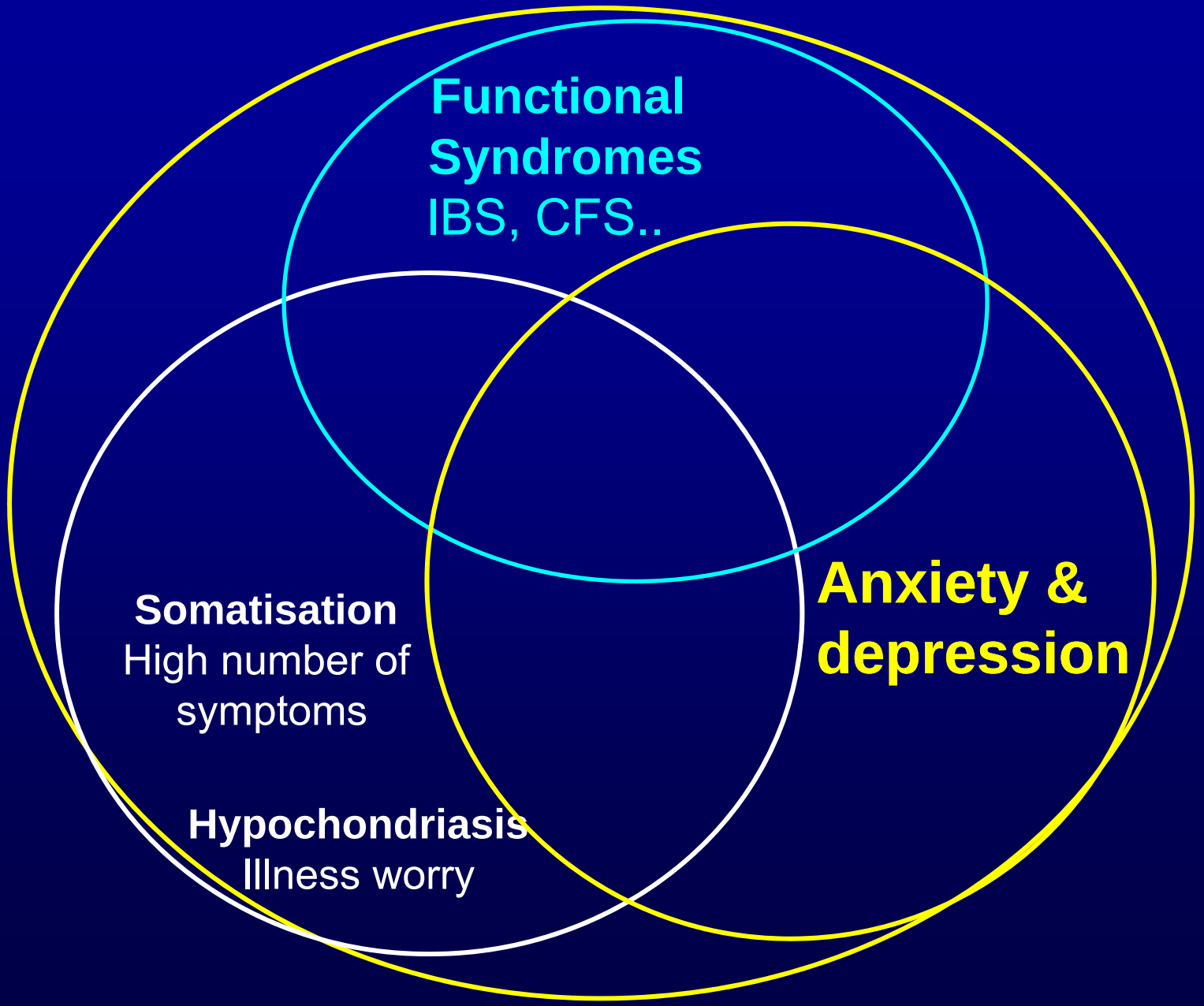
Medically Unexplained symptoms



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MUS a major problem in medicine

- Why such little progress in explaining?
- Definition of Somatisation disorder
- Dualism - separating mind & body
- The way ahead
- A Psychosomatic perspective
- A New Classification?

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DSM-V workgroup
Somatic Symptom disorders

- Joel Dimsdale
- Arthur Barsky
- Francis Creed
- Javier Escobar
- Nancy Frasure-Smith
- Michael Irwin
- Francis Keefe
- Sing Lee
- James Levenson
- Michael Sharpe
- Lawson Wulsin

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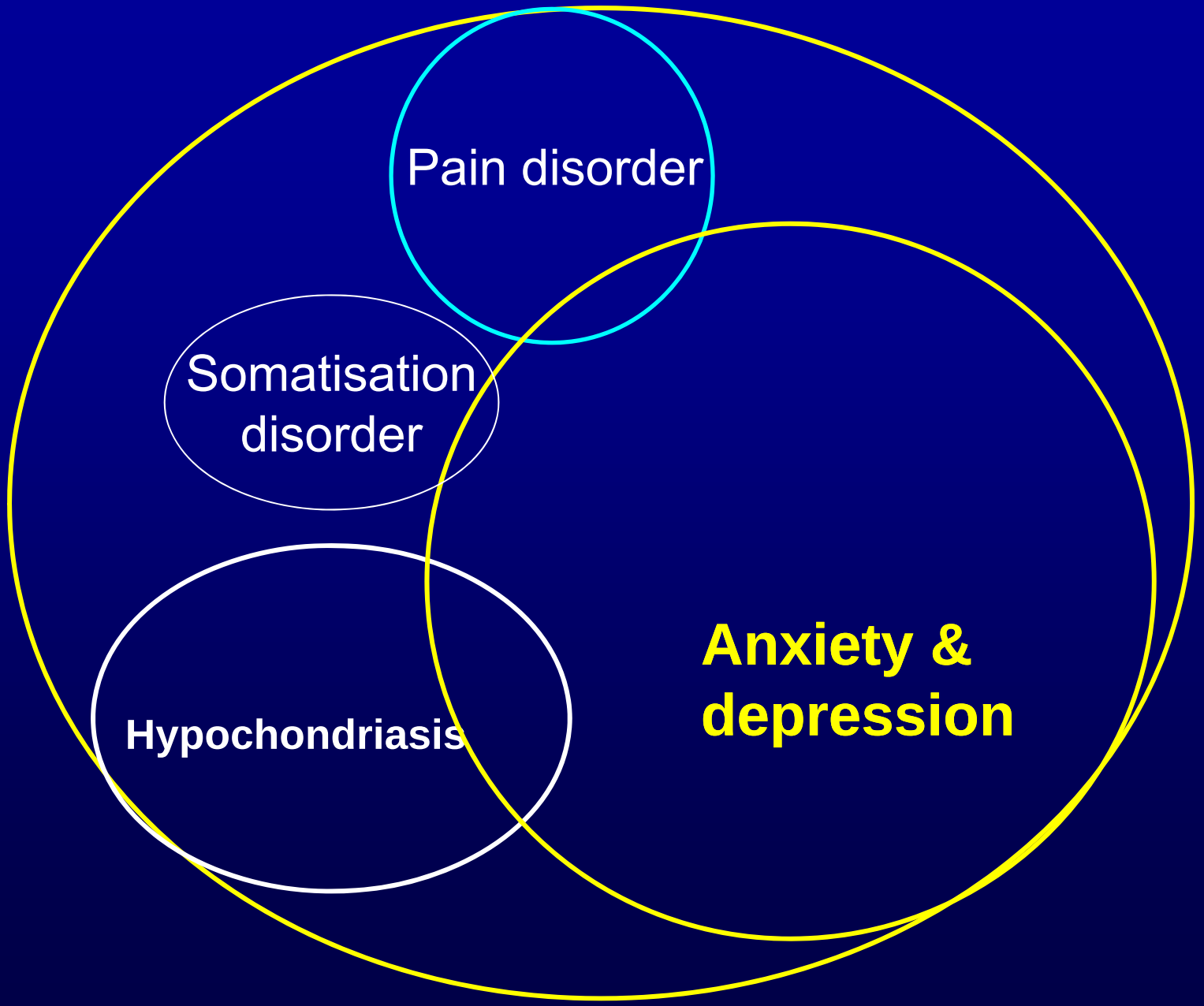
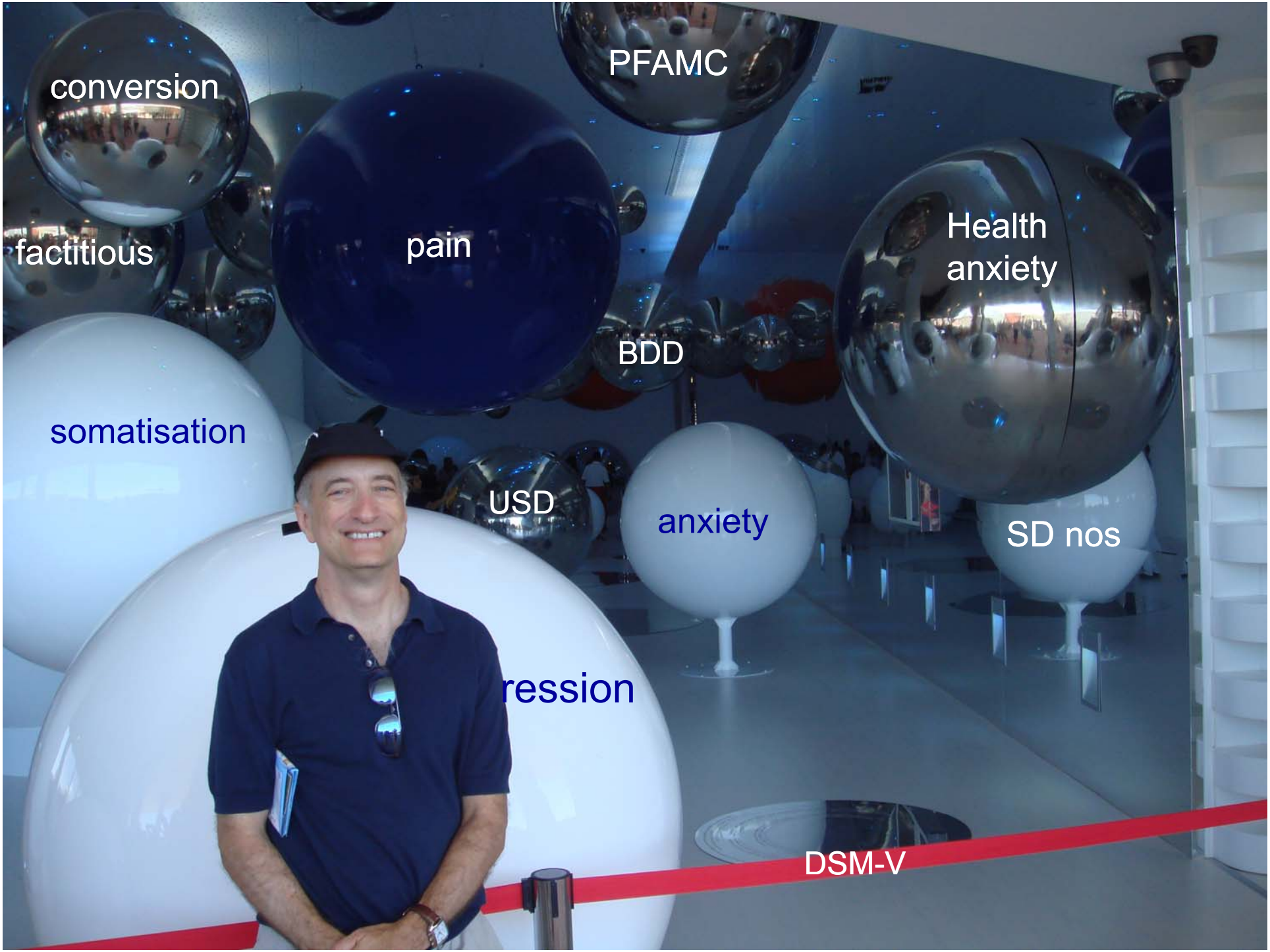
DSM Somatoform disorders




conversion
PFAMC
factitious
pain
Health anxiety
BDD
somatisation
USD
anxiety
SD nos
ression
DSM-V

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Proposed changes in DSM-V Somatic Symptom disorders

- Elimination of “medically unexplained” symptoms as a diagnostic criterion

- Somatisation,
- Hypochondriasis,
- Pain disorder

→ Complex Somatic Symptom disorder

Dimsdale & Creed J Psychosom Res 2009; 66(6):473-6.

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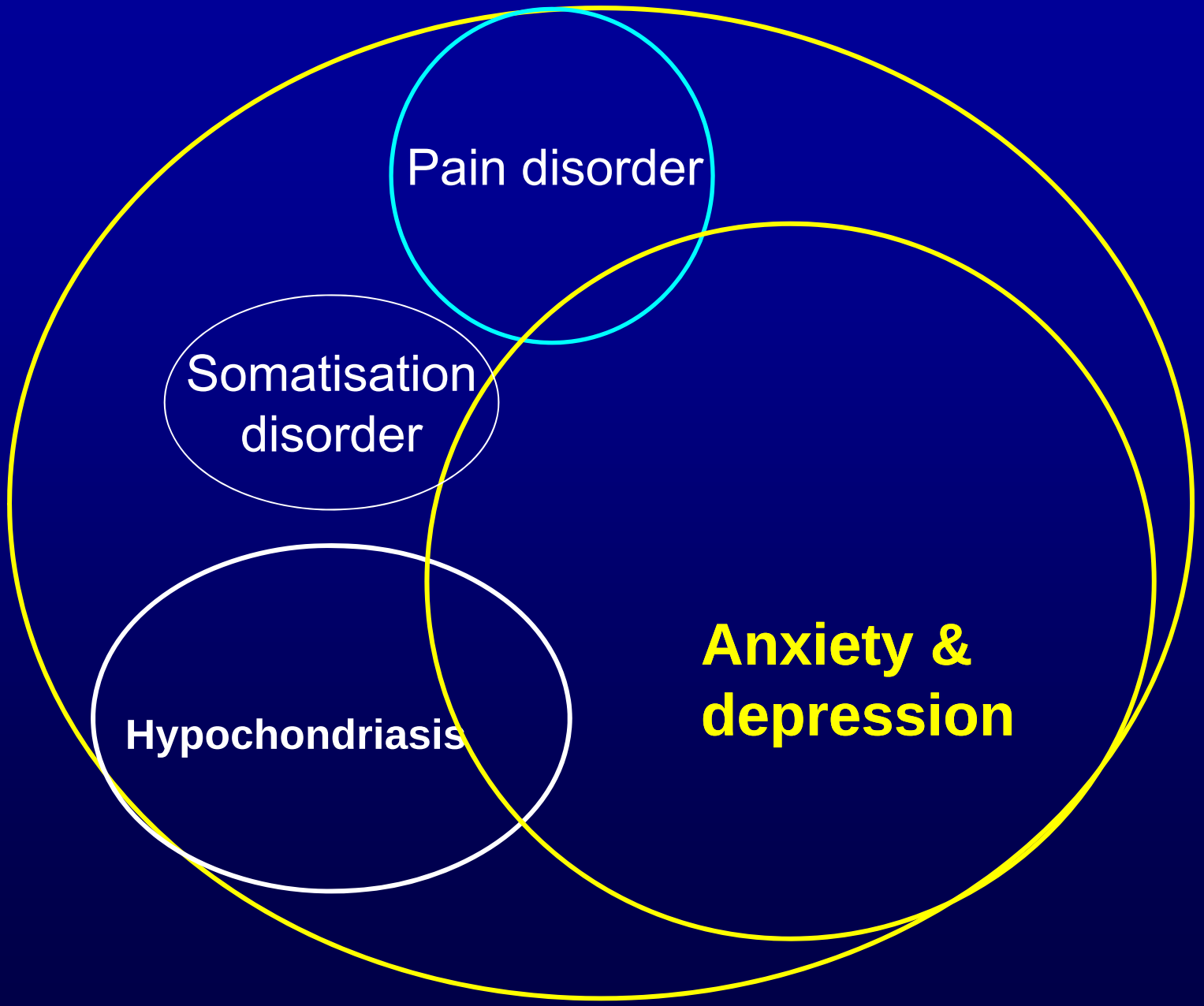
DSM IV Somatoform disorders



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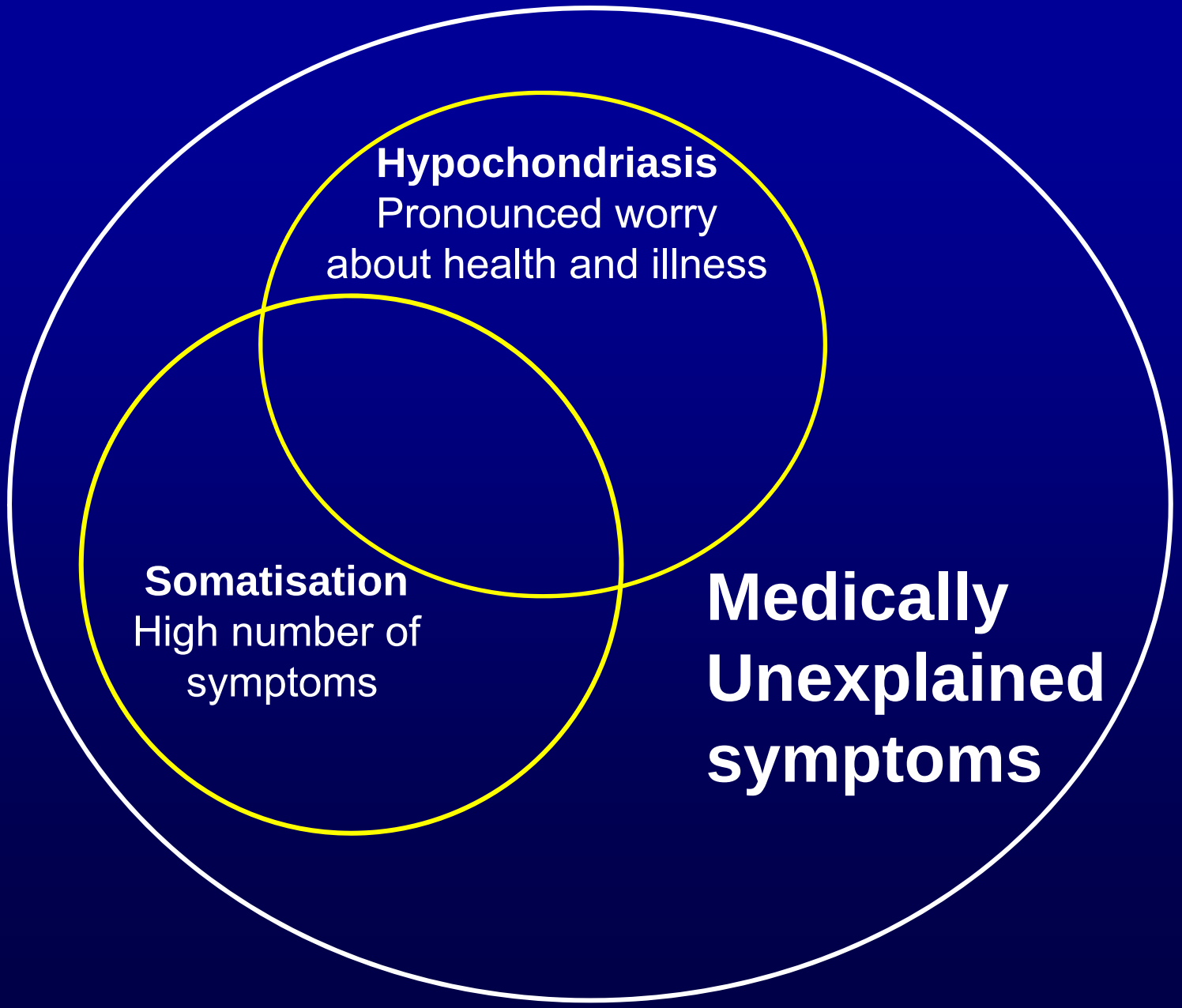

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Barsky score for hypochondriasis /somatisation

Med care 2001;39: 705-715

- total score - items are weighted scores for:
- somatic symptoms,]
- disease fear,] identified top
- bodily preoccupation,] 14% of primary
- disease conviction] attenders
- these are the 4 component symptoms of hypochondriasis.

Per Fink

Research Clinic for Functional Disorders and Psychosomatics Aarhus University Hosp., Denmark.

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A New, Empirically Established Hypochondriasis Diagnosis

Fink et al Am J Psychiatry 2004

Classification allowed definition of new diagnostic criteria for hypochondriasis……

In 75.9% of the patients with severe class 1 hypochondriasis, the primary care physicians reported - patient frequently consulted <u>because of medically unexplained functional symptoms</u>.

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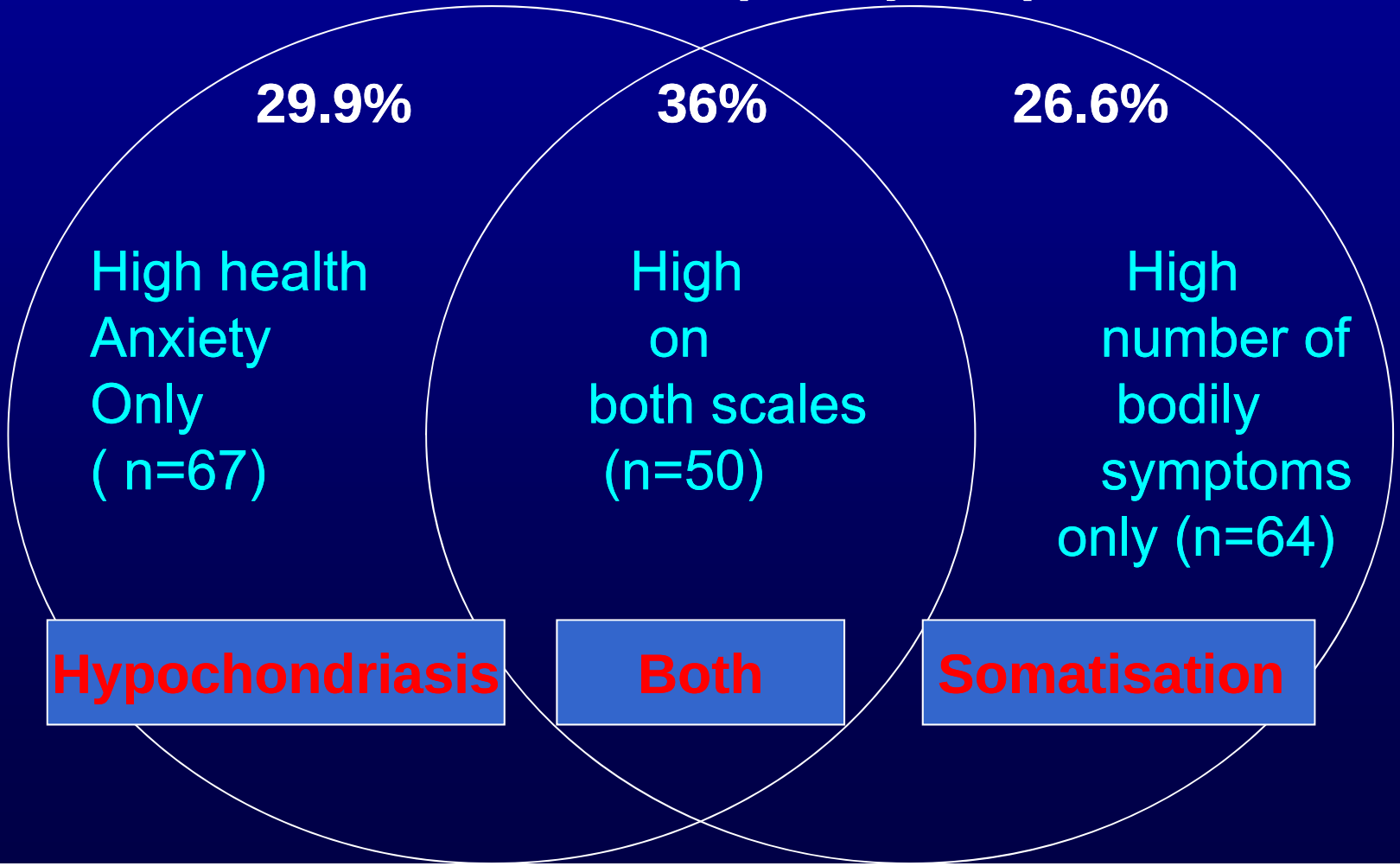
Population-based – Health anxiety & numerous bodily symptoms

% 4+ visits in subsequent year (control= 14.5%)



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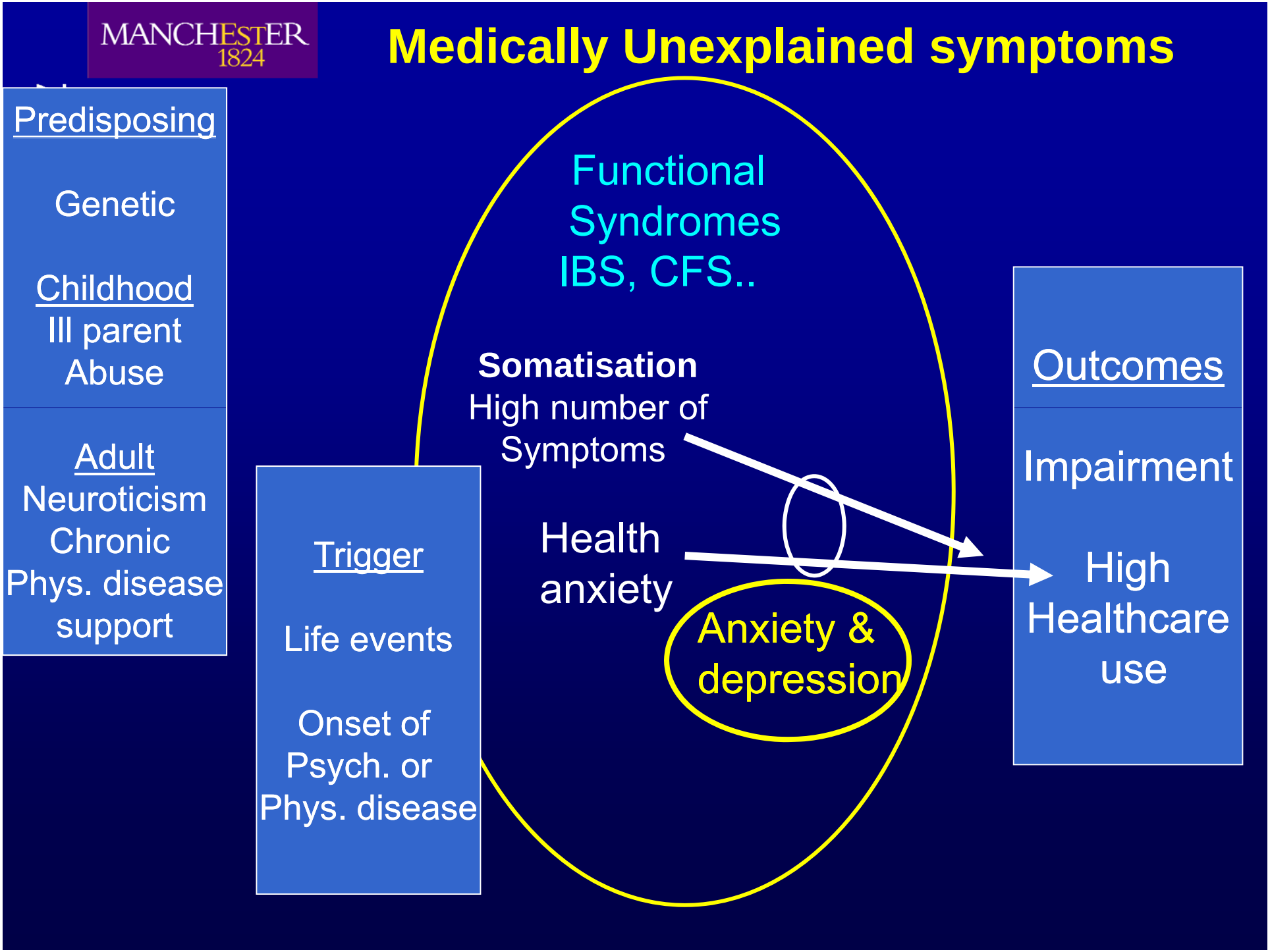
Medically Unexplained symptoms



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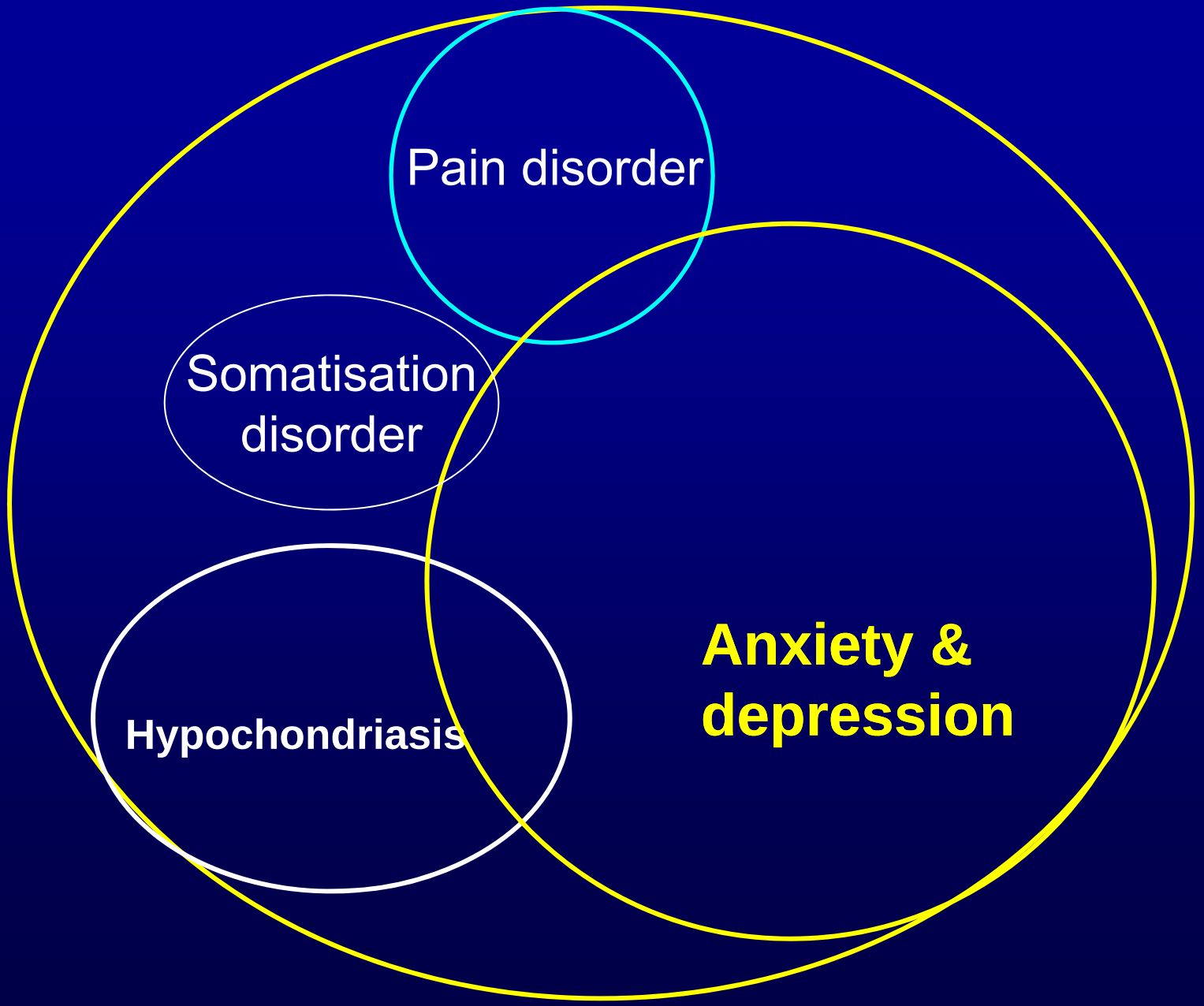
DSM Somatoform disorders



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Proposed changes in DSM-V Somatic Symptom disorders

- Elimination of “medically unexplained” symptoms as a diagnostic criterion

- Somatisation,
- Hypochondriasis,
- Pain disorder

→ Complex Somatic Symptom disorder

- If depressive disorder co-exists code both

Dimsdale & Creed J Psychosom Res 2009; 66(6):473-6.

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Proposed changes in DSM-V Somatic Symptom disorders

- New way of thinking
- What are the chances it will catch on?

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- Interesting to old age psychiatrists ?

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Not sure!

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- Of interest to those concerned with high healthcare costs and ways of reducing them?

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Unimpressed

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- Interesting for those concerned with physical disease and comorbid depression?

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Interesting

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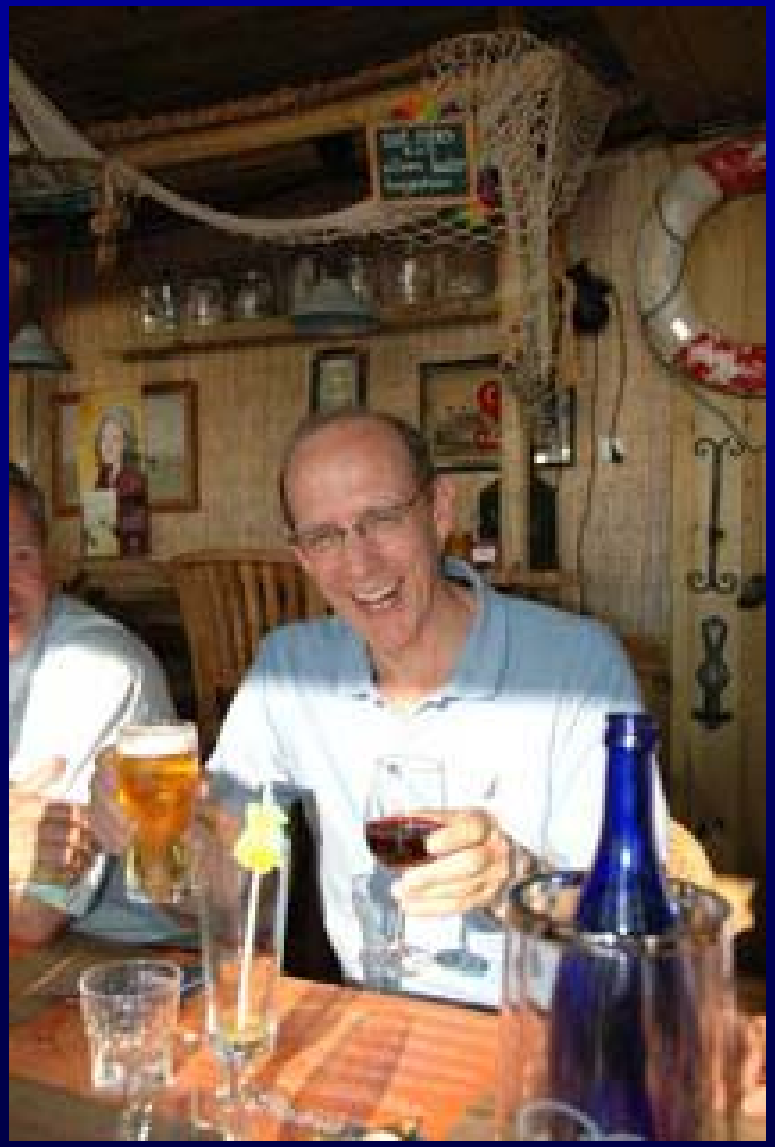
Ridiculous!



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Can we explain medically unexplained symptoms?

- Wrong question – shouldn't try and define group of patients which is poorly defined and heterogeneous
- Should define the processes that lead to poor outcomes (impaired functioning and high health use);
- If we understand the origin of these process and how they can best be treated we will improve our care of <u>all</u> patients with numerous somatic symptoms not just those which are described as "medically unexplained "

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Key references

- L. Wulsin & J. Dimsdale :DSM-V for Psychosomatic Medicine: Current Progress and Controversies
- DSM-V: Dimsdale & Creed J Psychosom Res 2009; 66(6):473-6.
- Improved management: Patients with medically unexplained symptoms and somatisation - a challenge for European healthcare systems. EACLPP Working document 2009. www.eaclpp.org
- Recent research: J Psychosom Res Special Issue April 2010

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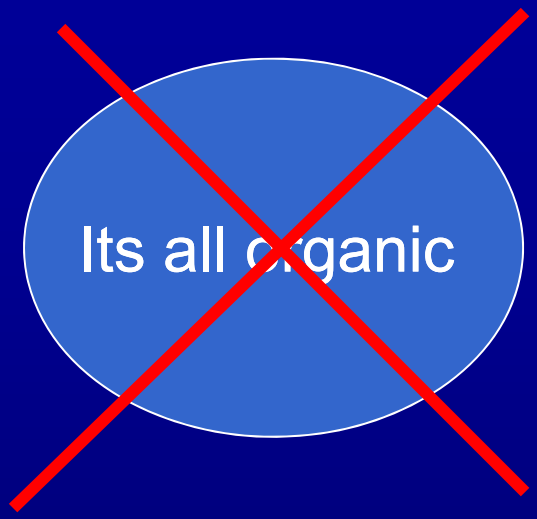

Its all psychological

Medically unexplained??

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Its all organic

Its all psychological

Psychosomatic

Measure all symptoms not just medically unexplained

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DSM-V project Collaborating Centres

"A dimensional approach to diagnosis of somatisation in DSM-V"

Centre	Investigator(s)	No of Subjects	Age	Measure
Bremen	Cecilia Essau	1035	12-17	SCL-90_R
Basel	R Lieb	1995	14-24	CIDI
Aarhus	P Fink	1457	18-70	SCL-90
Dresden	F Jacobi	4181	17-66	Zerssen
Groningen	J Rosmalen	1088	33-79	CIDI
Manchester	FHC/ JB	1443	25-65	SSI
Sri Lanka	Athula	6119	18-75	PHQ
Oslo	KA Leiknes	1247	18-91	CIDI
Marburg	W Rief	2510	14-93	PHQ

Francis Creed & Barbara Tomenson + collaborators

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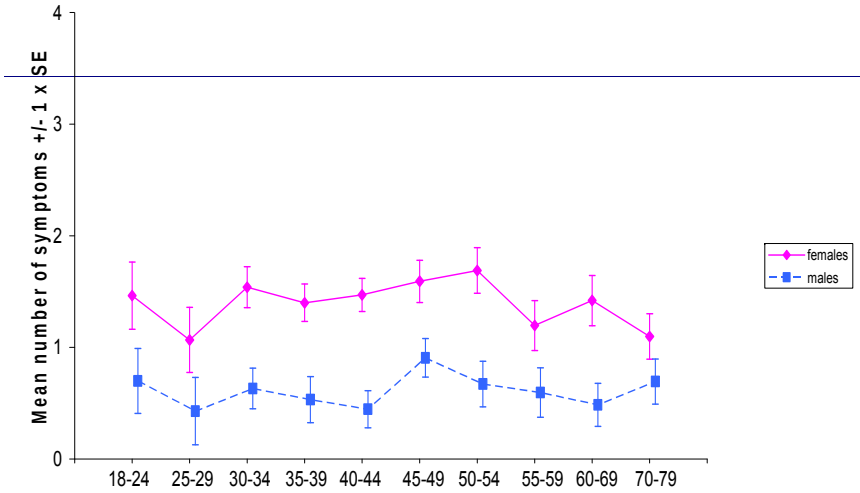
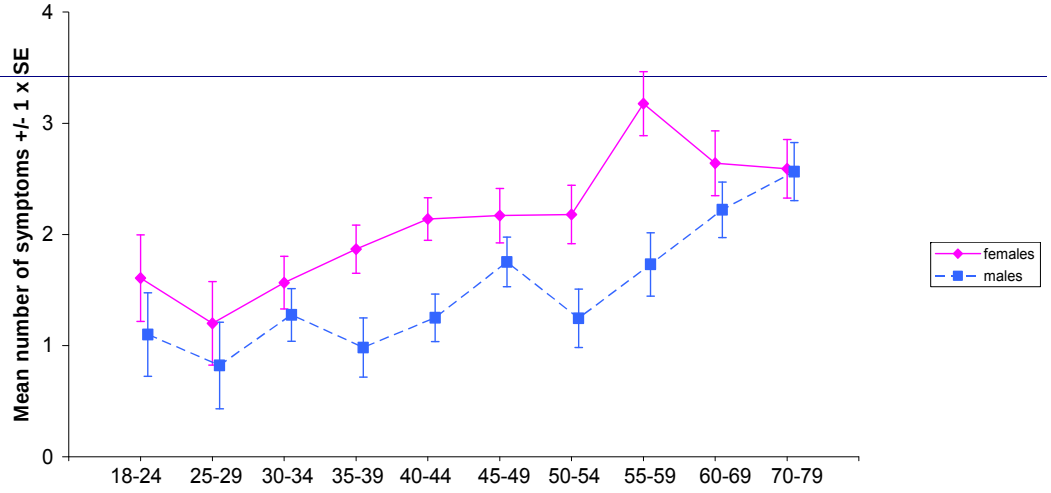
Medically unexplained

medically explained

Oslo - Kari Ann Leiknes
Number of Medically Unexplained Symptoms out of 42



Oslo - Kari Ann Leiknes
Number of Medically Explained Symptoms out of 42



Females have significantly more symptoms than males for both MUS and MES, but for medically explained symptoms there is a significant increase with age ($p<0.001$), which is not at all significant for MUS ($p=0.49$). There is no significant age group by sex interaction for either MUS or MES.

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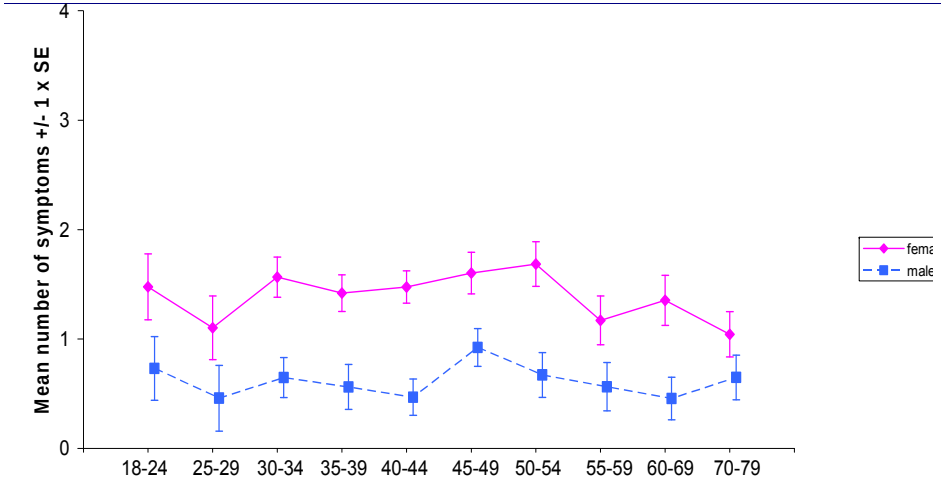
Medically unexplained medically explained

adjusted for physical illnesses

Oslo - Kari Ann Leiknes
Number of Medically Unexplained Symptoms out of 42
adjusted for number of physical diseases (out of a checklist of 13)



Oslo - Kari Ann Leiknes
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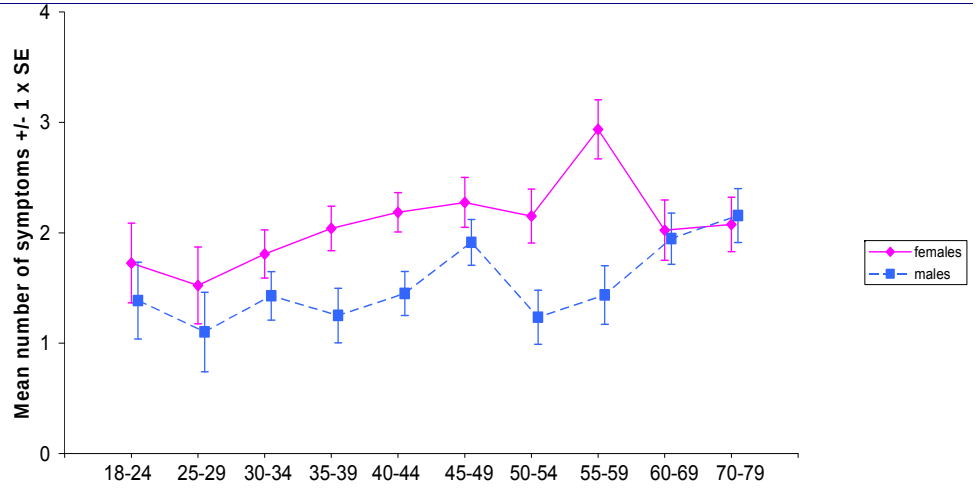

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Difference between the sexes is significant at p<0.001

- *Oslo,* adjusted for age and dep & physical disorders. This is true for both MUS and MES.
- *Dresden,* adjusted for MDD, panic, anx, and physical illnesses
- *Groningen,* adjusted for MDD, panic, anx, and physical illnesses. This is true for both MUS and MES.
- *Sri Lanka,* adjusted for age and physical diagnosis.
- *Manchester* adjusted for physical illness, anxiety & depression

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Correlation between the number of medically unexplained symptoms and all symptoms

- Few bodily symptoms: $r = .721$; $p \leq .001$
- Many bodily symptoms: $r = .703$; $p \leq .001$

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Provisional conclusion

- We can readily measure all bodily symptoms
- This may provide as reliable an indicator of the tendency to report bodily symptoms as measuring only medically unexplained symptoms.
- Need also other cognitive features?

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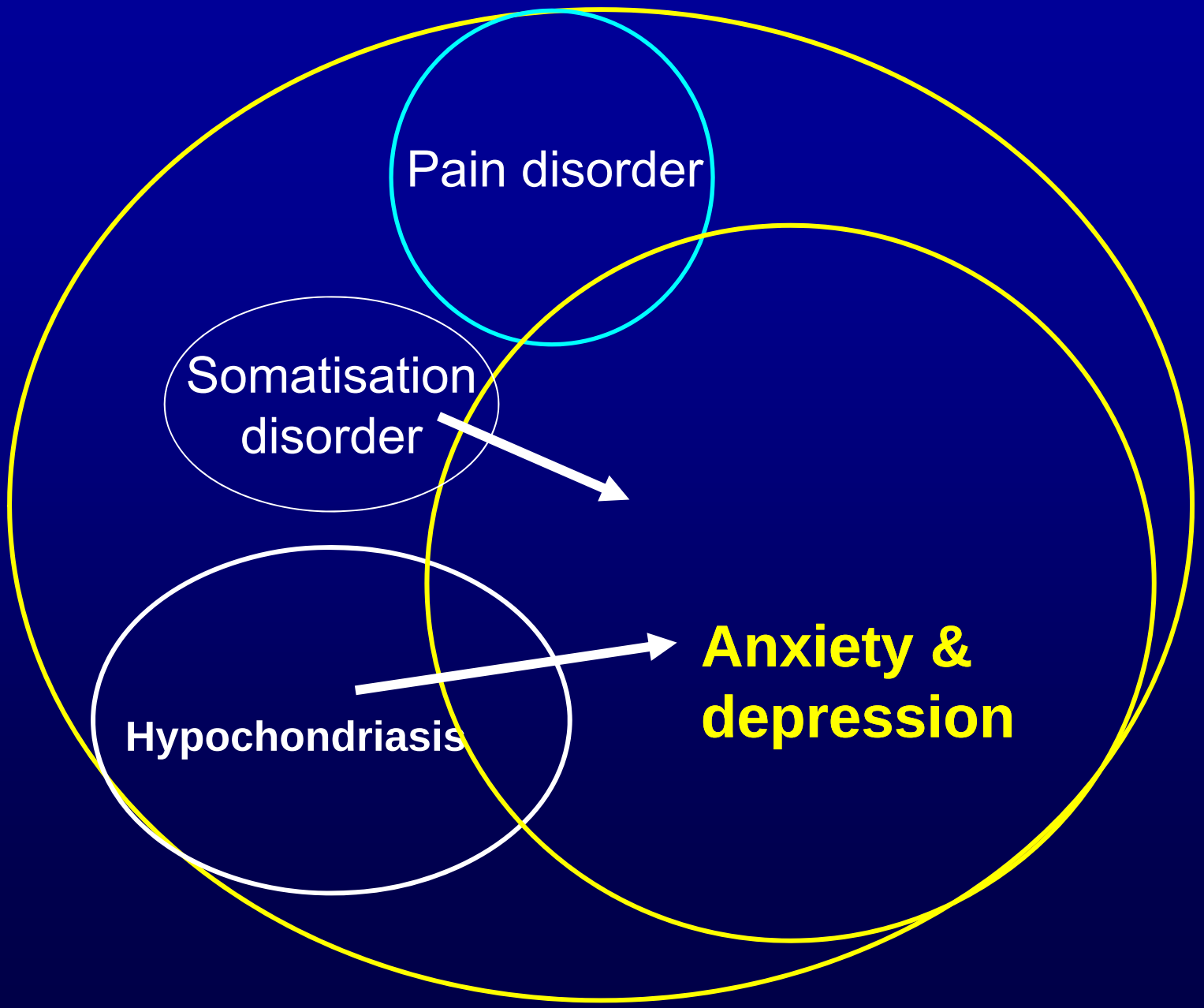
DSM IV Somatoform disorders



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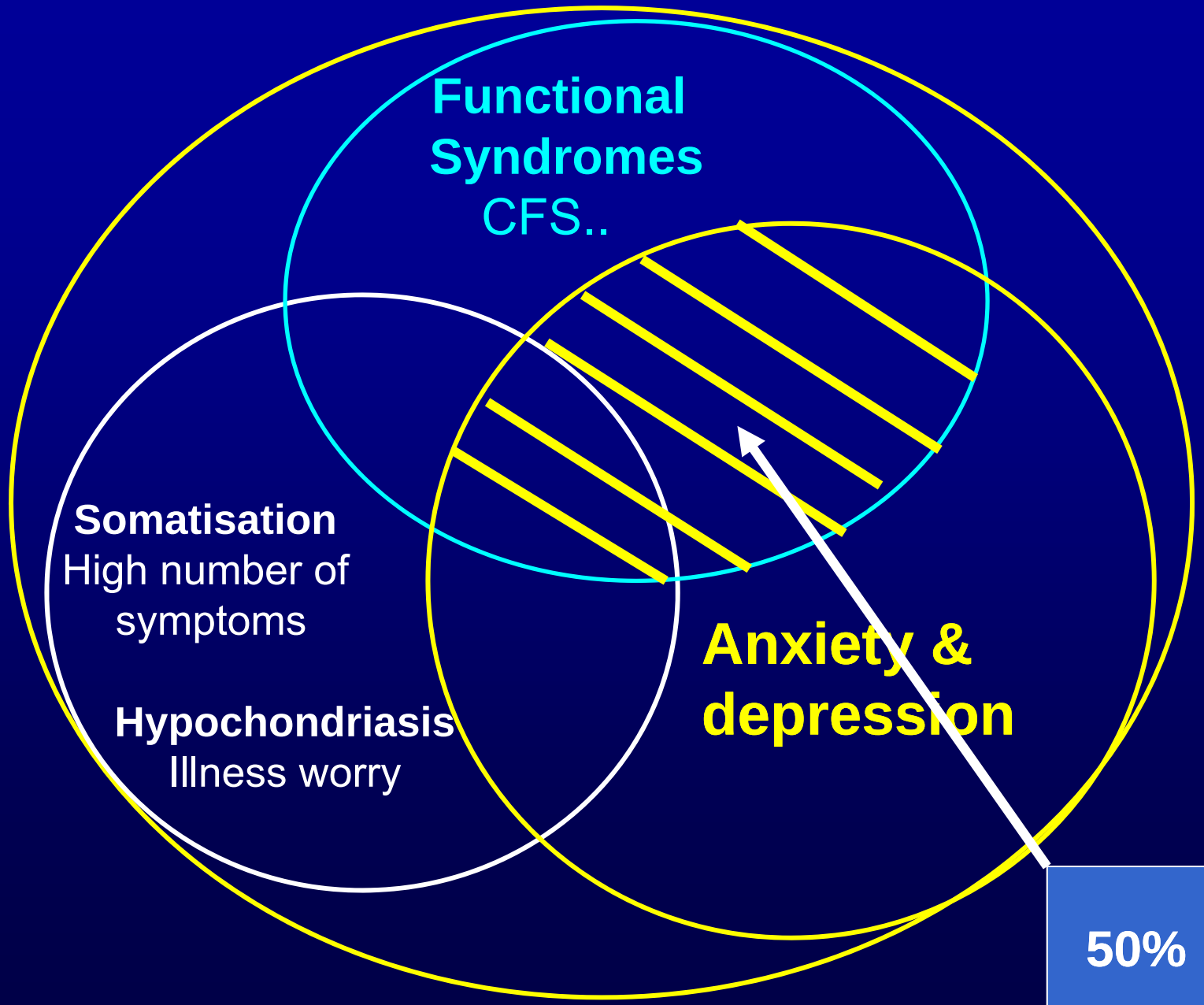
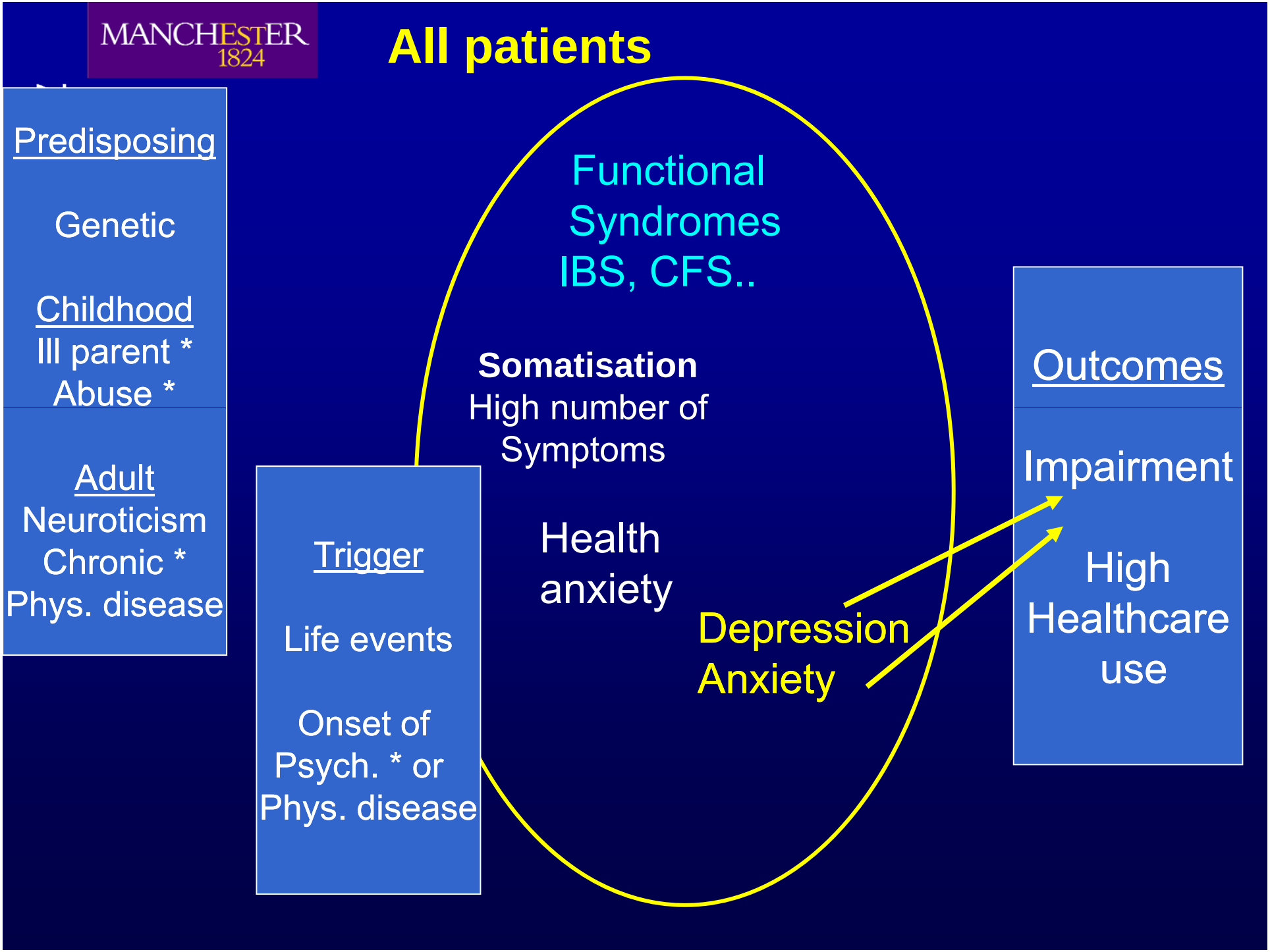
Medically Unexplained symptoms

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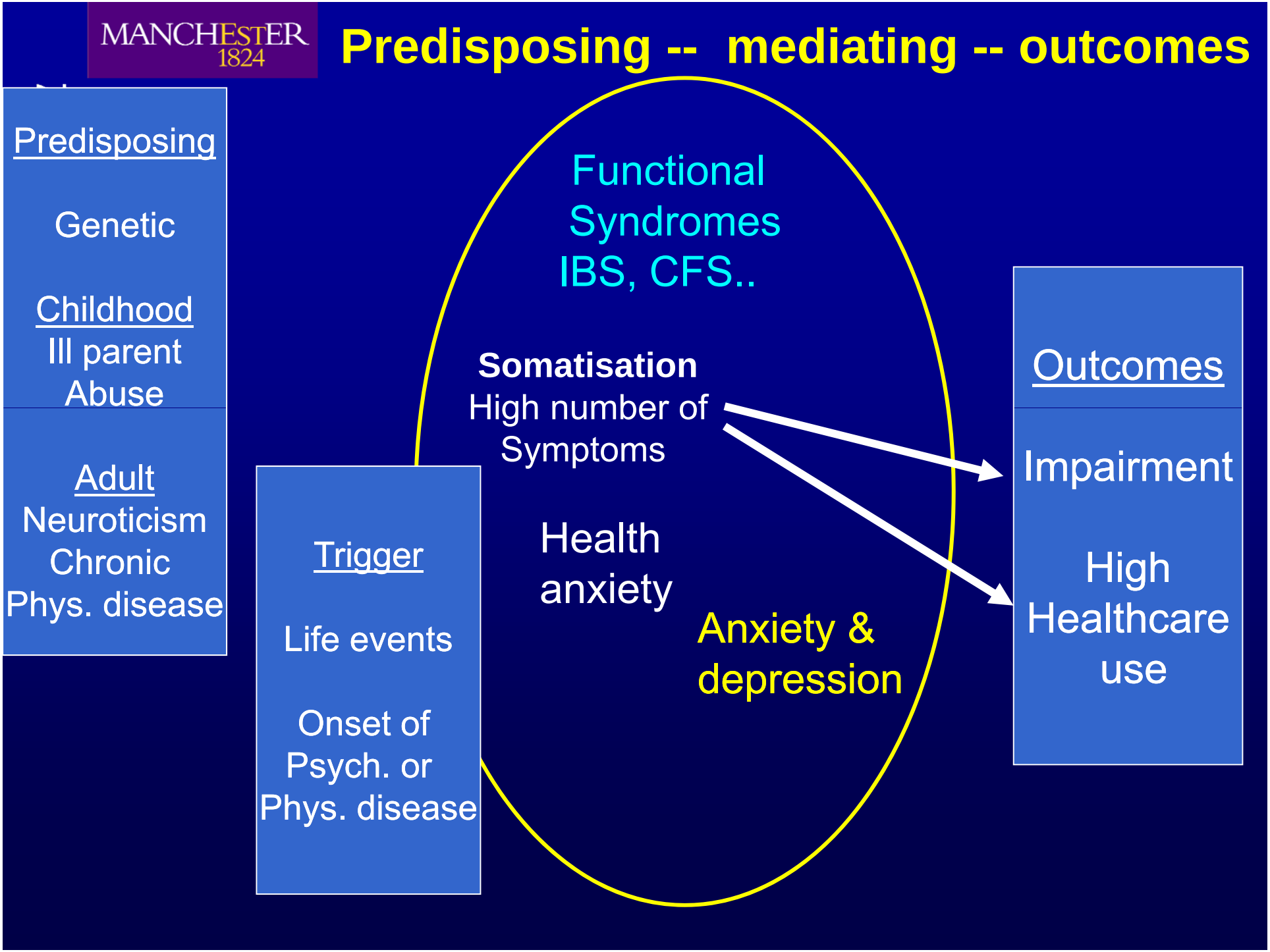
All patients
Predisposing
Genetic
Childhood
Ill parent *
Abuse *
Adult
Neuroticism
Chronic *
Phys. disease
Trigger
Life events
Onset of Psych. * or Phys. disease
Functional Syndromes IBS, CFS..
Somatisation
High number of Symptoms
Health anxiety
Depression
Anxiety
Outcomes
Impairment
High Healthcare use

Predisposing -- mediating -- outcomes



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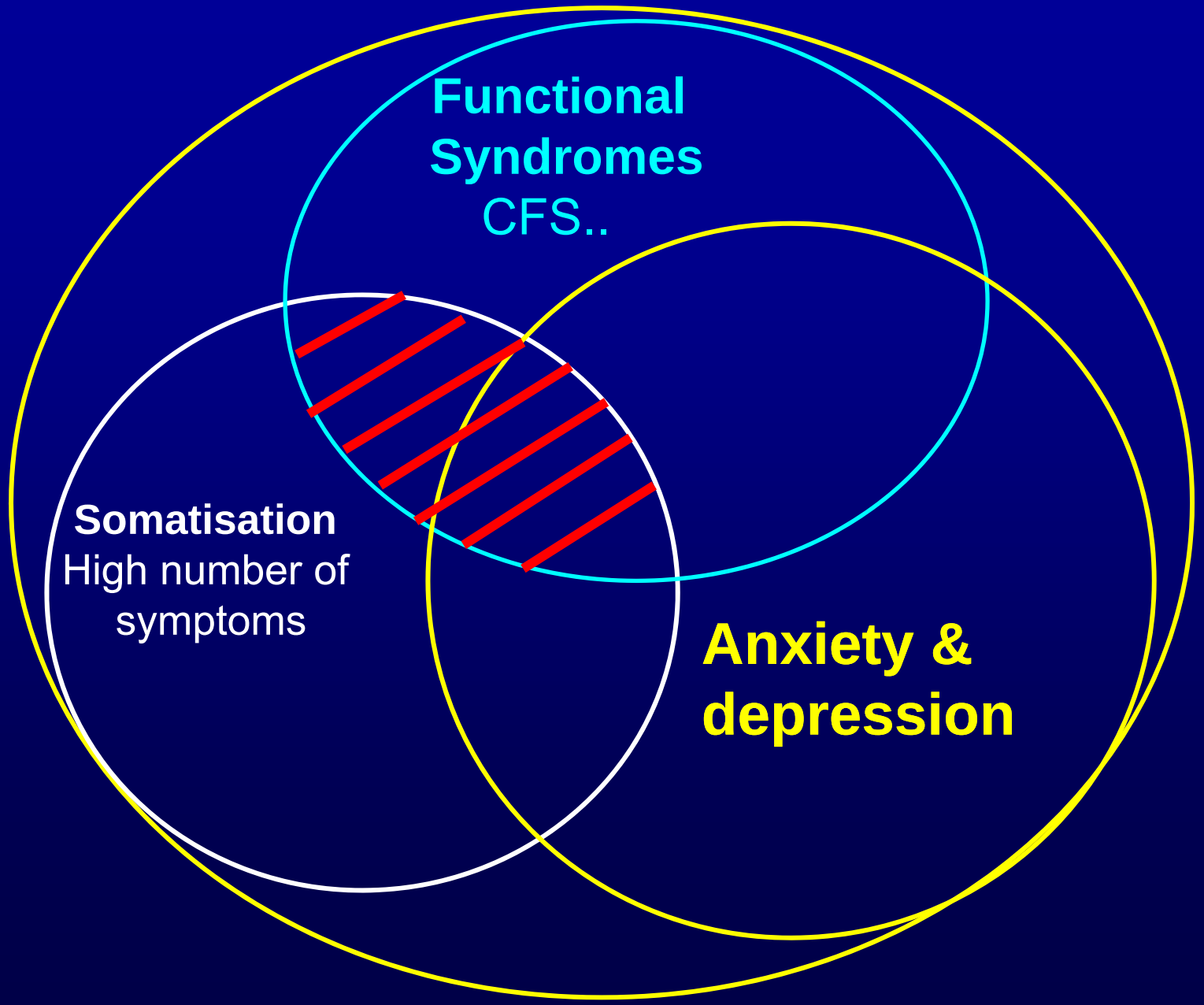
Medically Unexplained symptoms



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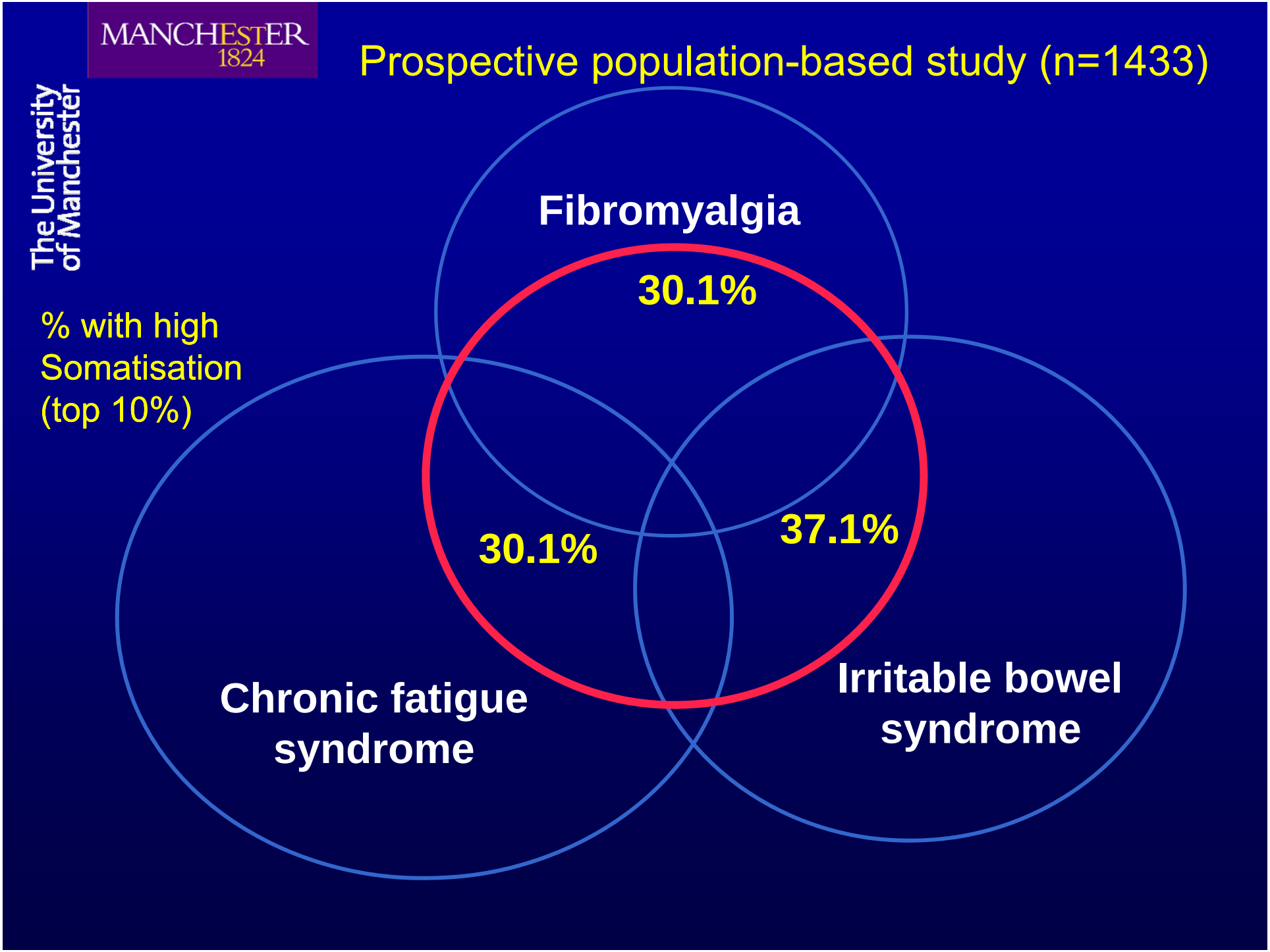
Prospective population-based study (n=1433)



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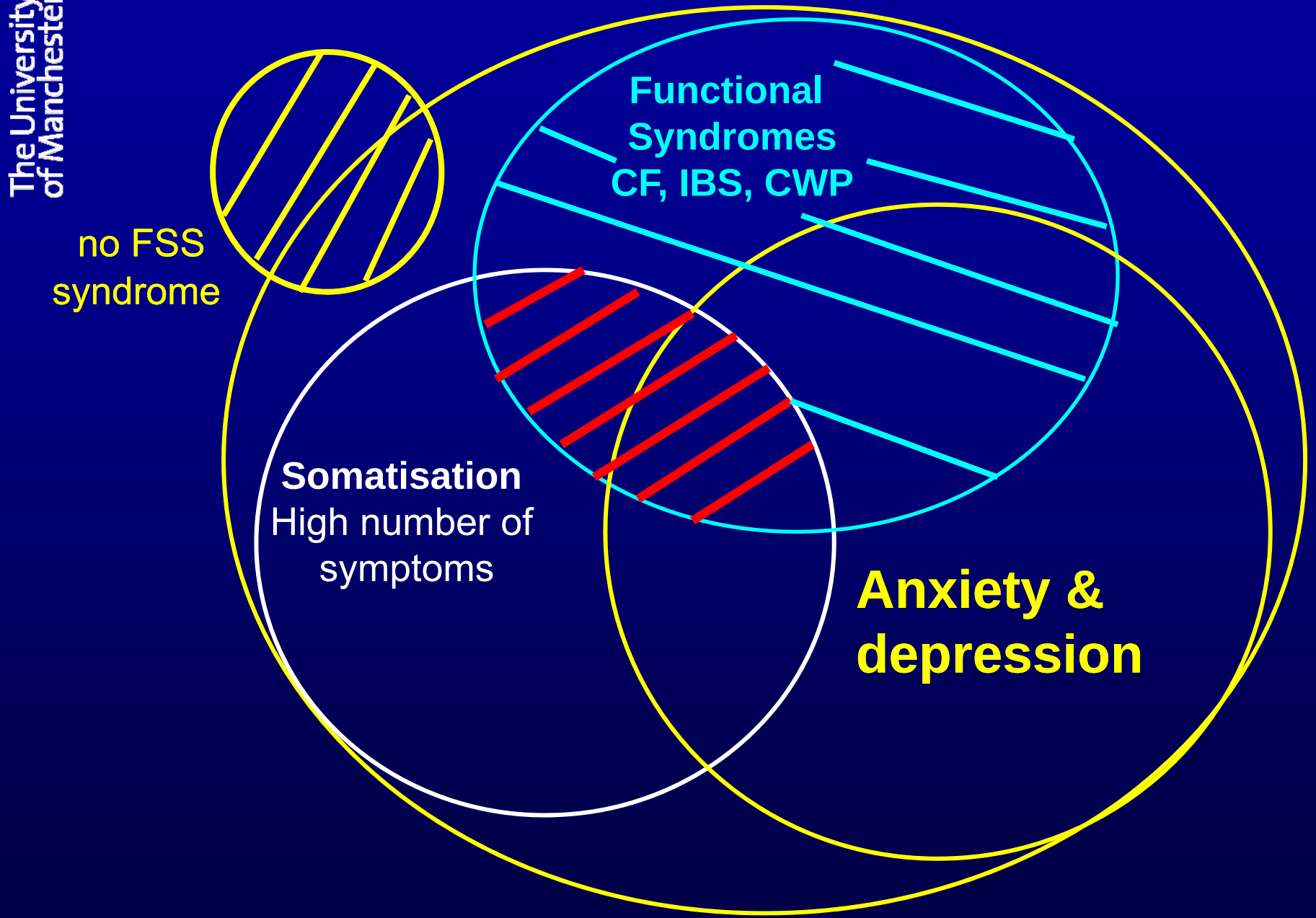
Medically Unexplained symptoms



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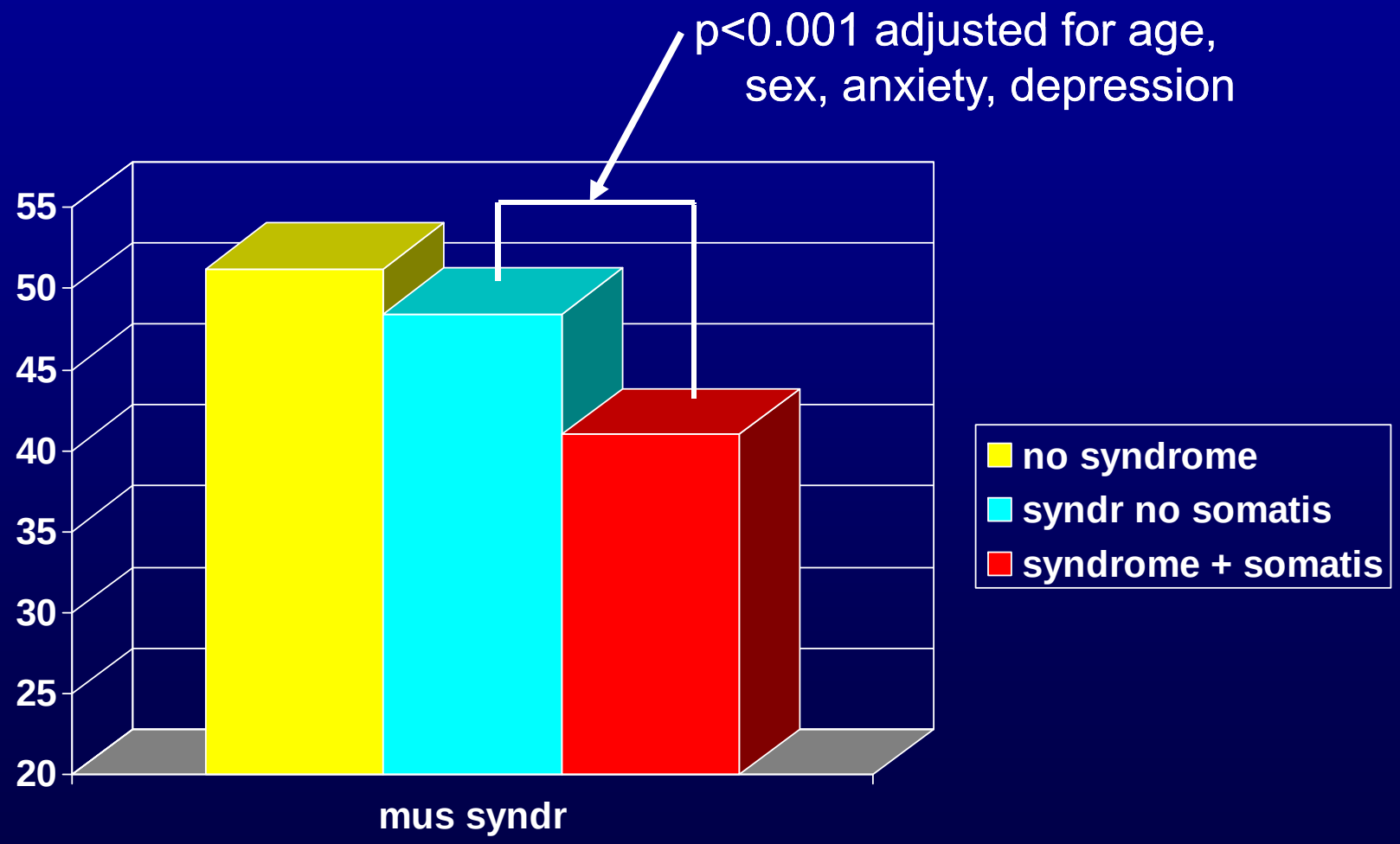
Health-related quality of life by syndrome and somatisation (top 10%)



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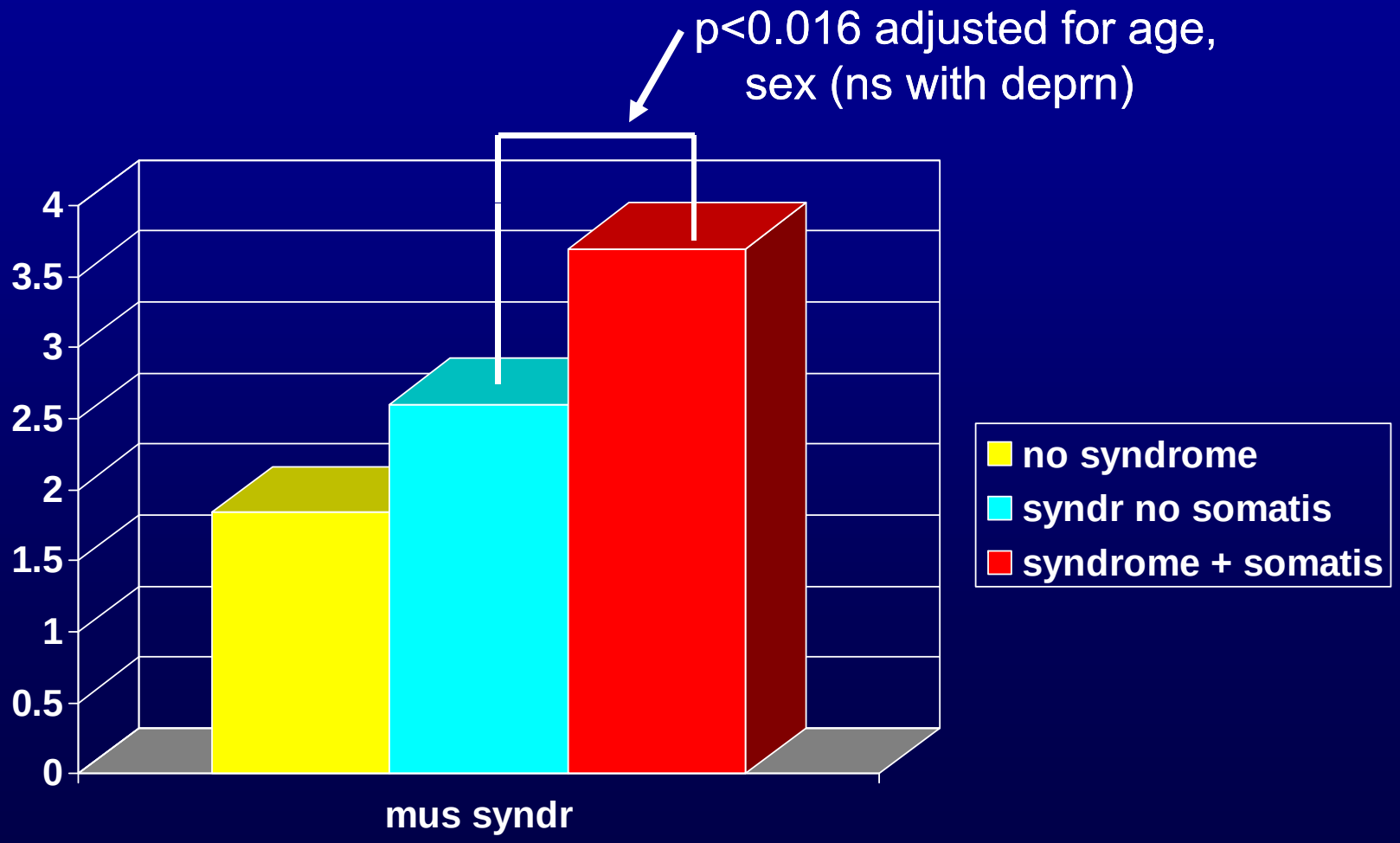
Dr visits by syndrome and somatisation (top 10%)



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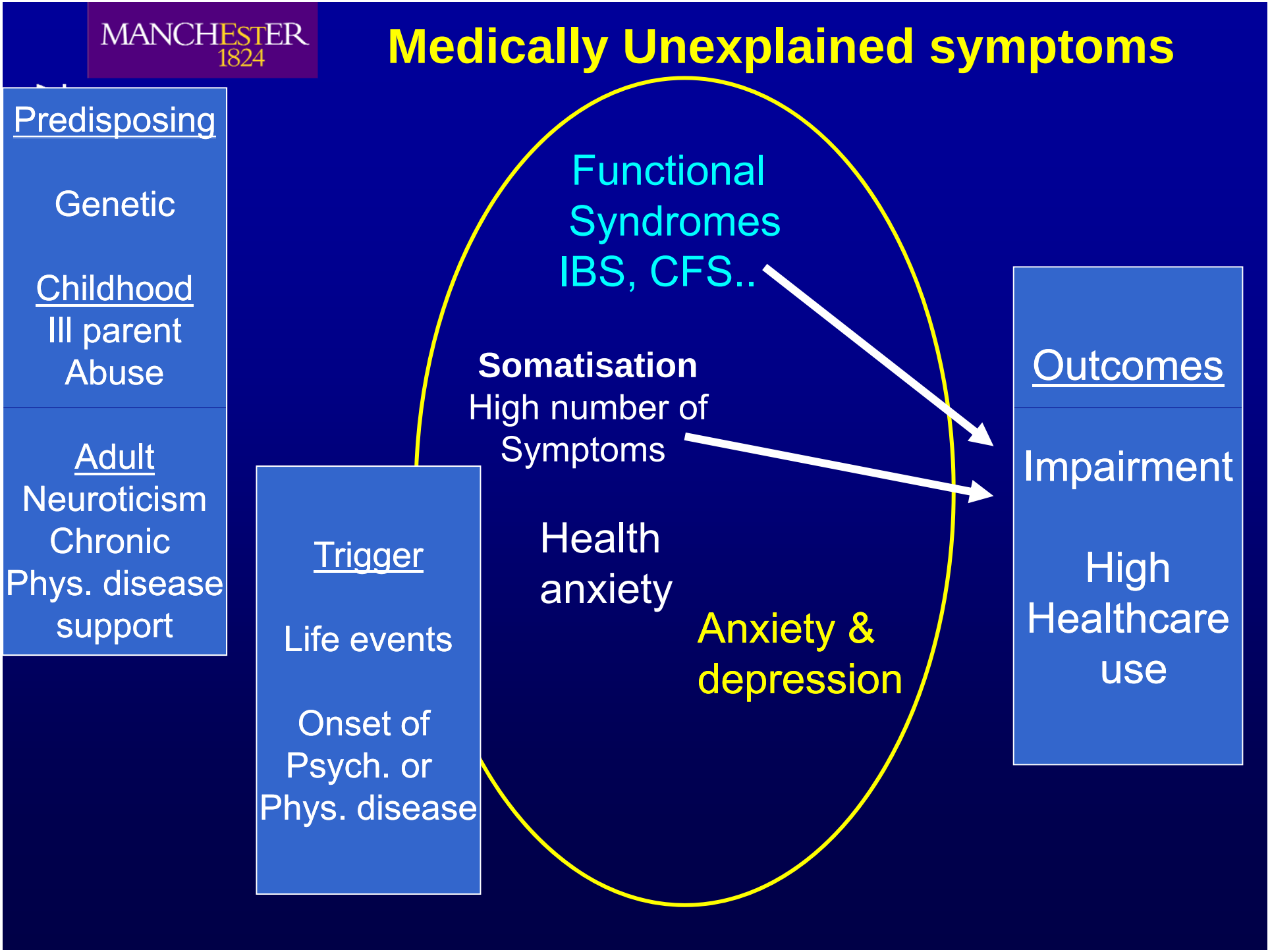
Conclusion

- Impairment and increased healthcare associated with both presence of Functional somatic syndrome (IBS, CF, fibromyalgia) and number of somatic symptoms.
- High number of somatic symptoms → powerful influence on outcomes

Medically Unexplained symptoms



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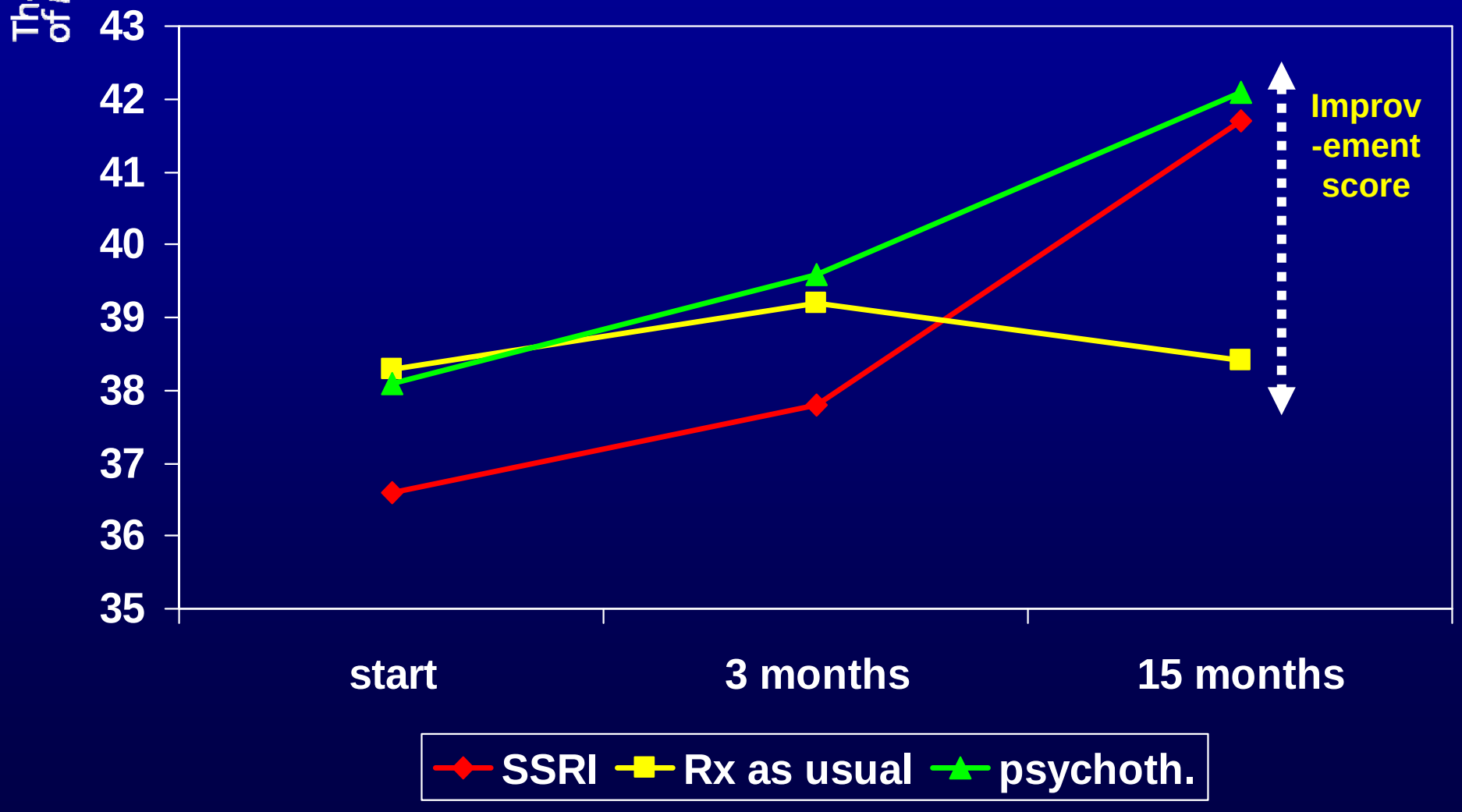
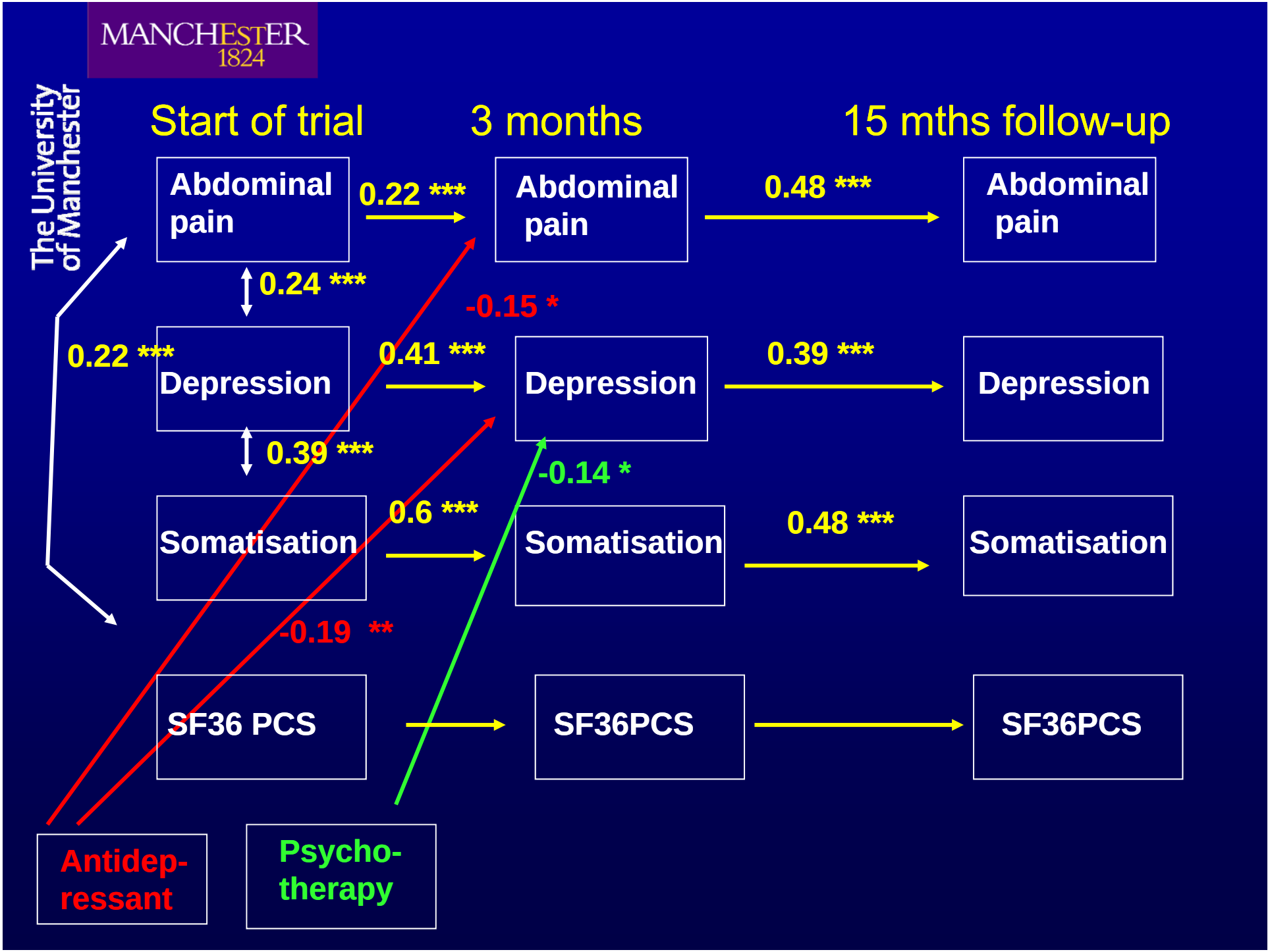
SF36 Physical component score

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Start of trial
3 months
15 mths follow-up
Abdominal pain
0.22 ***
Abdominal pain
0.48 ***
Abdominal pain
0.24 ***
-0.15 *
0.22 ***
Depression
0.41 ***
Depression
0.39 ***
Depression
0.39 ***
-0.14 *
Somatisation
0.6 ***
Somatisation
0.48 ***
Somatisation
-0.19 **
SF36 PCS
SF36PCS
SF36PCS
Antidep-ressant
Psycho-therapy

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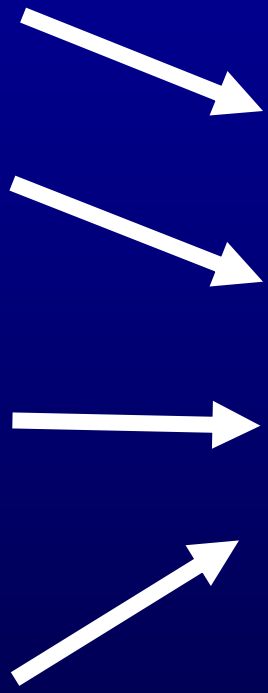
Change in Health status

Age, (- 0.11)
Abuse (0.1)
Unemployed (-0.19)

Baseline SF36 PCS (0.37)
Abdominal pain (- 0.18)
Change in abdo pain (0.2)

SCL somatisation (-0.32) ch 0.3)
SCL anxiety (0.28) (ch-0.2)
Change in depression (0.14)

Psychotherapy (0.16)
Paroxetine (0.15)



SF36 Physical Component score at follow-up

Creed et al *Aust NZ Psychiatry* 2005; 39: 807-15

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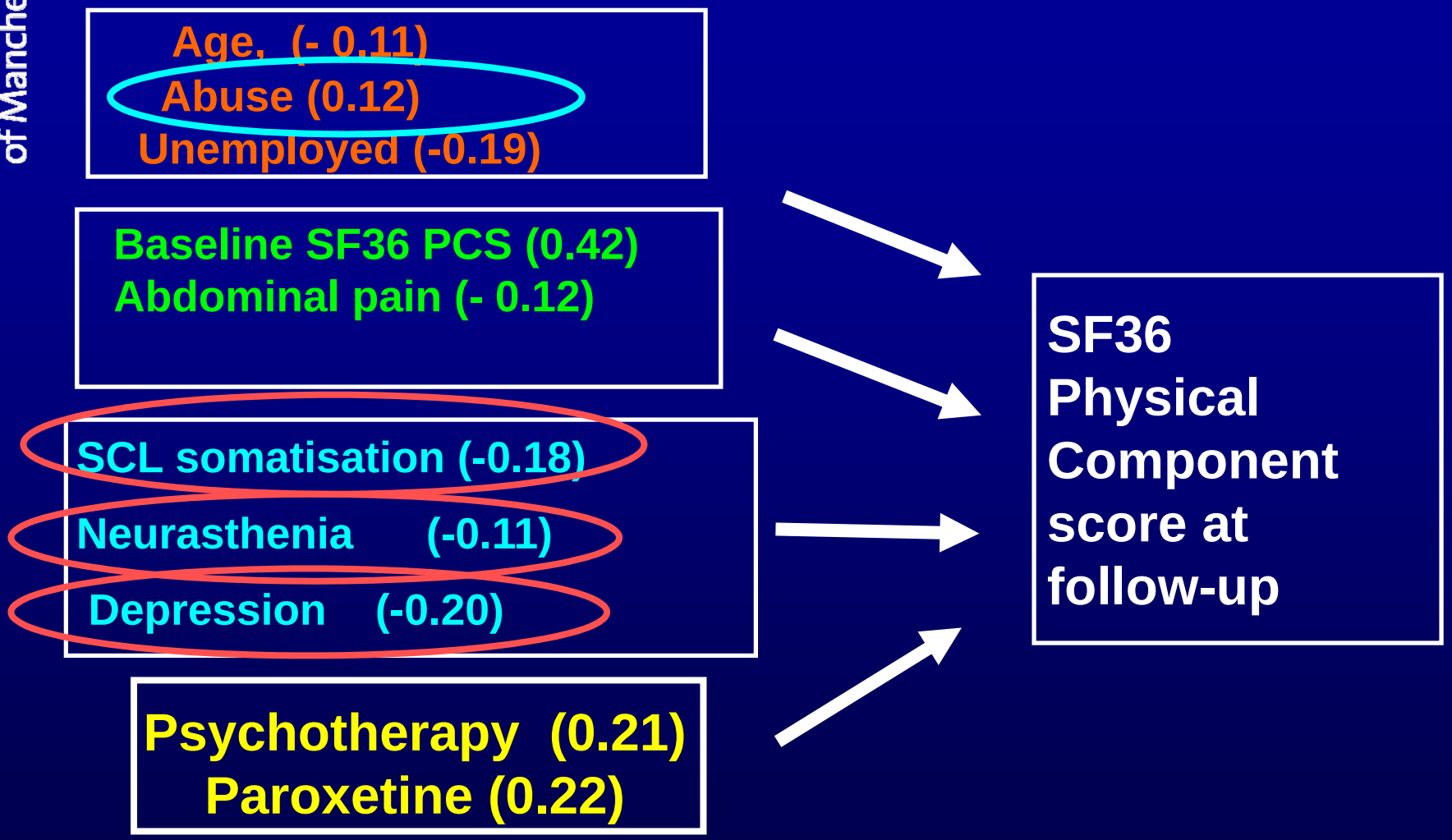
Change in Health status



Creed et al *Aust NZ Psychiatry* 2005; 39: 807-15

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Outcomes and treatments in IBS

	Outcome	Optimal treatment
Depressive disorder	Impairment Costs	Antidepressant
Fatigue (neurasthenia)	Impairment	Psychotherapy
Reported sex abuse	Costs	Psychotherapy
Somatisation	Costs & Impairment	Either

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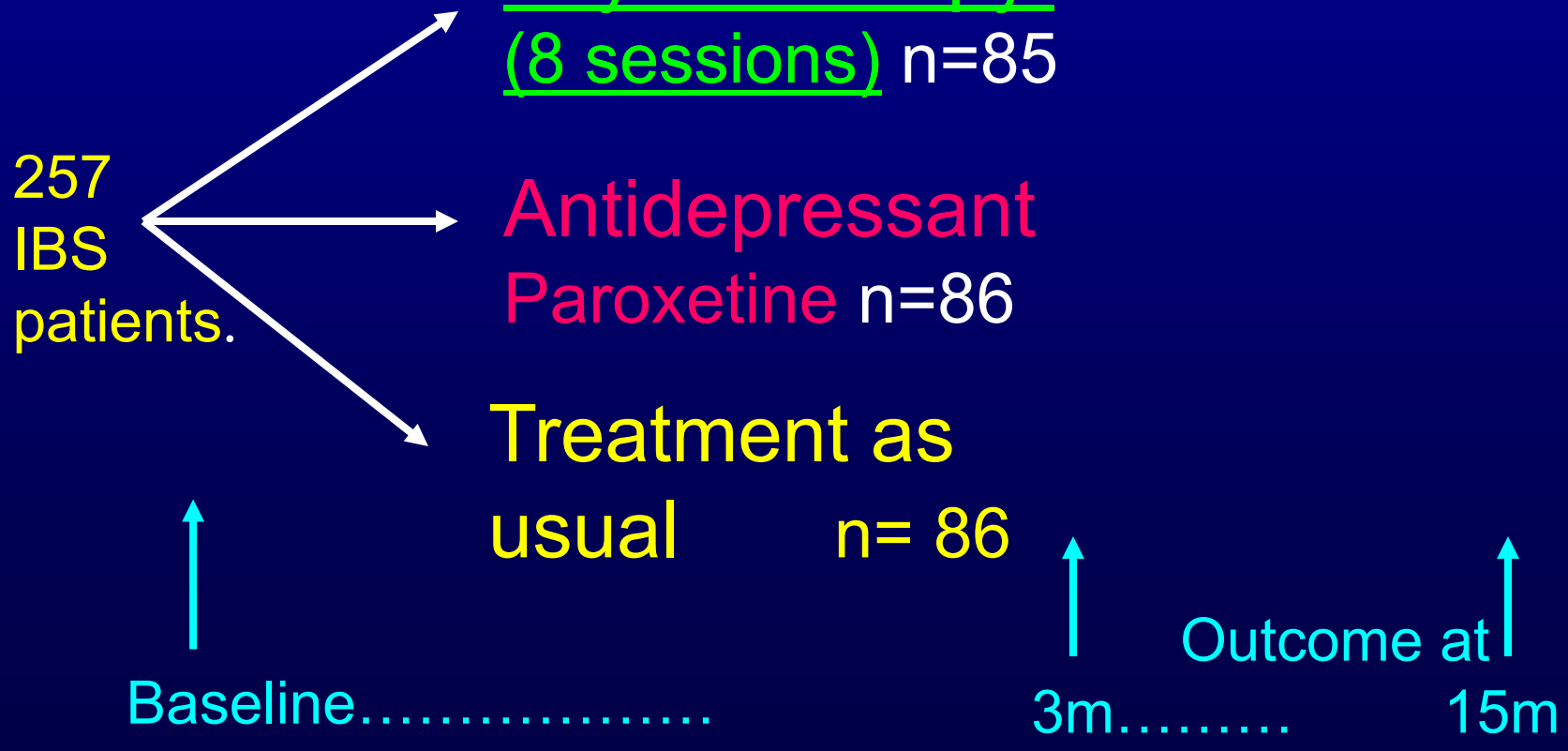
Randomised Controlled Trial

Creed et al *Gastroenterology 2003 124: 303-317*



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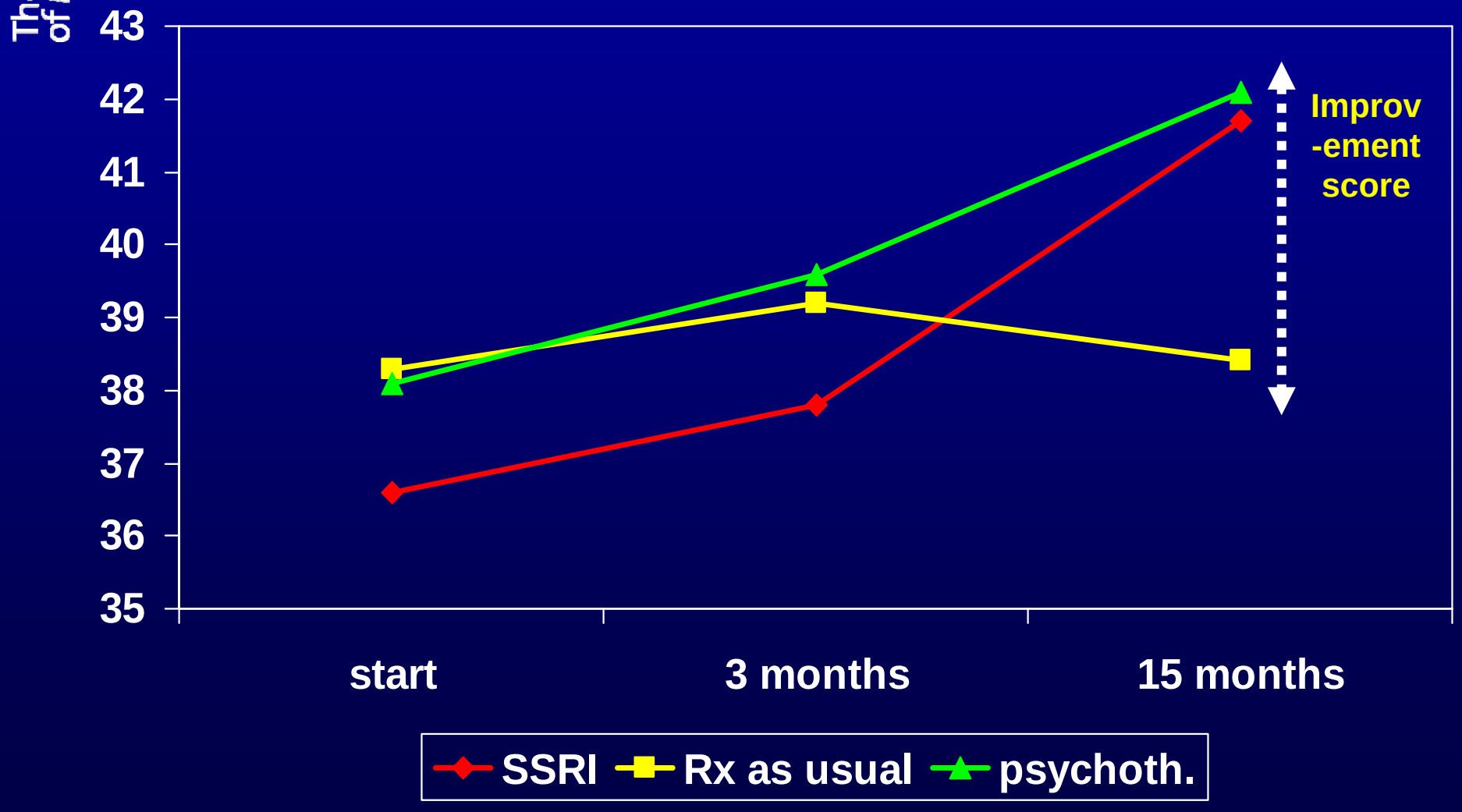
SF36 Physical component score



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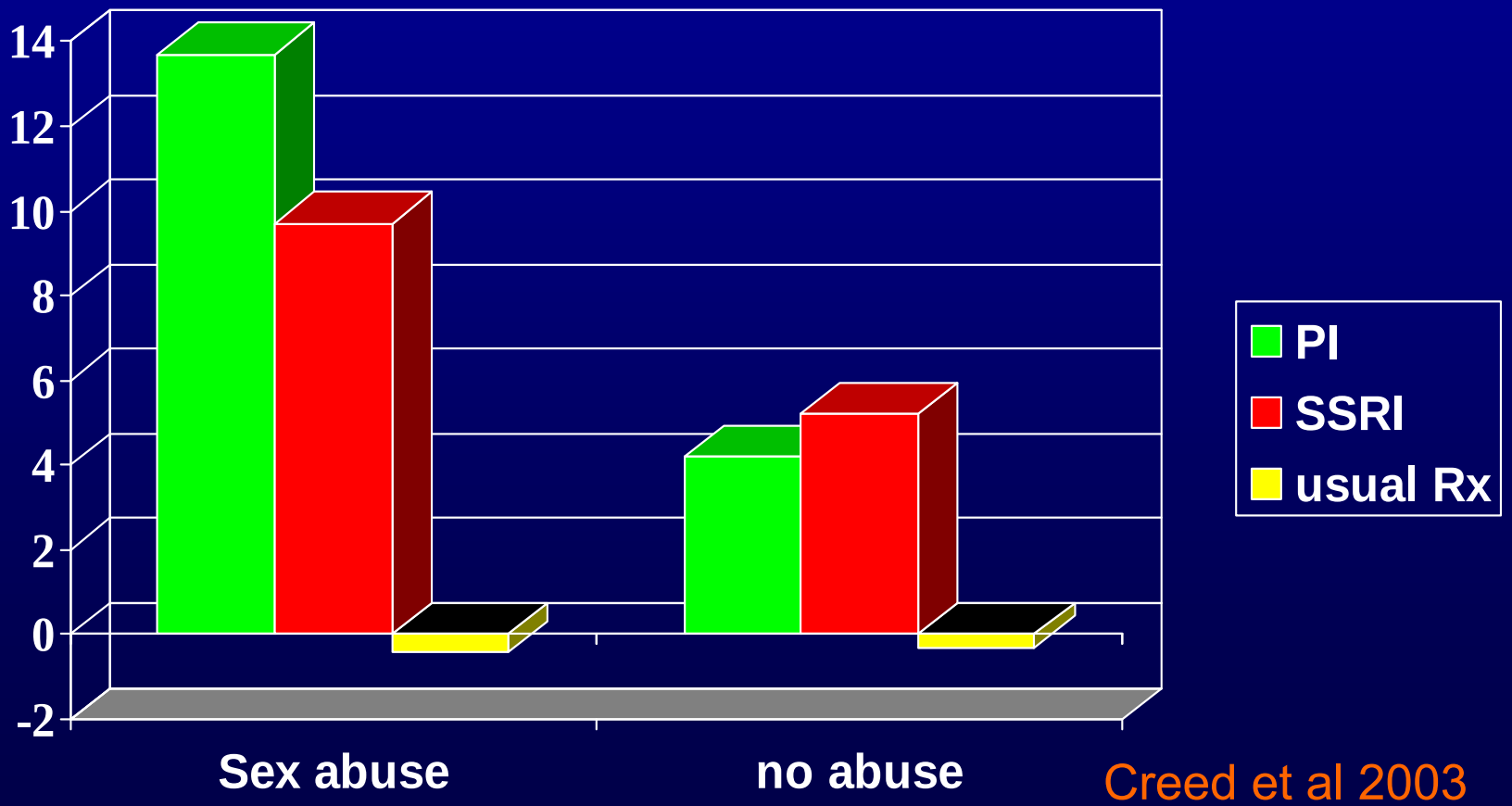
Improvement in SF36 Physical Component score by reported sexual abuse - scores adjust. for age, gender, deprn & baseline PCS score.

p=0.014, 0.10, 0.98



Creed et al 2003

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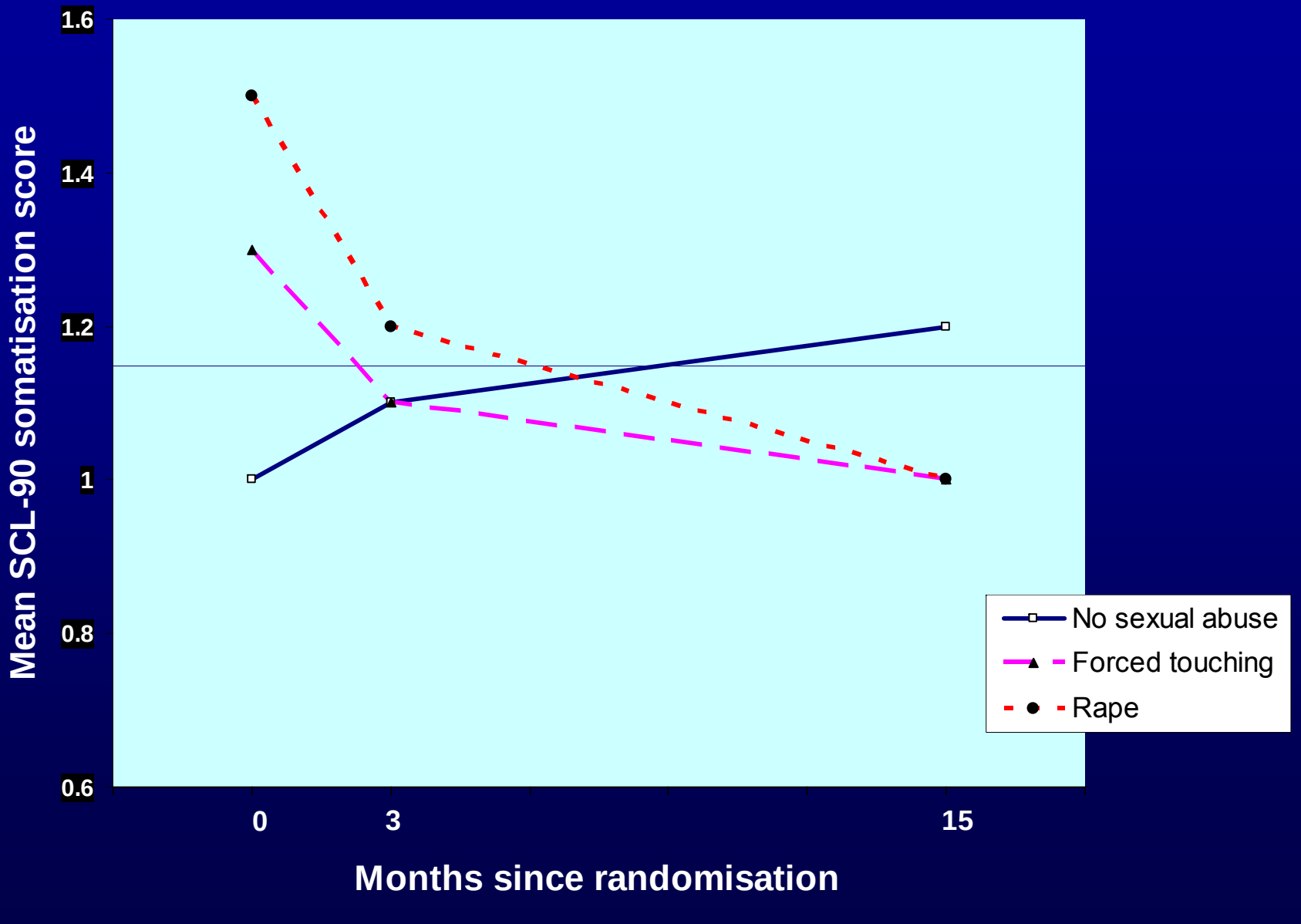

Creed et al Psychosomatic Medicine 2005; 67: 490-9

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Conclusion re history of sexual abuse

- Patients with a reported history of sexual abuse do particularly well with psychotherapy (NB small numbers)
- Change mediated by somatisation
- Change also in rectal distension threshold

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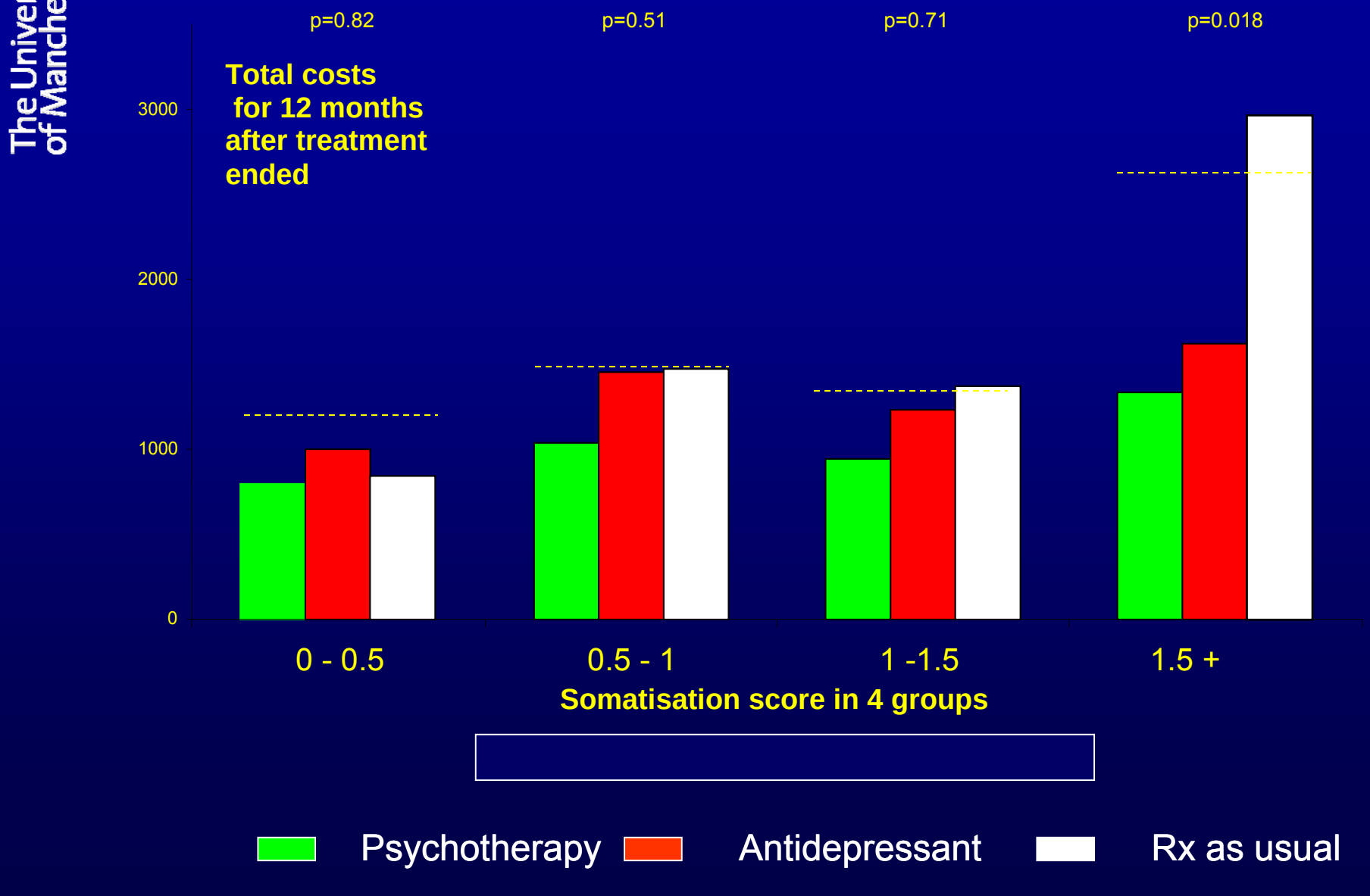
Total costs for 12 months after treatment



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Symptoms of the somatization dimension SCL-90.

			1	4
•	1	Headaches	0-4	little	mod+
•	4	Faintness or dizziness			mod
•	12	Pains in heart or chest			
•	27	Pains in lower back		little	q. a bit
•	40	Nausea or upset stomach		little	q. a bit
•	42	Soreness of muscles			q. a bit
•	48	Trouble getting your breath			mod
•	49	Hot or cold spells			mod+
•	52	Numbness or tingling in part of the body			mod
•	53	Lump in your throat			
•	56	Feeling weak in parts of your body			q. a bit
•	58	Heavy feeling in your arms or legs			q. a bit

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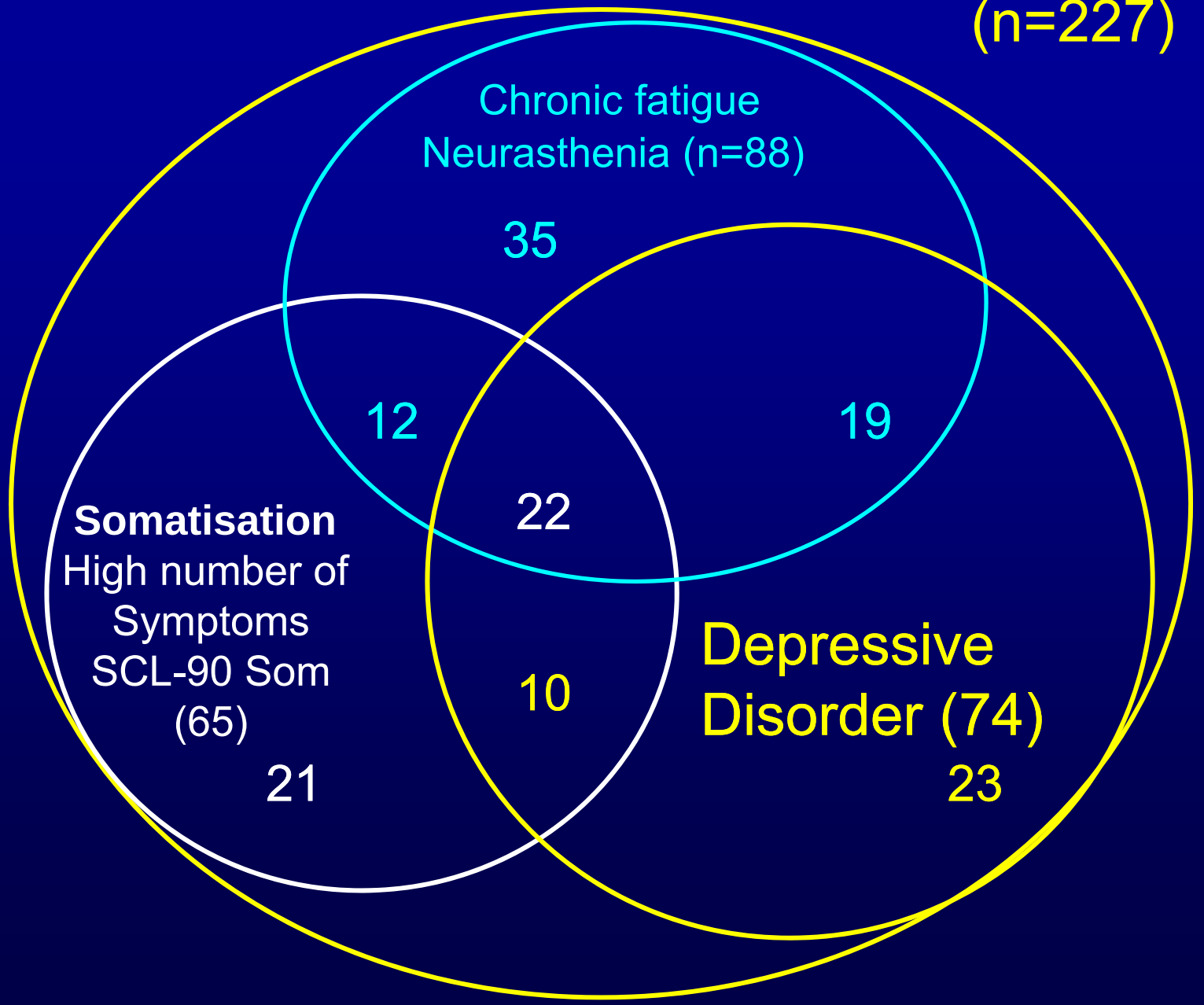
Severe Irritable Bowel Syndrome (n=227)



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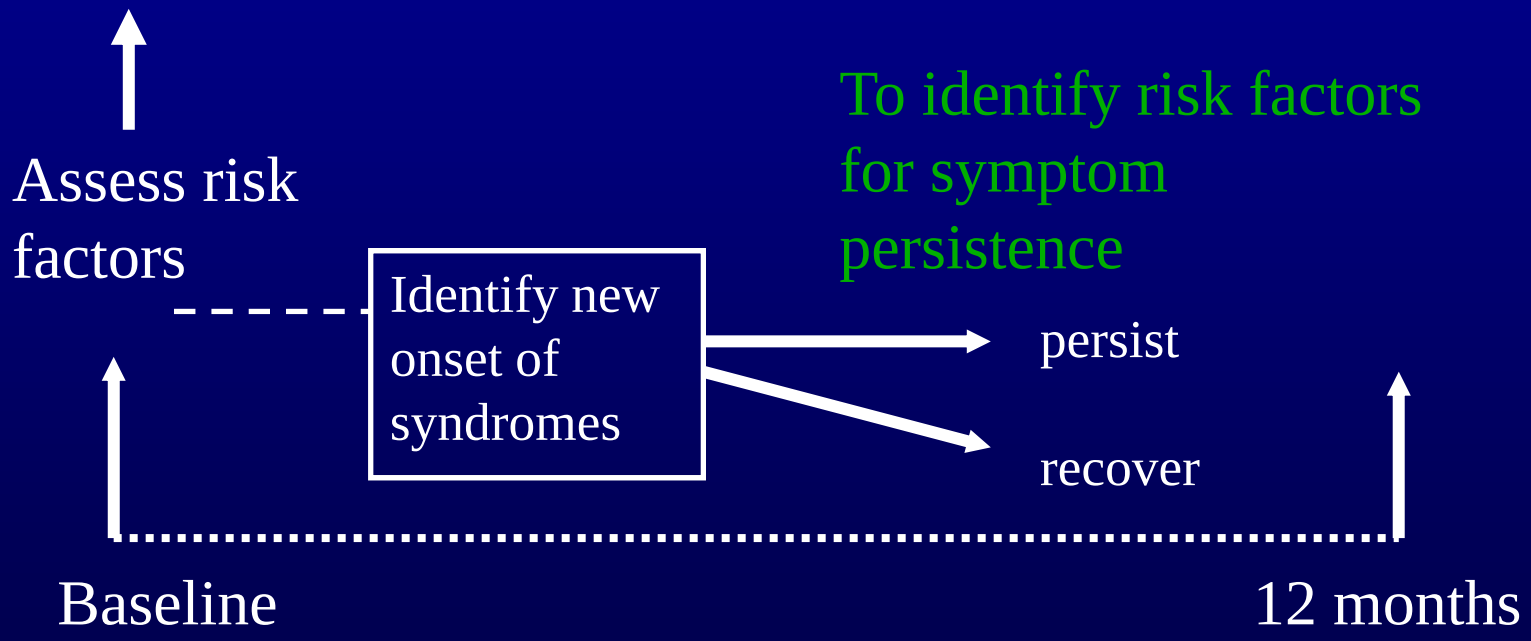
Prospective population-based study

Screen 2,000 population

11% chronic widespread pain

4% IBS 16% fatigue

76% = syndrome-free



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General Practice Symptoms Study

Francis Creed, Nav Kapur, Chris Dickens, (Psychiatrist)
John McBeth Gary Macfarlane, Alan Silman (Epidemiologists),
Andrew Pickles & Barbara Tomenson (Statistics),
Adrian Wells, (Psychologist)
Jonathan Hill (C & A Psych)
Arthur Barsky (Harvard), Wayne Katon (Seattle)
Funded by UK MRC

- n=1443 population-based sample - all bodily symptoms

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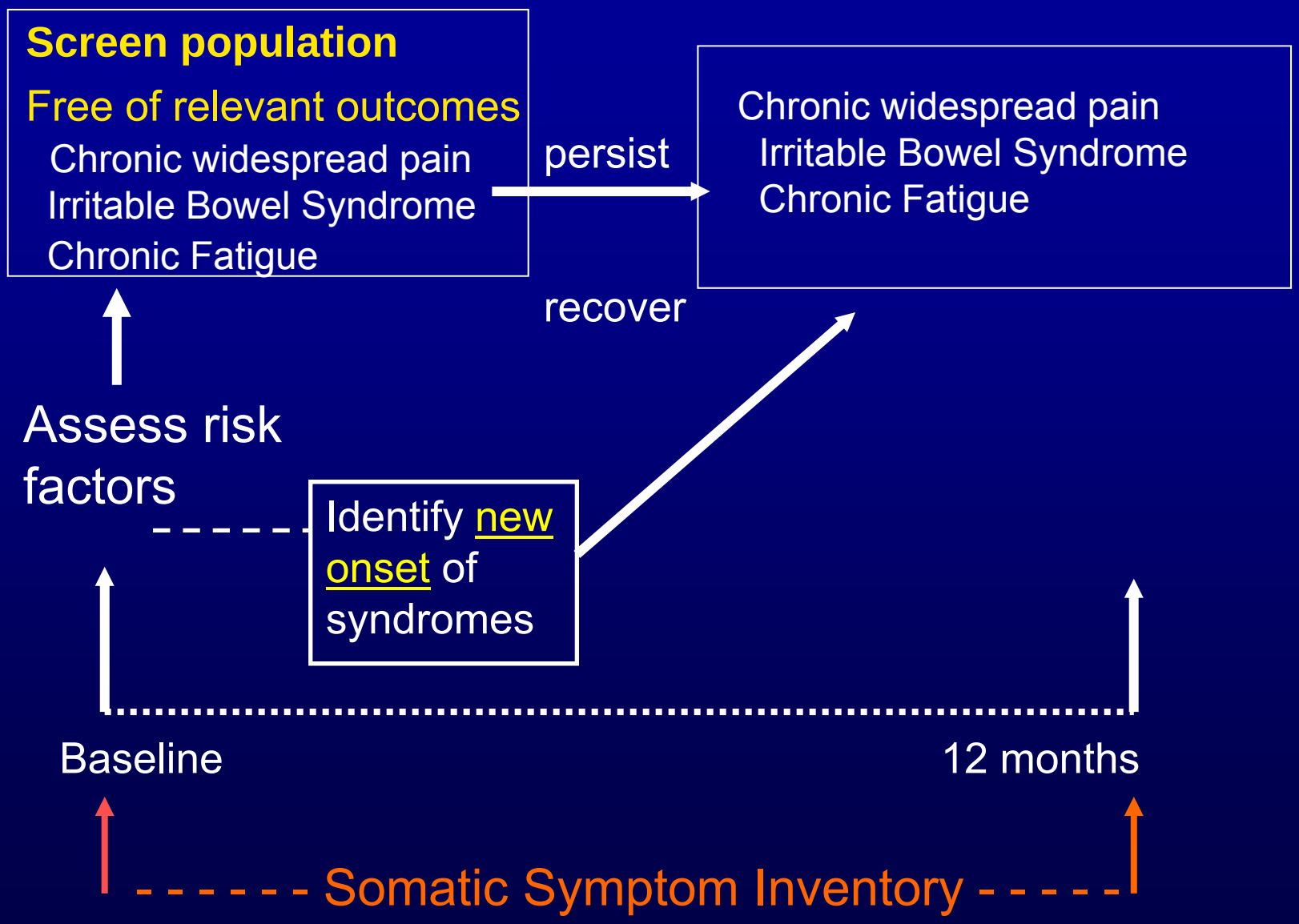
Prospective population-based study



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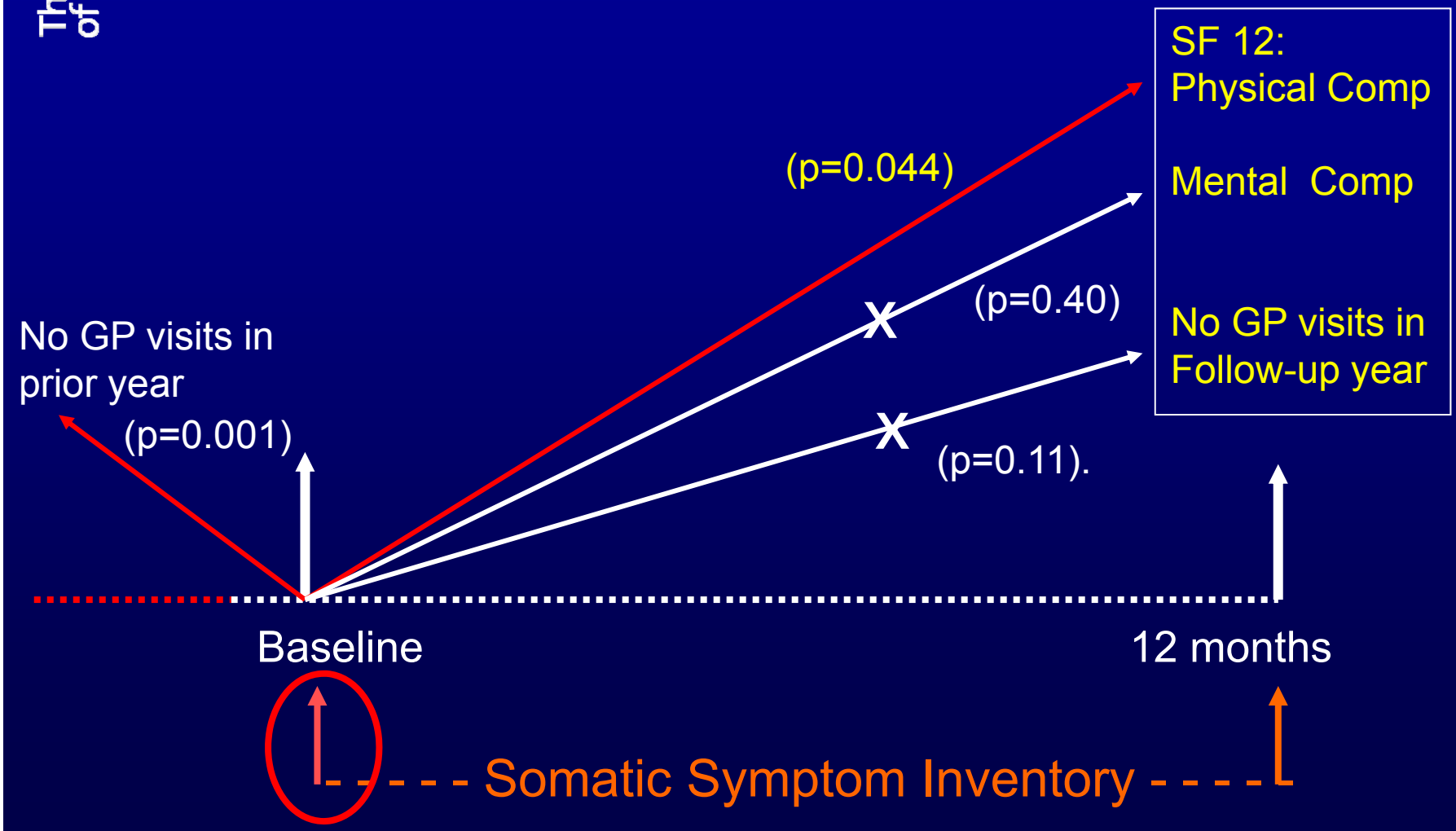
Multivariate analysis adjusting for all variables



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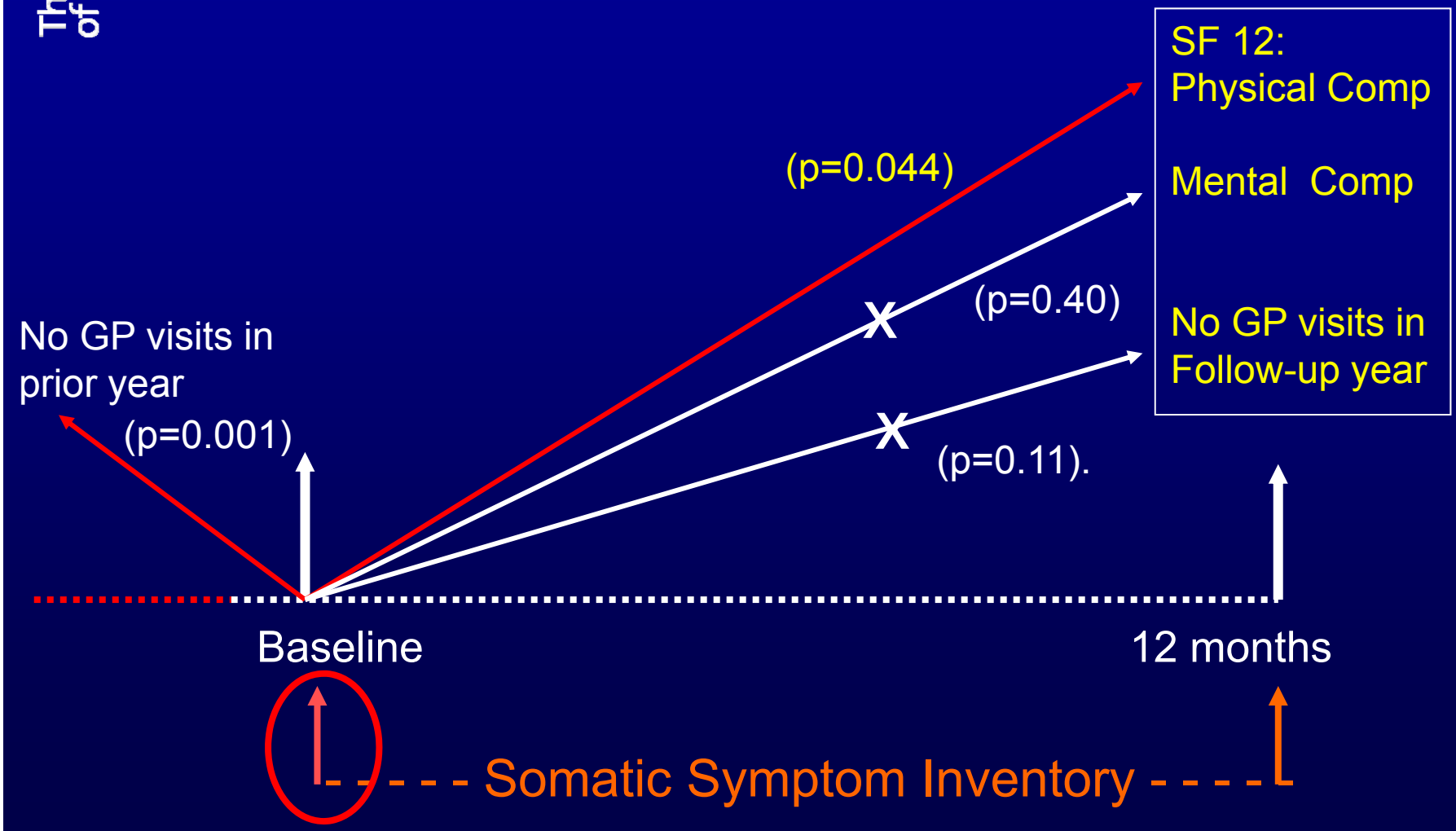
Multivariate analysis adjusting for all variables



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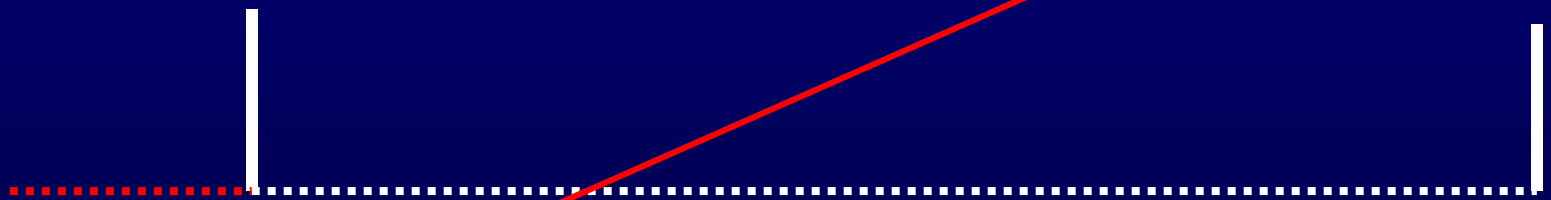
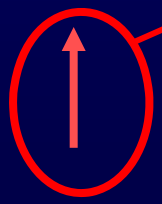
Multivariate analysis adjusting for all variables

No confidant
Number of general illnesses
No consultations year 1
Whitely
SSI x Whitely interaction

SF 12 (health status) Questionnaire

No GP visits in previous year (medical records)





Somatic Symptom Inventory

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Correlates of Extra-intestinal symptoms

- Extra-intestinal symptoms:
- headaches, backaches, wheeziness, insomnia, bad breath, fatigue, general stiffness, loss of interest in sex, frequent need to pass urine, dizziness, weakness, sensitivity to heat or cold, palpitations, and tightness or pressure in chest.

Lembo et al Am J Gastro 2009

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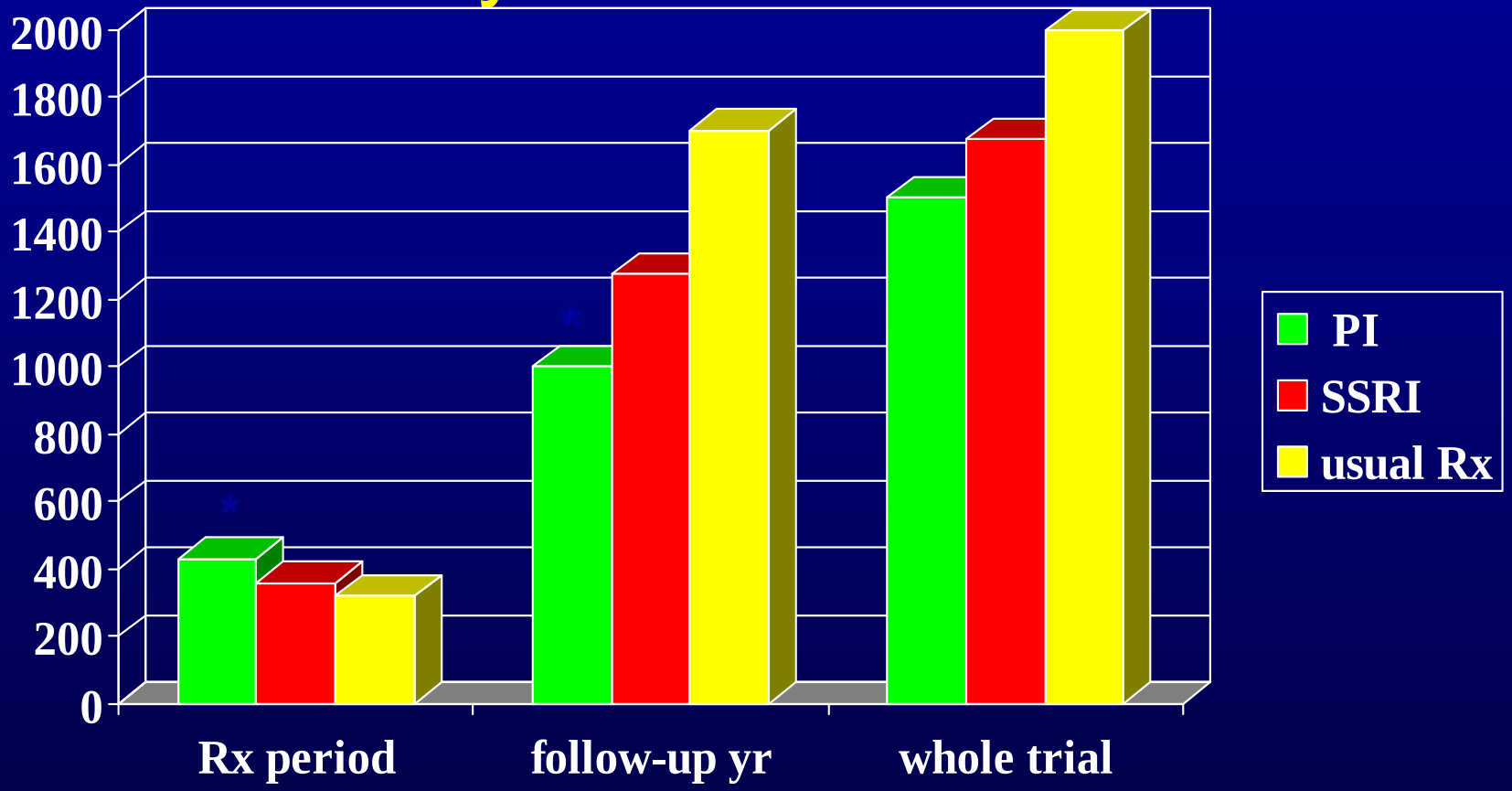
Mean direct healthcare costs for treatment period (12 weeks), follow-up 1 year and whole trial.



(Creed et al *Gastroenterology* 2003; 124: 303-317)

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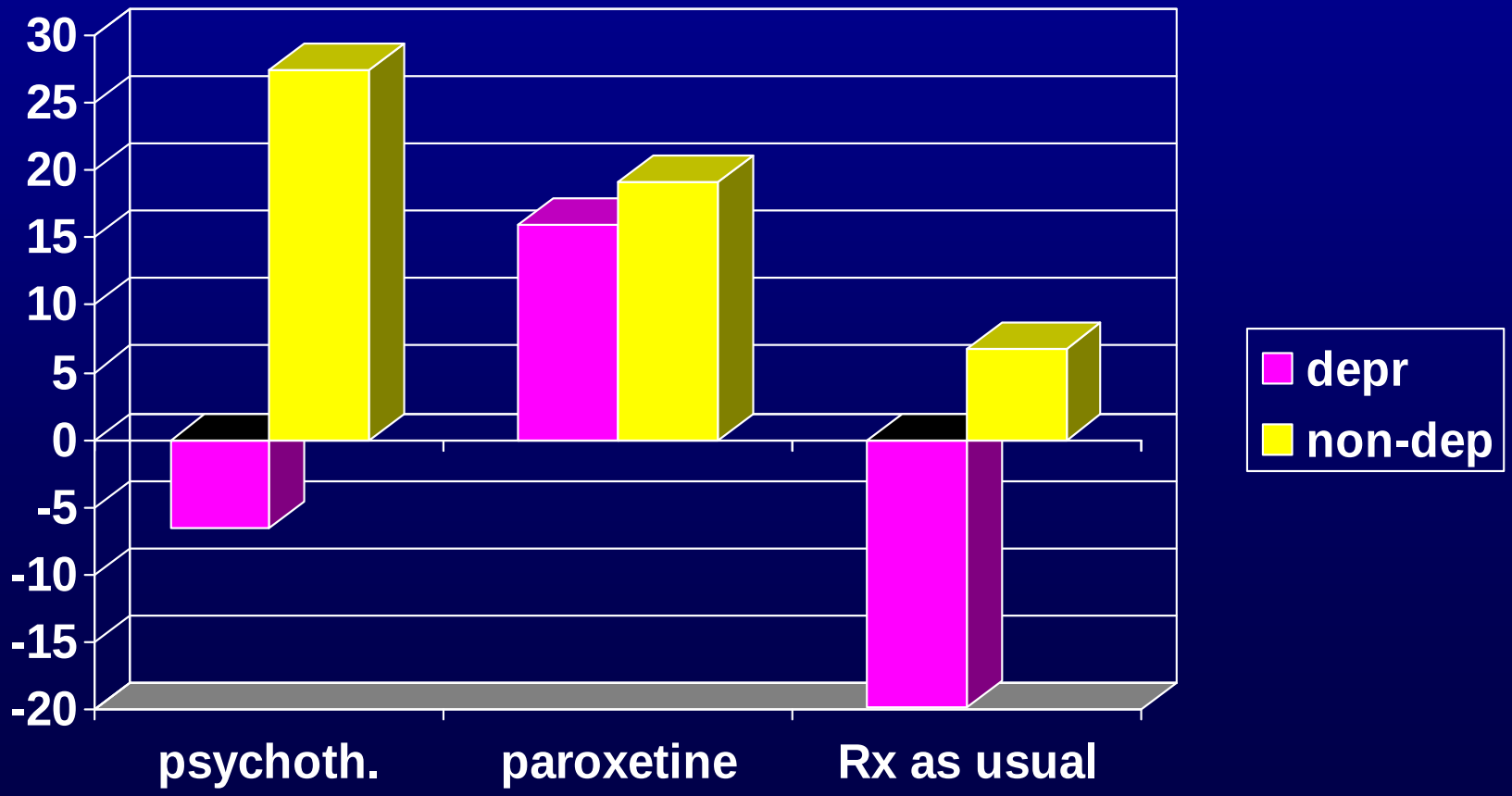
Change in SF36 role limitation score by Rx group & depressive disorder (p adj for age, sex, baseline score, pain and other medical conditions) Creed et al 2003



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Conclusion re depressive disorder

Patients with depressive disorder:

- Do poorly in treatment as usual group and in psychotherapy group
- Do well with paroxetine

i.e. Rx depressed IBS patients with paroxetine

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Patients with Neurasthenia

35% of patients had neurasthenia at start of trial

- This diagnosis predicted a worse outcome

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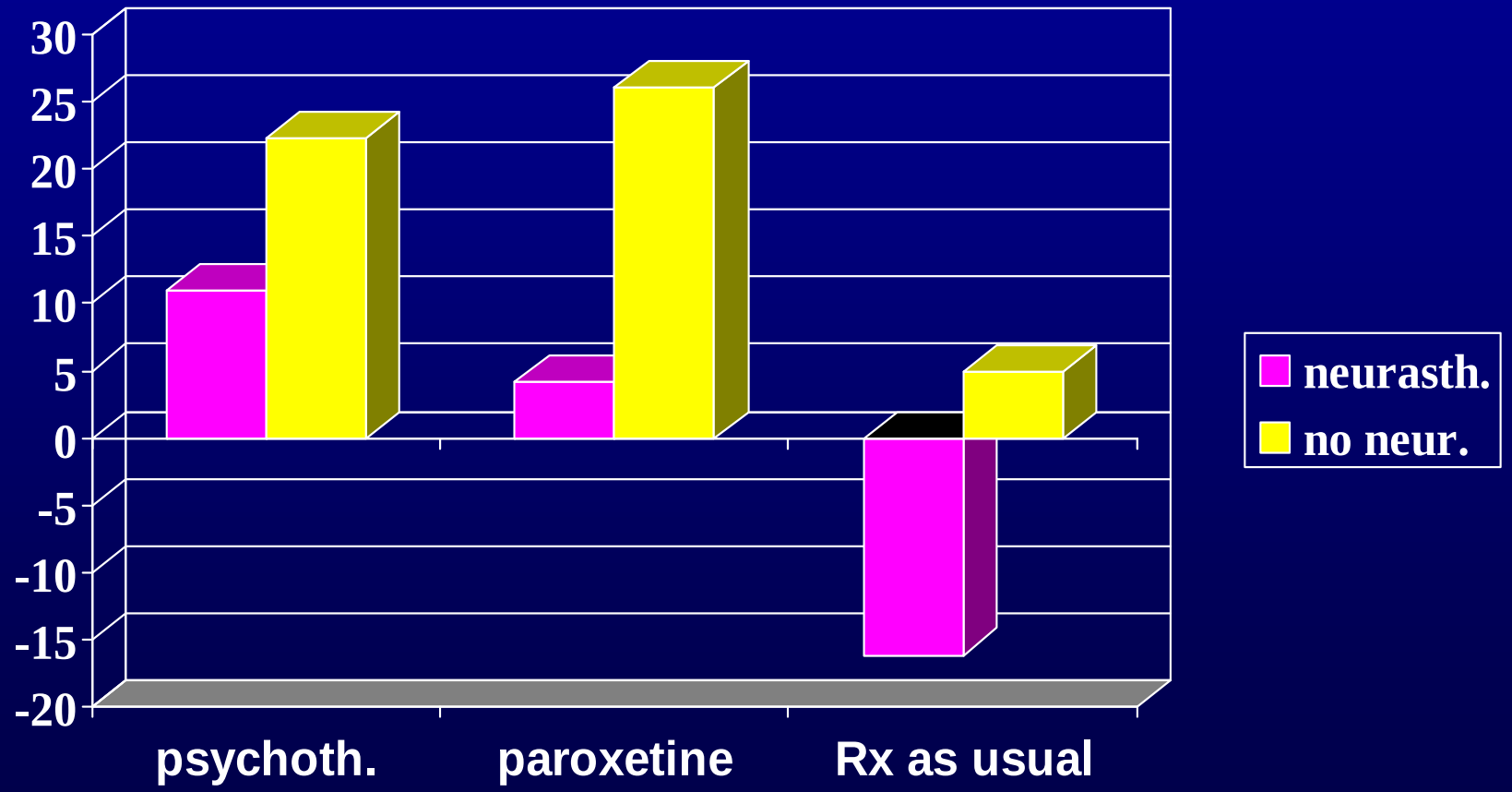
Change in SF36 role limitation score by treatment group – neurasthenia. p adjusted for age, sex, initial score, depression & pain



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Conclusion: Psychiatric diagnosis

- Neurasthenia predicts a poor outcome overall
- Patients with Neurasthenia do better with psychotherapy than with paroxetine.
- Depressive disorder also – poor outcome
- Patients with depressive disorder do better with SSRI antidepressant than psychotherapy

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	Monozygotic	Dizygotic
Age	ns	ns
gender	ns	ns
Co-twin has EIS ≥ 12	**6.82 (4.4 – 10.4)**	**2.71 (1.7 – 4.4)**
Neuroticism	1.14 (1.1 – 1.2)	1.27 (1.2 – 1.4)
Psych. Dis.	4.17 (2.3 – 7.6)	3.15 (1.8 – 5.6)
IBS	2.82 (1.7 – 4.6)	1.95 (1.1 – 3.3)