Can we now explain medically unexplained symptoms?

Francis Creed
University of Manchester, UK

Exeter
13th June 2013
Medical Symptoms not Explained by Organic Disease

Edited by: Francis Creed
Richard Mayou
Anthony Hopkins

Psychiatrists
Psychological
Psyche
LIAISON
Soma
Physical
Physicians

Royal College of Psychiatrists
Royal College of Physicians of London

1992
Aims

Can we now explain Medically Unexplained Symptoms?

No! Paucity of prospective studies

MUS - description or diagnosis?

Recent research → move away from MUS

New DSM 5 diagnosis

Clarify relationship with functional syndromes
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
- Rheumatology
- Neurology
- Irritable Bowel Syndrome
- Fibromyalgia
- Headache, Chronic Fatigue
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
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.
Kooiman CG Psychosomatic Medicine 2000
### Medically unexplained symptoms in medical out-patient clinics

<table>
<thead>
<tr>
<th>Study</th>
<th>No of pts</th>
<th>% unex</th>
<th>Clinics</th>
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</thead>
<tbody>
<tr>
<td>Nimnuan 2001</td>
<td>550</td>
<td>52%</td>
<td>Gynaecology, Neurology, Cardiology, Gastroenterology</td>
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<tr>
<td>Van Hemert ’93</td>
<td>191</td>
<td>52%</td>
<td>General medical</td>
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<tr>
<td>Hamilton 1996</td>
<td>324</td>
<td>35%</td>
<td>Neurology, Cardiology, Gastroenterology</td>
</tr>
<tr>
<td>Fiddler 2004</td>
<td>295</td>
<td>39%</td>
<td></td>
</tr>
<tr>
<td>Kooiman 2004</td>
<td>695</td>
<td>39-50%</td>
<td>General Medicine</td>
</tr>
<tr>
<td>Stone 2009</td>
<td>3781</td>
<td>30%</td>
<td>Neurology</td>
</tr>
</tbody>
</table>
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 10 care
- **Netherlands**: 5th most expensive category
- **USA**: 5th most frequent reason for clinic visits
  (60 million per annum)
  
Somatisation
High number of symptoms

Hypochondriasis
Pronounced worry about health and illness

Medically Unexplained symptoms
Medically Unexplained symptoms

Hypochondriasis
Pronounced worry about health and illness

Functional Somatic Syndromes
Irritable Bowel S,
Chronic Fatigue S.
Fibromyalgia

Somatisation
High number of symptoms
Medically Unexplained symptoms

- Functional Syndromes
  - IBS, CFS...

- Somatisation
  - High number of symptoms

- Hypochondriasis
  - Illness worry

- Anxiety & depression
Medically unexplained symptoms

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

= Major problem in medicine!

Generally not well managed

< 10% of patients with MUS receive specific psychological or antidepressant treatment

Hamilton et 1996, Fink JNNP 2003
Mangwana et al 2009, Hansen 2001
Medically unexplained symptoms
100 consecutive medical out-patients

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

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

• Don’t let hospital/primary care doctors think that all patients with MUS should see a psychiatrist - you will never go home at night!

• Do spend time helping general medical health professionals to develop their skills in managing these patients
DSM III & IV definition of somatisation disorder

- Multiple physical complaints before age 30:
- cannot be fully explained by known medical condition (after full investigation)
- → treatment seeking
  &/or
- impairment of function
No. of bodily symptoms required for diagnosis

- Briquet’s syndrome
  - DSM-III: 12(m) 14(f)
  - DSM IV: 8 symptoms
- Undiff Som Dis: 1 symptom

The University of Manchester
Prevalence of these disorder in primary care

DSM IV Somatization disorder <1%

DSM IV Undifferentiated somatoform disorder 79%

Lynch DJ et al Prim Care Companion J Clin Psychiatry 1999
DSM-IV Definition of somatisation disorder

• “Multiple physical complaints ..............:
• cannot be fully explained by known medical condition (after full investigation)

Difficult to measure
Dualistic thinking
Medically unexplained symptoms
Doctors do not agree?

• 37 GPs - % of patients rated as MUS?
• Answers ranged between 4% and 37%
• But symptom checklist scores - similar prevalence across all practices

Fink et al. Aust NZ J Psych 2005
Medically Unexplained symptoms

**Somatisation**
- High number of symptoms
- Hypochondriasis
  - Illness worry

**Functional Syndromes**
- IBS, CFS...

**Anxiety & depression**
The term: “Medically unexplained symptoms”

- Negative definition - defines group by what it is not
- We should move away from the “either/or” notion - that symptoms are either due to organic disease or psychological abnormalities.

- Creed et al. Psychosom Res 2010
Its all organic

Its all psychological

organic

psychological
Its all organic

Psychosomatic!

Its all psychological
Aetiological model of IBS

- Inflammation – post infective
- Psychological factors
- Data suggest an interaction between infection and psychosocial factors
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
Another aspect of Psychosomatic model

- What about all patients?
- Patients with Medically Unexplained symptoms
- and
- Patients with symptoms explained by organic disease?
Medical out-patients: Neurology, Cardiology & Gastroenterology

- 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

Fiddler et al. Gen Hosp Psych 2004
Jackson et al. J Psychosom Res. 2006
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)
Dr visits increases with number of bodily symptoms

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

MUS

Organic

0 to 5  6 to 7  8 to 9  10 to 12
Health status impaired with many bodily symptoms

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

MUS
Organic

0 to 5 6 to 7 8 to 9 10 to 12
### Predictors of health status

**SF36 PCS 6 months**

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Symbol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>*</td>
</tr>
<tr>
<td>Mus v organic</td>
<td>ns</td>
</tr>
<tr>
<td>Anxiety</td>
<td>**</td>
</tr>
<tr>
<td>Depression</td>
<td>**</td>
</tr>
<tr>
<td>Somatic symptom score</td>
<td>***</td>
</tr>
<tr>
<td>Fear of illness and death</td>
<td>***</td>
</tr>
<tr>
<td>Health worry &amp; preoccupation</td>
<td>**</td>
</tr>
</tbody>
</table>

Fiddler et al Gen Hosp Psych 2004
Number of bodily symptoms - childhood adversity and anx/dep as risk factors

Fiddler et al Gen Hosp Psych 2004

p = 0.002  <0.0005

[mus vs organic bar chart with Ad- Dep-, Adv +, Dep+, Ad+ Dep+ categories]
Medically Unexplained symptoms

Processes that affect all patients

Functional Syndromes
IBS, CFS...

Somatisation
High number of symptoms

Hypochondriasis
Illness worry

Anxiety & depression
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
Changes in DSM 5
Somatic Symptom disorders

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

- Somatisation,
- Hypochondriasis,
- Pain disorder

Somatic Symptom Disorder (includes DSM-IV [undifferentiated] somatisation disorder, hypochondriasis, pain disorder)

A. Somatic symptoms
• 1+ somatic symptoms - distressing +/- disruption of daily life.

B. Excessive thoughts, feelings, and behaviours re somatic symptoms:
• (1) Disproportionate and persistent thoughts about the seriousness of one’s symptoms.
• (2) High level of anxiety about health or symptoms
• (3) Excessive time and energy devoted to these symptoms or health concerns

C. Chronicity: symptomatic for > 6 months.
Distressing Somatic symptoms
Marked health anxiety
Persistent thoughts
serious illness

Somatic symptom disorder

Distressing Somatic symptoms

Medically Unexplained symptoms

DSM 5 Somatic symptom disorder
Somatisation

High number of symptoms

Pronounced worry about health and illness

Medically Unexplained symptoms

Somatic symptom disorder

Illness Anxiety Disorder

Medically Unexplained symptoms
Future research will study these together.

- **Somatisation**
  - High number of symptoms

- **Hypochondriasis**
  - Pronounced worry about health and illness

- **Medically Unexplained symptoms**
Death of somatoform disorders

- DSM-V proposals for Somatic Symptom disorders
- www.dsm5.org Somatic Symptom Disorders
- Elimination of “medically unexplained” symptoms
- Somatic Symptom disorder:
  - Uses total somatic symptom count for all patients
- Relationship with functional somatic syndromes,
- Anxiety & depression and general medical illness

Medically Unexplained Symptoms, Somatisation & Bodily Distress  Ed Creed F, Henningsen P, Fink P
Is it OK to move away from medically unexplained symptoms?
## DSM-V project population-based studies

“A dimensional approach to diagnosis of somatisation in DSM-V”

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

Tomenson et al. BJPsych in press
Medically unexplained  Gronigen  Medically Explained

[Graphs showing data distribution for Males (n=506) and Females (n=588)]
Medically unexplained symptoms formed 46.3% of lifetime CIDI somatic symptoms at Groningen and 58.1% at Oslo
# Correlates of somatic symptoms

<table>
<thead>
<tr>
<th>Location</th>
<th>Medically unexplained</th>
<th>Medically explained</th>
</tr>
</thead>
<tbody>
<tr>
<td>Groningen</td>
<td>Age (b=-.02), g med illness (b=0.60), MDD, panic or GAD (b=0.97)</td>
<td>female (b=0.96), g med illnesses (b=1.16)</td>
</tr>
<tr>
<td>Oslo</td>
<td>female (b=0.38), g med illness (b=0.12) anxiety and/or depression (b=0.71)</td>
<td>Age (b=0.21), female (b=0.26), g med illness (b=0.53) anxiety and/or depression (b=0.55)</td>
</tr>
<tr>
<td>Dresden</td>
<td>female (b=1.26), g med illnesses (b=2.02), MDD (b=2.08) anxiety (b=3.27)</td>
<td>Age (b=0.07), female (b=1.26), g med illnesses (b=2.02), MDD (b=2.08),</td>
</tr>
<tr>
<td>Munich adolescents</td>
<td>female (b=0.25) Anxiety (b=0.60) Depression (b=0.42), g med illness (not incl)</td>
<td>Age (b=0.10), female (b=0.38) Anxiety (b=0.71) Depression (b=0.74), g med illness (not incl)</td>
</tr>
</tbody>
</table>
Is it OK to move away from medically unexplained symptoms?

There are more similarities than differences between medically unexplained and explained symptoms:

* distribution in the population
* correlations with sex, general medical illness and anxiety & depression
All somatic symptoms

- More numerous than medically unexplained
- Can be applied to all patients whereas Somatoform disorders only applies to “medically unexplained” symptoms and may exclude patients with organic disease who have numerous somatic symptoms.

Kroenke: Of cancer patients with depression &/or pain half (c. 10% of all cancer patients) had multiple somatic symptoms (15 or more). Patients with multiple somatic symptoms had more severe impairment.
Relationship between numerous somatic symptoms and Functional Somatic Syndromes

- What is the relationship between multiple somatic symptoms and Functional Somatic Syndromes?
  - A) outcome
  - B) risk factors
Prospective population-based study (n=1433)

Chronic widespread pain

Chronic fatigue

Irritable bowel syndrome
Chronic fatigue

Irritable bowel syndrome

Prospective population-based study (n=1433)

Chronic widespread pain

30.1%

30.1%

37.1%

% with many Somatic Symptoms (top 10%)
Chronic fatigue

Irritable bowel syndrome

Chronic widespread pain

Prospective population-based study (n=1433)

30.1%

% with many Somatic Sx (top 10%)
Health status by group – Chronic widespread pain

The University of Manchester

- no CWP
- CWP alone
- CWP + SSI >25

![Chart showing health status by group: Chronic widespread pain]
Irritable bowel syndrome
Health status by group – Chronic Fatigue

The University of Manchester

PCS  | MCS  | Thermom
---   | ---   | ---
50    | 40    | 80
40    | 30    | 70
30    | 20    | 60
20    | 10    | 50
10    | 0     | 40
0     | 0     | 30

Legend:
- **no CF**
- **CF alone**
- **CF + SSI>25**
FSS and Somatic symptom disorder

• Only some people with a Functional Somatic syndrome (e.g. Irritable bowel syndrome, Chronic Fatigue syndrome or Chronic Widespread pain) have features of Somatic Symptom disorder.

• People with both FSS and features of Somatic Symptom disorder have greater impairment of health-related quality of life (Creed et al Int J Behav Med 2013)
Two patients with irritable bowel syndrome

<table>
<thead>
<tr>
<th>Woman aged 53 years</th>
<th>Woman aged 40 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBS 7 years</td>
<td>IBS 4 years</td>
</tr>
<tr>
<td>Abdominal pain relieved with defecation</td>
<td>Abdominal pain relieved with defecation</td>
</tr>
<tr>
<td>Bloating</td>
<td>Bloating</td>
</tr>
<tr>
<td>Disturbed bowel habit</td>
<td>Disturbed bowel habit</td>
</tr>
<tr>
<td>Many “extra-GI” symptoms</td>
<td>Few Extra-GI symptoms</td>
</tr>
<tr>
<td>Fear of serious illness</td>
<td>Chronic arthritis</td>
</tr>
<tr>
<td>Repeatedly asking for tests to identify physical cause</td>
<td>Accepted reassurance of gastroenterologist - no serious physical disease</td>
</tr>
<tr>
<td>Psychological distress,</td>
<td></td>
</tr>
</tbody>
</table>
Two patients with irritable bowel syndrome

<table>
<thead>
<tr>
<th>Woman aged 53 years</th>
<th>Extra-intestinal symptoms include:</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBS 7 years</td>
<td>pains in muscles and joints, lower back pain, headaches, chronic fatigue, urinary frequency dyspareunia</td>
</tr>
<tr>
<td>Abdominal pain relieved with defecation</td>
<td></td>
</tr>
<tr>
<td>Bloating</td>
<td></td>
</tr>
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<tr>
<td>Psychological distress,</td>
<td></td>
</tr>
</tbody>
</table>

Extra-intestinal symptoms are associated with impaired Health-related quality of life after adjustment for psychiatric disorders, (Lembo et al Am J Gastro 2009)
Relationship between numerous somatic symptoms and Functional Somatic Syndromes?

- A) outcome – marked impairment only when there is co-existing multiple somatic symptoms
- B) risk factors?
Reported Childhood abuse

- No syndr
- Syndr alone
- Syndr + SSI26

CWP
- p=0.082

IBS
- p=0.16

CF
- p=0.038
Recent threatening life events

- **No syndr**
- **Syndr alone**
- **Syndr + SSI26**

<table>
<thead>
<tr>
<th>Condition</th>
<th>CWP</th>
<th>IBS</th>
<th>CF</th>
</tr>
</thead>
<tbody>
<tr>
<td>CWPSSI diff other 2</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>IBSSSI diff no syndr</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>No syndr diff both</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
</tr>
</tbody>
</table>
Case history – 63 yr old woman

Age 52 -62 years – heart failure (Ejection fraction = 25%).

• Marked physical limitation but well-adjusted
• Age 62 : further chest pains – Tests → heart function unchanged
• Non-cardiac / G-I pain? → Gastroenterologist
• Retrosternal chest pain, heartburn, lower abdominal pain,
• Over 12 months : extensive G-I + further cardiac investigations → All normal.
Case history – 65 yr old woman

Over 12 months
• Experienced “all kinds of aches and pains”: multiple distressing bodily symptoms
• Had “all the tests its possible to have” – no help → preoccupied ++ with bodily symptoms
• “frightened of husband leaving me alone even in the house”: extreme health anxiety
• Excessive time and energy devoted to these symptoms or health concerns.
• Occurred after relative developed heart disease and cardiac medication affected eyesight
Case history – 65 yr old woman

Subsequent 3 months prior to referral to Psych: Depressive syndrome developed with panic attacks (wanted husband to be in sight for fear of heart attack)

- Symptoms developed after death of close friend
- Treated with antidepressants → improved but still anxious about her health and preoccupied with somatic symptoms
- CBT for health concerns → returned to non-anxious state of previous 10 years
This case illustrates:

- Somatic Symptom Disorder in presence of medical illness and anxiety/depression
- distressing somatic symptoms
- preoccupation with bodily symptoms [ SSD
- marked health anxiety
- Independent predictors of:
  - High health care use/costs
  - Impairment of quality of life
### Predictors of healthcare use

<table>
<thead>
<tr>
<th>Kapur et al 2004 (5 years) n= 738</th>
<th>Frostholm 2005 (2 years) n=1765</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex</td>
<td>Female sex</td>
</tr>
<tr>
<td>Older age</td>
<td>Older age</td>
</tr>
<tr>
<td>Fear of serious illness</td>
<td>Thoughts of persisting illness / serious symptoms</td>
</tr>
<tr>
<td>Worry re symptoms</td>
<td>Chronic physical disorders, psychological distress, Number of somatic symptoms (Health anxiety)</td>
</tr>
<tr>
<td>Chronic physical and chronic psychiatric disorders, Number of somatic symptoms Psychological distress,</td>
<td></td>
</tr>
</tbody>
</table>
Prospective population-based study
(Creed et al J Psychosom Res 2012)

<table>
<thead>
<tr>
<th>Baseline</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;12 years education</td>
<td>-2.25 (-3.79 to -0.70)</td>
</tr>
<tr>
<td>No. of medical illness</td>
<td>-2.32 (-3.47 to -1.17)</td>
</tr>
<tr>
<td>HADS anxiety</td>
<td>0.34 (0.10 to 0.59)</td>
</tr>
<tr>
<td>HADS depression</td>
<td>-0.51 (-0.85 to -0.18)</td>
</tr>
<tr>
<td>Somatic symptom score</td>
<td>-0.36 (-0.51 to -0.22)</td>
</tr>
</tbody>
</table>

SF 12 Physical score & EUROQOL

Baseline | 12 months

Somatic Symptom Inventory – number of bothersome symptoms like PHQ 15.
This case illustrates aspects of treatment

- **Kroenke 2006** Systematic review:
  - CBT > Behav therapy > antidepressants
  - Improved: Abridged Somatisation disorder > MUS
  - Somatic symptoms improved independent of improvement in depression/anxiety
  - CBT effective in Som Dis *(Allen 2006)* not mediated by improved depression
  - Hypochondriasis *(Barsky 2004)*
  - CBT no better than sophisticated routine care for MUS *(Sumathipala 2008)*
Move away from Medically Unexplained Symptoms

Prospective studies:
Multiple Somatic Symptoms +
Health anxiety and preoccupation with illness are predictors of outcome
→ DSM 5 diagnosis Somatic Symptom Disorder

Consider these dimensions in addition to:
• anxiety/depression,
• general medical illness and
• functional somatic syndromes
In clinical practice:

- Assess: number of somatic symptoms - ask questions about all bodily systems not just one
- Has patient consulted re different symptoms?

Ask: “Do you think your symptoms are serious? What caused/exacerbates them? How much do you worry about them? What are the feared consequences?”

- Past experience of illness in family/self
- Recent stresses/anxiety/depression
In clinical practice:

**Management:**

1) Explanation – pain does not mean pathology, factors that lead to health anxiety

2) Assess existing general medical illness and reasonable undetected gen med illness

3) Treat anxiety & depression

4) Principles of CBT – monitoring, avoidance, seeking reassurance...
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