Protocol information

Authors

Marianne Rosendal¹, Chris Burton², A H Blankenstein³, Per Fink⁴, Kurt Kroenke⁵, Michael Sharpe⁶, Morten Frydenberg⁷, Richard Morriss⁸

¹Research Unit for General Practice, Institute of Public Health, University of Århus, Århus, Denmark

²Community Health Sciences, General Practice Section, Edinburgh, UK

³Department of General Practice, EMGO Instituut (VU), Amsterdam, Netherlands

⁴Research Clinic for Functional Disorders and Psychosomatics, Århus University Hospital, Århus, Denmark

⁵Department of Medicine and Regenstrief Institute, Indiana University, Indianapolis, IN, USA

⁶School of Molecular & Clinical Medicine, University of Edinburgh, Edinburgh, UK

⁷Department of Biostatistics, Institute of Public Health, Århus University, Århus, Denmark

⁸Psychiatry, University of Nottingham, Nottingham, UK

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Contact person

Marianne Rosendal

Research Unit for General Practice, Institute of Public Health University of Århus Vennelyst Boulevard 6 Århus DK-8000 Denmark

E-mail: m.rosendal@alm.au.dk

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What's new

Date	Event	Description	
History			
Date	Event	Description	

Abstract

Background Objectives Search strategy Selection criteria Data collection and analysis Main results Authors' conclusions Plain language summary

Background

Description of the condition

Patients with physical symptoms which cannot be explained by pathologically defined disease are common in primary care (Fink 1999a; Kroenke 1989; Peveler 1997; Toft 2005; Verhaak 2006). They represent a spectrum of conditions ranging from mild self-limiting symptoms to severe and disabling disorders (Katon 1991; Rosendal 2007). As the number and severity of symptoms increases, so does the disability and the prevalence of psychological distress and dysfunctional illness cognitions (Hansen 2007; Kroenke 1994); there is good epidemiological evidence that the physical and psychological processes are inter-related (Aggarwal 2006; Hotopf 1998).

For the purposes of this review, the term Functional Somatic Symptoms (FSS) is used to refer to the presence of physical symptoms that are not attributable to organ pathology or any conventionally defined disease and which meet additional criteria such as the number of symptoms or other clinical characteristics. This term is used in preference to the alternative term of Medically Unexplained Symptoms (MUS). Patients with severe FSS have impaired health related quality of life (Gureje 1997; Smith 1986), disproportionate healthcare costs (Barsky 2001; Fink 1999a; Smith 1986) and lower satisfaction with their healthcare providers (Frostholm 2005; Lin 1991).

There is no universally agreed way of classifying FSS (<u>Sharpe 2006</u>). FSS includes functional somatic syndromes: clusters of related symptoms which are typically specific to one organ system or medical speciality. Some of the best known are irritable bowel syndrome, fibromyalgia and chronic fatigue syndrome. At least 29 such syndromes have been described (<u>Henningsen 2007</u>); new syndrome definitions continue to appear and old ones to evolve. Importantly, there is substantial overlap between syndromes (<u>Deary 1999</u>; <u>Wessely 1999</u>) and most adult patients with FSS, regardless of which symptoms they present, experience symptoms in a range of bodily systems (<u>Fink 2007</u>). Psychiatric classifications typically view individuals on a spectrum of severity from the most severe Somatisation Disorder, through somatoform disorder to the mildest abridged somatisation (<u>Escobar 1989</u>). Some patients on the FSS spectrum will also demonstrate pathological health anxiety or hypochondriasis (<u>Francis 1994</u>; <u>World Health Organisation 1993</u>). While many patients with FSS meet criteria for co-morbid anxiety or depressive disorders, these are not invariably present and the concept that FSS might simply represent somatised psychiatric illness is not tenable.

The prevalence of FSS in primary care depends on the sampling strategy and the definitions used. Studies of the reason for consulting find that approximately 15% of patients seeing their GP do so for a symptom not obviously explained by organic disease (Peveler 1997; Rosendal 2003), but the proportion consulting repeatedly for an unexplained symptom is considerably lower (Verhaak 2006). 20–30% of GP consulters aged 18–65 meet criteria for somatoform disorders (Arnold 2006;Fink 1999a;Toft 2005) but not all will present unexplained symptoms at that consultation. Less than 1% of GP consulters have the most severe Somatisation Disorder (Fink 1999a;Toft 2005). The natural history of FSS varies between individuals and symptom patterns frequently change over time. Overall approximately half of patients with FSS will improve spontaneously over a year (Barsky 1998; Craig 1993; Gureje 1999;Lieb 2002).

Description of the intervention

Methods of treating FSS

Historically, attempts to treat FSS have used a psychosomatic perspective, whereby physical symptoms are thought to arise from (hidden) mental distress. Mind body interactions are now seen as more complex but can be usefully viewed within a cognitive-behavioural model. This perspective has led to effective treatment by specialists for somatoform disorders (Kroenke 2000) and some specific syndromes (Henningsen 2007). An evolving family of brief therapies for primary care, originally termed "reattribution" (Goldberg 1989) has been developed for use in primary care; such therapies have features in common with the more detailed cognitive behavioural models. The original reattribution model targeted psychiatric illness, i.e. presenting somatisation (Goldberg 1989) and was built on problem-solving therapy. Later the model was extended by Gask and Morriss to a wider range of somatisation processes (Morriss 2006). A recent extended reattribution model integrated elements from cognitive therapy such as "reframing " in a way which integrated mind and body using a descriptive approach to FSS rather than implying causation (Fink 2002).

Enhanced care

'Enhanced care' is defined as the use of a structured treatment model which draws on explanations for symptoms in broad bio-psycho-social terms and, or, encourages patients to develop additional strategies for dealing with their physical symptoms. It includes "reattribution" (Goldberg 1989) and "reframing" (Fink 2002) models. Treatment is delivered by primary care clinicians to their own patients after the training of these physicians in the enhanced care model. Primary care clinicians include doctors and other health care professionals providing first contact care across a wide range of clinical domains (Boerma 1999; Starfield 1994; World Health Organisation 2001). Typically, training will involve experienced primary care clinicians taking time from their routine work and being taught both a theoretical framework and practical techniques to use within consultations with their own patients. Following the training, additional time for longer consultations may, or may not, be made available for the trained clinicians.

How the intervention might work

Early studies of reattribution training in primary care used a before and after evaluation with no randomisation. They showed that GP's skills were improved (<u>Kaaya 1992</u>) in a way which improved patient wellbeing (<u>Morriss 1999</u>) and reduced healthcare costs (<u>Morriss 1998</u>), these findings were taken to support the notion that making the link between psychological distress and physical symptoms led to better outcomes.

Subsequent studies have suggested various additional mechanisms, including providing extra time for patients, allowing expression of emotions or building useful explanations (Brody 1990;Dowrick 2004; Salmon 2007). Given that FSS is an umbrella term for a heterogeneous group of patients and disorders, it is likely that different psychological and physiological processes will be relevant for different individuals. It is also plausible that paradoxical effects of psycho-social intervention will be seen whereby some patients benefit while others become more distressed, at least in the short term. There is some epidemiological (Kirmayer 1991) experimental (Graugaard 2003) and interventional (Schweickhardt 2005) evidence to support this conjecture.

Given the variety of patient groups, psychological processes and physical symptoms we consider enhanced care as a complex intervention <u>Campbell 2001</u>.

Why it is important to do this review

We are currently aware of several studies which have evaluated enhanced care models, partially or fully based on reattribution, for patients with FSS. While these have shown positive effects on GP's attitude (<u>Rosendal 2005</u>) and diagnostic awareness (<u>Rosendal 2003</u>), effects on patient outcomes have been modest and insignificant in individual trials. We wish to carry out a systematic review and meta-analysis of the clinical effectiveness of these interventions.

This review fits alongside another Cochrane review, 'Patient consultation letters for medically unexplained symptoms' ((<u>Hoedeman 2008</u>) which involves specialist assessment of individual patients). This review includes some studies in the broader review of psychosocial interventions delivered by general practitioners (<u>Huibers 2007</u>) but we focus only on FSS and include more recent studies.

Objectives

This review aims to evaluate the clinical effectiveness of enhanced care interventions for FSS by primary care professionals. The review focuses on patient outcomes.

Methods

Criteria for considering studies for this review

Types of studies

All randomised controlled trials of enhanced care compared againts treatment as usual.

Studies will be restricted to the primary care setting and to treatment models which are specific to that setting. Studies of specialist interventions hosted in primary care (for example prolonged contact with a psychotherapy specialist at the primary care clinic rather than hospital) will not be included.

Studies will be included without regard to the unit of randomisation, i.e. whether individual clinicians or clusters of clinicians are randomised. Crossover studies will not be included because the nature of the intervention – a change in practice – permits crossing over in one direction only.

Types of participants

Clinicians

Studies will be restricted to those in which treatment is delivered by generalists such as general practitioners, nurse practitioners or other health care professionals working within the primary care setting with first contact and ongoing care for patients regardless of their presenting problems. This excludes care provided by mental health professionals. No exclusions will be made on the basis of age, years of practice, practice type, and previous psychological training.

Studies must include specific training of participating clinicians; in groups where practitioners work together, this may be either to individuals or to the whole group.

Patients

Studies will be limited to those involving adults (at least 18 years old) with FSS, identified either by case finding or by the primary care clinician's assessment of the presenting problem. In the absence of universally agreed criteria for FSS, studies in which patients are included based on their clinician's own assessment of the presenting problem as "medically unexplained" will be included. Case finding studies will be required to use validated instruments for FSS such as rating scales and interviews (Table 1). Studies of a single functional syndrome (e.g. Irritable Bowel Syndrome) will be included provided they meet the other criteria.

Studies where the primary entry criterion is a specific non-somatoform mental health disorder (e.g, depression, anxiety, post-traumatic stress disorder) will be excluded. However, the presence, or continuing treatment, of one or more common mental disorders such as depression and anxiety in patients included with FSS will not lead to automatic exclusion. Our definition of FSS excludes factitious disorder and psychiatric illness arising as a

complication of an organic disease (for example depression in a patient with heart disease).

Types of interventions

Experimental condition

Studies will be included if they employ a model of enhanced care, based on reattribution or reframing of symptoms, characterised by psychosomatic explanations for physical symptoms and "making the link" between symptoms and mental distress. The intervention must be delivered by either a generalist after additional training or a generalist acting as an intermediate specialist such as a general practitioner with a specific interest. Delivery may be provided either within routine consultations or during additional dedicated appointments which may be longer than usual or involve specific reimbursement.

The duration, content and degree of formalisation (eg written manual) of the training will be described for studies but we will not specify criteria in advance as different methods may be applicable in different professional cultures. Studies will be restricted to the primary care setting and to treatment models which are specific to that setting. Studies of specialist interventions hosted in primary care (for example prolonged contact with a psychotherapy specialist at the primary care clinic rather than hospital) will not be included.

The review does not include organisational changes involving shared care models with mental health professionals (Cochrane consultation letter group (<u>Hoedeman 2008</u>). Trials of pharmacological treatment will be excluded but pharmaceutical treatment is permitted as part of the general treatment.

Control comparators

Studies for inclusion should have, as a control comparison group, patients receiving treatment as usual.

Types of outcome measures

Primary outcomes

The primary outcome measure is patient health status measured by a validated quality of life tool. Specifically, for SF-36 and related tools (SF-12, SF-8) the primary outcome will be the physical and mental component summary scores.

Secondary outcomes

- 1. Measures of symptom load (number and/or severity of symptoms), for instance using a checklist such as PHQ-15 (Kroenke 2002) or Somatic Symptom Index. While symptoms are likely to be related to health related quality of life, the number and intrusiveness of symptoms appears to be a central characteristic of FSS.
- 2. The patients' illness beliefs, using a validated tool such as the Illness Perception Questionnaire Weinman 1996
- 3. Depression and anxiety measured by questionnaire (eg Hospital Anxiety & Depression Scale)
- 4. Functional status measured as sick leave
- 5. Patient satisfaction with care
- 6. Health care utilisation: The review will analyse medical consumption if stated outcomes can be compared either as number of visits and days in care or as health care costs
- 7. Attrition from studies

We will analyse both primary and secondary outcomes as continuous measures and will test for positive and negative treatment effects in by looking for changes in measures.

Outcomes will be categorised as short term (0-5 months), medium term (6-11 months) or long term follow-up (12 or more months). The primary focus will be on 12 month follow-up data where available.

Search methods for identification of studies

Search of literature will be limited to the time period 1966 to publication of this review.

No language restriction will be employed.

Electronic searches

We will use a broad search strategy for Functional Somatic Symptoms (FSS) but limit the search to RCTs and primary care.

Searches will be conducted in: The CCDAN specialised registers (CCDANCTR-Studies and CCDANCTR-References, <u>Appendix 1</u>), the Cochrane Central Register of Controlled Trials (CENTRAL), the Database of Abstracts of Reviews of Effectiveness (DARE), Medline (1950-) (<u>Appendix 2</u>), Embase (1980-), PsychINFO (1806-), CINAHL (1982-), PSYNDEX, SIGLE, and LILACS.

All reference lists of relevant papers will be screened and author names from identified studies will be searched electronically.

Searching other resources

The electronic searches will be supplemented by hand searches in:

- Conference proceedings: I nternational P sychosomatic R esearch, European liaison-psychiatry and the Academy of Psychosomatic Medicine
- Reference lists of retrieved and potentially relevant papers, as well as relevant systematic reviews,

dissertations, theses and literature reviews

Furthermore, we will contact first authors of identified studies and other experts in the field for information about published or unpublished studies (this includes contact to research groups that have been taught reattribution by Linda Gask).

Data collection and analysis

Selection of studies

MR and CB will independently screen all study abstracts identified by the search strategy. When there are disagreements about the selection of a trial a third review a uthor (MS or KK) will be asked to assess the trial and the evaluation by MR and CB. In view of the relatively small field of interest and the involvement in the review of several trial investigators, we believe that blinding of review authors is not possible.

Data extraction and management

The study characteristics of selected trials will be extracted by two of three review authors (MR, CB, NB) thereby avoiding investigators reviewing their own studies. The extraction will be conducted independently by two authors. Disagreements between the authors will be resolved by discussion with a third author (PF). The provisional data extraction form is presented in <u>Table 2</u> and will be pilot tested by MR and CB on five studies before implementation.

Assessment of risk of bias in included studies

We will assess the risk of bias using the Cochrane Collaboration's tool for assessing risk of bias and report the results in a standard Risk of Bias table assessing the following domains

1) Sequence generation: Was the allocation sequence adequately generated?

2) Allocation concealment: Was allocation adequately concealed?

3) Blinding of participants, personnel and outcome assessors for each main outcome or class of outcomes: Was knowledge of the allocated intervention adequately prevented during the study?

4) Incomplete outcome data for each main outcome or class of outcomes: Were incomplete outcome data adequately addressed?

5) Selective outcome reporting: Are reports of the study free of suggestion of selective outcome reporting?6) Other sources of bias: Was the study apparently free of other problems that could put it at a high risk of bias?

A description of what was reported to have happened in each study will be provided, and a judgement on the risk of bias will be made for each domain within and across studies, based on the following three categories: A. Yes (low risk of bias)

B. Unclear

C. No (high risk of bias).

The study quality will be assessed by two reviewers independently (MR, CB, NB) and disagreements will be resolved by consulting MS or KK. Where necessary, the authors of the studies will be contacted for further information. The primary analysis will include all studies. A secondary sensitivity analysis will be conducted including only studies rated as at low to moderate risk of bias.

Measures of treatment effect

Continuous outcomes: whereIf the patient populations are comparable but outcome measures vary between studies, effect sizes will be extracted as standardised mean difference (SMD) with 95% confidence intervalsfrom continuous measures.

Dichotomous outcomes: these outcomes will be analysed by calculating a pooled relative risk (RR) for each comparison, with 95% confidence intervals. Where overall results are significant, the number-needed-to-treat (NNT) to produce one outcome will be calculated.

Unit of analysis issues

As these are studies of interventions at the GP level, but with outcomes at the patient level, cluster effects are possible and should ideally be addressed in the study design. For trials which do not use a cluster randomised design we will carry out an adjustment to effective sample size. For this, we will attempt to derive an intracluster correlation coefficient from other studies within the review, or failing this assume an intra-cluster correlation of 0,05 based on the finding that the intra-cluster correlation is typically lower than 0,05 for outcome variables in primary care (Campbell 2001).

.Studies with different clinical entry criteria or diagnostic groups will all be included in the same analysis rather than carrying out separate analyses.

Dealing with missing data

In the first instance we will approach original authors to obtain missing data. If this is not available then missing dichotomous data will be managed through intention to treat (ITT) analysis, in which it will be assumed that patients who dropped out after randomisation had a negative outcome. Best / worse case scenarios will also calculated for the clinical response outcome, in which it will be assumed that dropouts in the active treatment group had positive outcomes and those in the control group had negative outcomes (best case scenario), and

that dropouts in the active treatment group had negative outcomes and those in the control group had positive outcomes (worst case scenario), thus providing boundaries for the observed treatment effect.

Missing continuous data will either analysed on an endpoint basis, including only participants with a final assessment, or analysed using last observation carried forward to the final assessment (LOCF) if LOCF data were reported by the trial authors. Where SDs are missing, attempts will be made to obtain these data through contacting trial authors. Where SDs are not available from trial authors, they will be calculated from t-values, confidence intervals or standard errors, where reported in articles (<u>Deeks 2007a</u>; <u>Deeks 2007b</u>). If these additional figures are not available or obtainable, the study data will not be included in the comparison of interest.

Rachel I'm not happy with this last and am checking with Debbi....

Assessment of heterogeneity

Statistical heterogeneity will be formally tested using the natural approximate chi-square test, which provides evidence of variation in effect estimates beyond that of chance. Since the chi-squared test has low power to assess heterogeneity where a small number of participants or trials are included, the p-value will be

conservatively set at 0.1. Heterogeneity will also be tested using the I^2 statistic, which calculates the percentage of variability due to heterogeneity rather than chance. We will take I^2 values over 50% as suggestive of substantial heterogeneity but will take care to consider the direction and magnitude of effects.

Assessment of reporting biases

Where sufficient numbers of trials allow a meaningful presentation, funnel plots will be constructed to establish the potential influence of publication bias.

Data synthesis

If a sufficient number of comparable studies with low risk of bias are available we will carry out meta-analyse s in which studies will be weighted by size. While we will look for heterogeneity between studies (see above) we do not have any *a priori* expectation of this, hence we will use a fixed effects meta-analysis. The meta-analysis will be performed by CB and MF in the first instance.

Subgroup analysis and investigation of heterogeneity

As the objective of the review is to compare broadly similar treatments in broadly similar individuals we propose to carry out only one subgroup analysis comparing two equal groups representing studies with more training of practitioners and those with less.

Sensitivity analysis

We plan to carry out sensitivity analyses by limiting the analysis to studies with – low or moderate risk of bias as determined by risk of bias domains, including:

- 1. Blinding of outcome assessors
- 2. Allocation concealment
- 3. Dropout rate lower than 20%

These sensitivity analyses will also be used to examine potential sources of methodological heterogeneity.

Results

Description of studies Risk of bias in included studies

Risk of blas in included studi

Effects of interventions

Discussion

Authors' conclusions

Implications for practice

Implications for research

Acknowledgements

Contributions of authors

Marianne Rosendal and Chris Burton wrote the protocol draft, other authors contributed with critical feedback and discussions of methods. All authors accepted the final version of the protocol.

Declarations of interest

Marianne Rosendal has been actively participating in the evaluation of RCTs cited in this review and is currently involved in the development of treatment guidelines for Danish primary care. The working hours spent on this Cochrane review has been part of standard employment at the Research Unit for General Practice. No other

conflicts of interest known.

Chris Burton: no conflicts of interest known.

Nettie Blankenstein has been the primary researcher in one of the RCTs on reattribution cited in this review. Currently, she is involved in the development of a multi-disciplinary treatment guideline on somatoform symptoms and disorders for Dutch primary and secondary health care. She has contributed to the development of a training course for general practitioners on cognitive-behavioural treatment for functional symptoms. Her contribution to this Cochrane review is part of her employment at the department of general practice of the VU university medical center. No further conflicts of interest known.

Per Fink has been involved in RCTs on treatment of medically unexplained symptoms in primary care and is currently participating in the development of treatment guidelines for Danish primary care. No other conflicts of interest known.

Kurt Kroenke has had research support from Eli Lilly and Pfizer and honoraria from them plus Forest in relation to research in depression. No other conflicts of interest known.

Michael Sharpe: no conflicts of interest known.

Morten Frydenberg: no conflicts of interest known.

Richard Morriss has been the chief investigator of one of the RCTs cited in this review as well as a previous non-randomised treatment trial. No other conflicts of interest known.

Differences between protocol and review

Published notes

Characteristics of studies

Characteristics of included studies

Footnotes

Characteristics of excluded studies

Footnotes

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

Summary of findings tables

Additional tables

1 Instruments for the assessment and sampling of functional somatic symptoms and disorders (preliminary overview)

Type of instrument Name		references		
Questionnaire Abridged criteria		Escobar 1989		
	PHQ-15	Kroenke 2002		
	SCL-som	Derogatis 1977		
	Whiteley-7	Fink 1999		
Interview	SCAN	World Health Organisation 1998		
	DIS	Eaton 2000; Robins 1989		
	CIDI	Andrews 1995; World Health Organisation 1990		
Health care use	Frequent attendance Blankenstein 2001; <u>Katon 1992;Portegijs 1996;</u> <u>Schilte 20</u>			

Footnotes

The table may be supplemented by specific instruments for functional somatic syndromes

The final review will also include a table of names and classification terms

2 Data extraction form

Rubric		Reviewer 1	Reviewer 2	Conclusion
Author name				
Title of paper				
Name of study				
Personal notes (e.g. name of disorder used)				
Reason for exclusion				
Study characteristics				
	Assessment of methods (table 2)			
	Setting of the study (the primary care organisation)			
	Level of randomisation and measures of clustering			
	The risk of contamination (control patients receiving intervention unintentional or vice versa)			
	Doctor characteristics and sampling (previous training, years in practice, GP age)			
	Patient characteristics (inclusion, exclusion, ethnicity, diagnosis, symptom duration, psychiatric co-morbidity) and sampling (population screening, waiting room screening, GP assessment, diagnostic instruments used)			
	Intervention* in active group			
	Intervention in control group			
	Outcome measure and instrument for assessment (primary outcome, secondary outcome, subgroups)			
	Length of maximum follow-up			
	Results			

Footnotes

* Interventions

- Training (duration, content, skills training, supervision)
- Treatment model: reattribution and how close it is to the original, psychosocial interventions other than reattribution). To which degree does the model for patients stipulate that physical symptoms are secondary to psychosocial distress.
- Clinicians (GP, nurse, other)
- Organisation (flagging of patients, consultation duration, number of consultations, no changes)

References to studies

Included studies

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Ongoing studies

Other references

Additional references

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Other published versions of this review

Classification pending references

Data and analyses

Figures

Sources of support

Internal sources

- Research Unit for General Practice, Århus, Denmark
- Community Health Sciences, General Practice Section, University of Edinburgh, UK
- Department of General Practice, EMGO Instituut (VU), Amsterdam, Netherlands
- The Research Clinic for Functional Disorders and Psychosomatics, Århus University Hospital, Denmark
- Department of Medicine and Regenstrief Institute, Indiana University, USA
- School of Molecular & Clinical Medicine, University of Edinburgh, UK
- Department of Biostatistics, Institute of Public Health, University of Århus, Denmark
- Department of Psychiatry, University of Nottingham, UK

External sources

• No sources of support provided

Feedback

Appendices

1 CCDAN Registers search strategy

CCDANCTR-Studies

Treatment setting = "general practice" or "family practice" or "primary care"

and

Diagnosis= "medically unexplained" or "frequent attend*" or "high util*" or somat* or neurasthen* or hyprochondria* or hysteri* or pain or "chronic fatigue"

CCDANCTR-References

Free-text = "general practi*" or "family practi*" or "primary care" or "primary health*" or "physicians, family" or Title/Abstract = GP*

and

Free-text = "medically unexplained" or "frequent attend*" or "high util*" or somat* or neurasthen* or hyprochondria* or hysteri* or "chronic fatigue"

2 MEDLINE search strategy

- 1. SOMATOFORM DISORDER/ or NEURASTHENIA/ or HYPOCHONDRIASIS/
- 2. NEUROCIRCULATORY ASTHENIA/
- 3. (somatoform or somati#ation or somati#ing or somati#ed or somatic symptom\$ or somatic syndrome\$ or symptom syndrome\$ or multisomat\$ or neurastheni\$ or hypochondria\$).ti,ab.
- 4. ((medic\$ adj3 (unexplain\$ or inexplic\$)) or unexplained symptom\$).ti,ab.
- 5. (((frequent or high) adj1 attend\$) or high utili#er\$ or repeat\$ present\$).ti,ab.
- 6. functional symptoms.ti,ab.
- 7. reattribution.ti,ab.
- 8. exp ABDOMINAL PAIN/
- 9. stomach ache\$.ti,ab
- 0. exp BACK PAIN/
- 1. COLONIC DISEASES, FUNCTIONAL/
- 2. CYSTITIS, INTERSTITIAL/
- 3. painful bladder syndrome.ti,ab.
- 4. urethral syndrome.ti,ab.
- 5. cardiac neuros\$.ti,ab.
- 6. ((non cardiac or non-cardiac) adj chest pain).ti,ab.
- 7. ((nonorganic or non organic or non-organic) adj pain).ti,ab.
- 8. effort syndrome.ti,ab.
- 9. DIZZINESS/
- 20. FIBROMYALGIA/
- 1. FATIGUE SYNDROME, CHRONIC/
- 2. myalgic encephalomyel\$.ti,ab.
- 2. (post viral or postviral or post-viral) adj (fatigue or syndrome).ti,ab.

- 24. exp HEADACHE
- 25. exp HEADACHE DISORDERS
- 26. exp HYPERVENTILATION
- ?7. exp HYSTERIA
- 28. Briquet's syndrome.ti,ab.
- 29. IRRITABLE BOWEL SYNDROME/
- 30. MULTIPLE CHEMICAL SENSITIVITY/
- 1. exp PELVIC PAIN
- 2. exp PREMENSTRUAL SYNDROME
- 3. PSYCHOPHYSIOLOGIC DISORDERS
- :4. (psychalgia or psychogenic or psychoseizure\$ or psychosomatic).ti,ab.
- 5. TEMPOROMANDIBULAR JOINT DYSFUNCTION SYNDROME
- 6. urethral syndrome.ti,ab.
- 37. or/1-36
- 38. exp PRIMARY HEALTHCARE/
- 39. PHYSICIANS, FAMILY/
- 0. FAMILY PRACTICE/
- 1. FAMILY HEALTCARE/
- 2. NURSE PRACTIONERS/
- 13. ((family or community) adj (medic\$ or doctor\$ or physician\$ or nurs\$ or health))).ti,ab.
- 14. ((general or family or nurs\$) adj1 (practice\$ or practitioner\$)).ti,ab.
- 15. (primary care or primary healthcare or primary health care or primary health service\$ or homecare or care in the community).ti,ab.
- 16. GP\$ or generalist\$.ti,ab.
- 17. or/38-46
- 8. randomized controlled trial.pt.
- 19. controlled clinical trial.pt.
- 0. randomi#ed.ab.
- i1. placebo\$.ab.
- 32. exp Clinical Trials as Topic/
- 3. randomly.ab.
- i4. trial.ti.
- 5. or/48-54
- 6. (animals not (humans and animals)).sh.
- 7. 55 not 56
- i8. 37 and 47 and 57

Graphs