Behavioural modification interventions for medically unexplained symptoms in primary care: systematic reviews and economic evaluation

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Scientific summary

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Background

The term 'medically unexplained symptoms' is used to describe a wide range of persistent bodily complaints for which adequate examination and appropriate investigations do not reveal sufficient explanatory structural or other specified pathology. Use of the term medically unexplained symptoms does not require that the physical symptoms have a psychogenic origin, as somatoform disorders do. The term may be applied to patients presenting with single or multiple symptoms, or clusters of symptoms specific to a particular organ system or medical specialty, often referred to as functional somatic syndromes (e.g. fibromyalgia, irritable bowel syndrome or chronic fatigue syndrome). Medically unexplained symptoms is a controversial term and debate is ongoing regarding its continued use or a move to alternative terminology. Medically unexplained symptoms is a portfolio term covering a wide range of presentations. The term 'medically unexplained' does not exclude physical pathology.

Medically unexplained symptoms can cause distress to the patient. A range of prevalence rates of medically unexplained symptoms in primary care are suggested, with UK estimates of around 18% of consecutive attenders to general practitioners to worldwide estimates of between 25% and 50% of primary care patients presenting with such symptoms. The financial cost to the UK NHS has been estimated at > £3B. A wide range of interventions has been implemented in the treatment of medically unexplained symptoms. These include pharmacological treatments, such as antidepressants; psychological therapies including psychodynamic therapy; cognitive–behavioural therapy; behaviour therapy, such as reducing unhelpful coping behaviours (e.g. reassurance seeking); and relaxation therapies, such as meditation-based stress reduction. Physical therapies have also been implemented, such as graded exercise therapy, aerobic or strengthening exercises, or alternative therapies, such as acupuncture or hypnotherapy.

Current evidence for the effectiveness of interventions for medically unexplained symptoms is not conclusive, with beneficial effects found for psychological interventions conducted in secondary care but evidence that such therapies are less beneficial when conducted by general practitioners. Treatment intensity has been proposed as a moderator of effects, with some reviews indicating that more intense treatments show more beneficial effects. To our knowledge, no review to date has specifically explored the effectiveness of behavioural modification interventions for a range of medically unexplained symptoms populations in primary care settings.

Objectives

1. To determine the clinical effectiveness of behavioural modification interventions for medically unexplained symptoms in primary care and community-based settings, by undertaking a full systematic review of quantitative literature.
2. To evaluate the barriers to and facilitators of effectiveness and acceptability of behavioural modification interventions for medically unexplained symptoms from the perspective of both patients and service providers, by undertaking realist synthesis following a systematic review of the available qualitative research literature.
3. To undertake meta-analysis of available evidence on clinical effectiveness, including a network meta-analysis, where appropriate.
4. To identify and synthesise evidence on health economic outcomes such as health-care resource use (e.g. general practitioner appointments), and health-related quality-of-life data from the studies included in the clinical effectiveness review.

5. To provide new evidence on the cost-effectiveness of behavioural modification interventions for medically unexplained symptoms conducted in a primary care or community setting, by conducting a systematic review of existing economic analyses and undertaking a de novo model-based evaluation where there is an absence of high-quality published analyses that are directly applicable to our research question.
6. To explain which interventions are appropriate for which medically unexplained symptoms patients under which circumstances (via realist synthesis).

Methods for quantitative review

A systematic review of the literature was undertaken to identify relevant studies to evaluate the clinical effectiveness of behavioural modification interventions for medically unexplained symptoms in a primary care or community-based setting. A systematic search strategy using a combination of free-text terms and thesaurus searching was used. Eleven electronic sources (e.g. MEDLINE, Cumulative Index to Nursing and Allied Health Literature, PsycINFO and EMBASE) were searched for systematic reviews and randomised controlled trials, between 20 November 2015 and 7 December 2015. In addition, reference sections of included studies and existing systematic reviews were scrutinised for potentially relevant studies. Inclusion criteria are summarised as follows:

- study design – randomised controlled trials with no minimum duration of follow-up
- population – adult participants meeting the inclusion criteria for medically unexplained symptoms, including 'medically unexplained symptoms', somatoform disorders, chronic unexplained pain, the functional somatic syndromes (e.g. irritable bowel syndrome, fibromyalgia, chronic fatigue syndrome)
- intervention – behavioural interventions meeting the inclusion criteria including a range of psychotherapies, exercise-based interventions; multimodal therapies; general practitioner interventions (e.g. reattribution); promoting a biopsychosocial approach towards the management of medically unexplained symptoms
- outcomes – improvement in specific physical symptoms; improvement in symptoms of emotional distress (e.g. depression/anxiety); physical function; impact of illness on daily activities
- setting – primary care or community settings.

Methods for network meta-analysis

A network meta-analysis was used to synthesise the evidence and allow a simultaneous comparison of all evaluated interventions in a single coherent analysis. Standardised mean differences were computed for the continuously distributed outcomes to allow the inclusion of studies that evaluated outcomes using different scales. Separate network meta-analyses were performed for three time points: end of treatment, short-term follow-up (< 6 months since end of treatment) and long-term follow-up (≥ 6 months after end of treatment).

Methods for qualitative review

A qualitative evidence synthesis was conducted to provide added value to the quantitative analysis by exploring patient and service provider issues around the acceptability of behavioural modification interventions in primary care settings. A systematic search strategy was developed to identify UK-based qualitative studies, using a combination of free-text terms and thesaurus searching. Searches were conducted on 4 July 2016. Specifically, thematic synthesis was used to aggregate the findings. The framework developed for data extraction was used to shape the synthesis of the findings. Themes were then developed within the framework elements.

Methods for realist synthesis

The aim of the realist synthesis was to provide an overview and analysis of the evidence for the contribution of contextual factors associated with the ongoing primary care consultation and the patient's interaction with primary care professionals to the success or failure of behaviour modification interventions ('behavioural interventions') for medically unexplained symptoms. A search was conducted for relevant 'theories' in the literature. A list of programme theories was drawn up, which were subsequently grouped, categorised and synthesised. A theoretically based evaluative framework was designed, which was then 'populated' with evidence.

Methods for cost-effectiveness

A systematic review was conducted to identify published economic evaluations, conducted in the UK, which measured benefits using quality-adjusted life-years. A systematic search strategy was developed using a combination of free-text terms and thesaurus searching. Searches were conducted between 15 and 25 August 2016. Economic evaluations that did not report quality-adjusted life-years were narratively summarised for cost outcomes. Applicability to the National Institute for Health and Care Excellence's reference case and methodological quality were assessed using the checklist provided in the National Institute for Health and Care Excellence's guidelines manual.

An independent economic assessment was conducted with the aim of generating a within-study estimate of cost-effectiveness for each trial included in the clinical effectiveness review. Incremental costs compared with usual care were estimated for each behavioural modification intervention and for any active comparators. Cost estimates were based on the duration of time spent by health-care professionals delivering the intervention and the unit cost for the relevant health-care professional.

Our aim was to estimate quality-adjusted life-years based on utilities from the UK version of the EuroQol-5 Dimensions, but studies reporting utility values using the Short Form questionnaire-6 Dimensions or non-UK valuations of the EuroQol-5 Dimensions were considered acceptable alternatives. Where these data were not available, we estimated utility values by mapping from the Short Form questionnaire-12 items or the Short Form questionnaire-36 items to the UK EuroQol-5 Dimensions whenever possible.

Incremental quality-adjusted life-years were estimated using an area under the curve approach up to the last time point for which utility data were reported or estimable for each study. Utility values were adjusted for baseline differences. Uncertainty in the incremental quality-adjusted life-years because of uncertainty in the Short Form questionnaire-36 items/Short Form questionnaire-12 items study outcomes was explored through a two-way sensitivity analysis.

Results for quantitative review

In total, 59 randomised controlled trials were included in the quantitative review, providing data on 9077 participants. Studies were rated as being of variable quality, ranging from low to high quality. Owing to the nature of the interventions and control arms, few studies reported blinding participants. The number of participants in a single trial ranged from 10 to 524. There was considerable heterogeneity within the populations and behavioural interventions studied, the outcomes measured and the detail of the study setting. Data relating to these and other potential sources of heterogeneity were extracted and a metaregression was planned to investigate the influence of these factors on effects. For population samples, 29 studies were of participants meeting inclusion criteria for 'medically unexplained symptoms'

or somatoform disorders; one trial studied participants with mixed 'medically unexplained symptoms' diagnoses; 12 studies were of participants with chronic fatigue; six studies were of participants with chronic unexplained pain at a single site on the body; seven studies were of participants with chronic unexplained pain at multiple sites on the body; three studies were of irritable bowel syndrome; and the remaining study was of a population of women with medically unexplained vaginal discharge. Within-population variation was identified, with differences in diagnostic/inclusion criteria used for some of the condition groups, in particular the 'medically unexplained symptoms' population.

Behavioural intervention arms were coded into one of 13 behavioural intervention types: high-intensity cognitive–behavioural therapy; low-intensity cognitive–behavioural therapy; graded activity; strength/endurance/sport; other psychotherapy; relaxation/stretching/social support/emotional support; guided self-help; multimodal interventions (interventions consisting of more than one intervention type); and general practitioner interventions with a behavioural modification basis that included general practitioner reattribution; general practitioner medically unexplained symptoms management; general practitioner-delivered cognitive–behavioural therapy; general practitioner-delivered other psychotherapy; and any other general practitioner-delivered behavioural intervention not fitting in any other category. Three non-behavioural comparator arms were also identified: medication; usual care (including treatment as usual and waiting list); and usual care plus (defined as enhanced usual care but not meeting the criteria for a behavioural intervention). Considerable heterogeneity was evident within intervention types, with variation in the number and duration of sessions, treatment duration and differences in treatment provider.

Owing to the heterogeneous populations, a diverse range of outcomes were measured across studies. Commonalities were sought and 10 key outcomes were identified where it was considered that sufficient similar data were available to attempt meta-analyses. These were specific physical symptoms (pain, fatigue, bowel symptoms); emotional distress (depression, anxiety or composite measures, e.g. mental health); symptom load (somatisation, generic physical symptoms); physical functioning; and impact of symptoms on daily activities. There was considerable heterogeneity between studies in the measures used to assess these outcomes.

There was also variation in the detail of setting, with participants in some studies recruited and treated by their own general practitioner at their own general practitioner practice, whereas in others treatment involved collaborative care with other health professionals or was co-ordinated by participants' GP but involved an external setting such as a fitness facility. In all studies, however, participants were primary care patients and were not recruited from tertiary care settings.

Results for meta-analysis

For all the results presented in this section, a positive SMD indicates a beneficial effect when compared with usual care. Cohen's categories were used to describe the magnitude of the effect size: small ($0.2 \leq \text{SMD} < 0.5$), medium ($0.5 \leq \text{SMD} < 0.8$) and large ($0.8 \leq \text{SMD}$) (Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. 2nd edn. Hillsdale, NJ: Lawrence Erlbaum Associates, Publishers; 1988). SMDs < 0.2 were described as 'not substantial'.

Immediately post treatment

The results were inconclusive for the majority of interventions that were included in the network meta-analysis but with the following exceptions. High-intensity cognitive–behavioural therapy was shown to be effective for four outcomes: pain, impact of illness on daily activities, anxiety and depression.

Relaxation/stretching/social support/emotional support was shown to be effective for two outcomes: fatigue and emotional distress. Multimodal therapy was shown to be effective for three outcomes: pain, fatigue and physical functioning. Low-intensity cognitive–behavioural therapy and graded exercise were shown to be effective for one outcome: fatigue. Other psychotherapy and strength/endurance/sport were shown to be effective for one outcome: emotional distress. Guided self-help was shown to be not effective for two outcomes: physical functioning and emotional distress. This result was based on a single study with an unusually large negative effect size compared with a multimodal intervention. Inconsistency checking showed this indirect comparison to be inconsistent with the direct comparison.

For physical symptom outcomes, it was found that high-intensity cognitive–behavioural therapy was the most beneficial intervention for pain when compared with usual care [a medium effect size, SMD 0.54 with 95% credible interval (CrI) 0.28 to 0.84]. Relaxation/stretching/social support/emotional support was the most beneficial intervention for fatigue when compared with usual care (a large effect size, SMD 0.87 with 95% CrI 0.20 to 1.55). High-intensity cognitive–behavioural therapy was the most beneficial intervention for somatisation when compared with usual care, a small effect size (SMD 0.32 with 95% CrI –0.12 to 0.75), but the result was inconclusive. Only other psychotherapy and usual care were included in the network meta-analysis on generic physical symptoms, and usual care was more effective than other psychotherapy, a small effect size of other psychotherapy versus usual care (SMD –0.25 with 95% CrI –0.77 to 0.30), but the result was inconclusive.

For physical functioning and impact of symptoms on daily activities, it was found that multimodal therapy was the most beneficial intervention for physical functioning when compared with usual care, a small effect size (SMD 0.33 with 95% CrI 0.09 to 0.59). Guided self-help was significantly worse than usual care (a medium effect size SMD –0.73 with 95% CrI –1.18 to –0.29) for physical functioning. High-intensity cognitive–behavioural therapy was the most beneficial intervention for impact of symptoms on daily activities when compared with usual care, a large effect size (SMD 1.30 with 95% CrI 0.59 to 2.00).

For emotional distress outcomes, it was found that high-intensity cognitive–behavioural therapy was the most beneficial intervention for both anxiety and depression when compared with usual care, with a medium effect size (SMD 0.52 with 95% CrI 0.06 to 0.96) for anxiety and a large effect size (SMD 0.80 with 95% CrI 0.26 to 1.38) for depression. Relaxation/stretching/social support/emotional support was the most beneficial intervention for emotional distress when compared with usual care, with a medium effect size (SMD 0.66 with 95% CrI 0.18 to 1.28). Guided self-help was significantly worse than usual care (a large effect size SMD –1.03 with 95% CrI –1.95 to –0.10) for emotional distress.

Short-term follow-up

The results were inconclusive for the majority of interventions that were included in the network meta-analysis but with the following exceptions. High-intensity cognitive–behavioural therapy was shown to be effective for four outcomes: pain, impact of symptoms on daily activities, anxiety and depression. Low-intensity cognitive–behavioural therapy was shown to be effective for one outcome: fatigue. Relaxation/stretching/social support/emotional support was shown to be effective for two outcomes: fatigue and emotional distress. Multimodal therapy was shown to be effective for two outcomes: physical functioning and emotional distress. Medication was shown to be effective for one outcome: impact of symptoms on daily activities.

For physical symptom outcomes, it was found that high-intensity cognitive–behavioural therapy was the most beneficial intervention for pain when compared with usual care, a medium effect size (SMD 0.73 with 95% CrI 0.10 to 1.39). Low-intensity cognitive–behavioural therapy was the most beneficial intervention for fatigue when compared with usual care (with a medium effect size SMD 0.62 with 95% CrI 0.11 to 1.14).

For physical functioning and impact of symptoms on daily activities outcomes, it was found that multimodal therapy was the most beneficial intervention for physical functioning when compared with usual care, with a medium effect size (SMD 0.78 with 95% CrI 0.23 to 1.40). High-intensity cognitive–behavioural therapy was the most beneficial intervention on impact on daily activities when compared with usual care, with a large effect size (SMD 2.25 with 95% CrI 1.34 to 3.16).

For emotional distress outcomes, it was found that high-intensity cognitive–behavioural therapy was the most beneficial intervention for both anxiety and depression when compared with usual care, a medium effect size (SMD 0.74 with 95% CrI 0.14 to 1.37) for anxiety and a large effect size (SMD 0.93 with 95% CrI 0.37 to 1.52) for depression. Relaxation/stretching/social support/emotional support was the most beneficial intervention for emotional distress when compared with usual care, with a large effect size (SMD 0.82 with 95% CrI 0.02 to 1.65).

Long-term follow-up

The results were inconclusive for the majority of interventions that were included in the network meta-analysis but with the following exceptions. Low-intensity cognitive–behavioural therapy was shown to be effective for two outcomes: fatigue and bowel symptoms. Guided self-help was shown to be not effective for four outcomes: pain, physical functioning, impact of symptoms on daily activities and emotional distress.

For physical symptom outcomes, it was found that medication was the most beneficial intervention for pain when compared with usual care, with a small effect size (SMD 0.41 with 95% CrI −0.16 to 0.98), but the result was inconclusive. Guided self-help was significantly worse than usual care (a large effect size SMD −2.27 with 95% CrI −3.30 to −1.23) for pain. Low-intensity cognitive–behavioural therapy was the most beneficial intervention for fatigue (with a medium effect size, SMD 0.64 with 95% CrI 0.05 to 1.20) and for bowel symptoms (with a large effect size, SMD 0.84 with 95% CrI 0.17 to 1.52) when compared with usual care. High-intensity cognitive–behavioural therapy was also the most beneficial intervention on somatisation when compared with usual care, with a small effect size (SMD 0.47 with 95% CrI −0.30 to 1.29), but the result was inconclusive.

For physical functioning and impact of symptoms on daily activities outcomes, it was found that high-intensity cognitive–behavioural therapy was the most beneficial intervention for physical functioning when compared with usual care, with a small effect size (SMD 0.47 with 95% CrI −0.49 to 1.44), but the result was inconclusive. Guided self-help was significantly worse than usual care (a large effect size SMD −2.98 with 95% CrI −4.00 to −1.96) for physical functioning. Low-intensity cognitive–behavioural therapy was the most beneficial intervention for impact when compared with usual care, with a large effect size (SMD 0.89 with 95% CrI −0.22 to 1.55), but the result was inconclusive. Guided self-help was significantly worse than usual care (a large effect size SMD −1.10 with 95% CrI −2.08 to −0.07) for impact of symptoms on daily activities.

For emotional distress outcomes, it was found that general practitioner 'other psychotherapy' was the most beneficial intervention for anxiety when compared with usual care, a small not substantial effect size (SMD 0.18 with 95% CrI −0.40 to 0.76), but the result was inconclusive. Multimodal therapy was the most beneficial intervention on depression when compared with usual care, with a small effect size (SMD 0.51 with 95% CrI −0.02 to 1.13), but the result was inconclusive. Multimodal was also the most beneficial intervention on emotional distress when compared with usual care, with a small effect size (SMD 0.56 with 95% CrI −0.31 to 1.45), but the result was inconclusive. Guided self-help was significantly worse than usual care (a large effect size SMD −1.44 with 95% CrI −2.60 to −0.30) for emotional distress.

Results for the qualitative review

The qualitative systematic review examined patient and health professional perspectives on the acceptability, relative benefits and potential harms of the interventions. In total, 10 papers reported evidence from eight studies, providing data from 130 patients and 38 health professionals. Some of the included studies were only of moderate or low quality and some findings were assessed as being of moderate or low confidence. The findings of the synthesis across all interventions showed that a major theme for patients was gaining support. Patients also highly valued receiving an explanation for their symptoms, together with learning self-management techniques and being provided with support for learning such techniques. The helpfulness of the intervention appeared to be facilitated by a good relationship between patients and the health professionals delivering the intervention.

Evidence from health professionals showed that important facilitators were training and supervision for delivery of the interventions and they found primary care or the community an appropriate and helpful setting for this. Barriers to intervention participation and success included both patients' and health professionals' own attitudes and beliefs, conflicts between health professionals and patients, health professionals' lack of confidence in their own skills and abilities to deal with medically unexplained symptoms, together with resource constraints. Health professionals were also concerned that the interventions may have inadvertently detrimental consequences for patients, and that they may be ill-equipped to deal with their own and patients' emotions. The implications of the findings suggest that, although a number of patients found interventions helpful, a minority did not find the intervention helpful or did not want to take part in the intervention at all; therefore, careful matching of patients to interventions should take place. Further considerations were continuity of care from the same health professional or team, that interventions do not end suddenly, or without adequate follow-up. The qualitative synthesis was also able to elucidate and provide potential explanations for some of the findings of the quantitative review, for example the variation in the number of sessions patients attended both within and between studies.

Results for realist synthesis

The realist synthesis explored eight programme theory components to explain why interventions for the target populations are found to be more or less successful, particularly when delivered within a primary care setting. Key factors contributing to success, across multiple interventions, included establishing and maintaining belief and trust as a foundation for the relationship between patient and professional, and negotiation of a shared biopsychosocial disease model. A focus on symptoms was also believed to be helpful particularly in moving towards an explanation considered sufficient at a specific point in time, but contingent as further clinical information and patient experience emerges.

Both patients and professionals sought to avoid perpetuation of an unproductive diagnostic cycle whereby a patient is shifted between referral to different consultants or different diagnostic tests. More equivocal was the value of a 'label' for patients' symptoms, with perceived differences in the value of a label such as 'chronic fatigue syndrome', which could be considered helpful, compared with the generic 'medically unexplained symptoms', which was considered manifestly unhelpful. Nevertheless, response to labels could also differ between patients. A particular tension was identified in whether or not the practitioner should explore psychosocial cues. It surfaced in some interventions that this was an essential feature of the consultation and subsequent treatment (e.g. reattribution therapies), whereas others recommended that psychosocial cues should only be initiated by the patient (e.g. the primary care symptom clinic). There was little evidence considering the inherent advantage of a primary care setting beyond arguments for continuity of care, which is increasingly being eroded by team-based delivery of primary care services, although delivery in non-medical settings was suggested for countering the stigma associated with the psychological framing of symptoms.

Results for cost-effectiveness

Only two studies were included in our review of UK cost-effectiveness studies. One study found that neither of the two behavioural modification interventions examined (graded activity; other psychotherapy) provided more benefits than usual care in patients with chronic fatigue. The other study found that in patients with chronic unexplained pain, high-intensity cognitive–behavioural therapy was cost-effective (when valuing a quality-adjusted life-year at £20,000) compared with usual care, and had greater benefit than strength/endurance/sport and a multimodal intervention combining both strength/endurance/sport and high-intensity cognitive–behavioural therapy. Five cost–consequences studies were identified, but again these had heterogeneous results, with only two reporting a statistically significant difference in costs between study arms.

For the independent assessment of cost-effectiveness, within-trial estimates of cost-effectiveness were estimated for 18 studies. There is a large degree of heterogeneity in the estimates of cost-effectiveness across individual studies. Some interventions were found to be dominated by usual care (i.e. they cost more and produced fewer quality-adjusted life-years) or dominated by other behavioural modification interventions. For those interventions that generated quality-adjusted life-year gains versus usual care, the mid-point incremental cost-effectiveness ratios ranged from £1397 to £129,267, but, where the mid-point incremental cost-effectiveness ratio fell below £30,000, the exploratory assessment of uncertainty suggested that it may be above £30,000. When comparing studies that had interventions in the same class, the estimates of cost-effectiveness were often inconsistent across studies. This may reflect differences between studies within the populations or in the exact delivery of the interventions.

Limitations

Results from the network meta-analysis are limited because of the sparsity of the networks. A lack of consistency in the point estimates between studies comparing the same type of interventions with usual care and moderate to high levels of statistical heterogeneity means that the results are not conclusive and should be interpreted with caution. It was not possible to conduct planned metaregressions to identify potential moderators because of insufficient replication of each intervention type in the network and, therefore, it was not possible to explain between-study heterogeneity of effects. In particular, it was not possible to determine whether or not different medically unexplained symptoms populations respond differently to similar interventions, although differences in individual point estimates within intervention types across populations suggest that there are differences, although there were overlapping confidence intervals.

Results from the cost-effectiveness analyses found considerable heterogeneity between individual studies, with a lack of consistency in duration/number of treatment sessions and the number of patients recruited and treated by individual providers. The main limitation of the independent economic evaluation is that the conclusions that can be drawn are limited to the direct comparisons presented in the subset of studies for which we were able to estimate quality-adjusted life-year differences.

Discussion and conclusions

Results of the clinical effectiveness review indicate that, when conducted in primary care settings, behavioural modification interventions, in particular high-intensity cognitive–behavioural therapy and multimodal therapies, show some beneficial effects for improvement of specific individual physical symptoms. However, for more complex outcomes, in particular for measures of symptom load (somatisation and generic physical symptoms), there was little evidence of their effectiveness. There were also some beneficial effects for improvement of mood, most commonly high-intensity cognitive–behavioural therapy but also for other psychotherapy, relaxation/stretching/social support/emotional support and strength/

endurance/sport interventions. Few beneficial effects were found at long-term follow-up. Results of the network meta-analyses showed no effects for behavioural interventions delivered by general practitioners themselves. All of these results are limited by a lack of studies for each intervention type and by considerable heterogeneity within intervention types, and between populations and outcomes, and should therefore be interpreted with caution. Differences in effects suggest that there is no specific intervention type that uniformly benefits all 'medically unexplained symptoms' populations included in the review, which might reflect the heterogeneity within medically unexplained symptoms. Cost-effectiveness also varies considerably depending on a number of factors, such as intensity of treatment, group size, and the number of patients recruited and treated by each trained general practitioner.

Patients value receiving an explanation of their symptoms and learning self-management techniques, with the support provided by a health professional being especially valued. A good relationship between patient and health professional is perceived to facilitate the effectiveness of behavioural modification interventions, particularly when based on a common understanding of the illness. Training for general practitioners in medically unexplained symptoms, although shown to have limited effectiveness as an intervention in itself, is perceived to be an influential factor in facilitating the doctor/patient relationship and the effectiveness of behavioural modification interventions. The primary care setting is perceived as both appropriate and helpful. A collaborative care model of interventions for medically unexplained symptoms patients may therefore be both acceptable and beneficial.

Potential research priorities

The following research priorities are suggested, based on the findings of the review:

1. Explanation of observed between-study differences in effects within the same intervention type. This may be addressed by:

    i. more detailed reporting of information regarding the defined mechanisms of the behavioural interventions under study, and how these map onto a theoretical and empirical understanding of the conditions
    ii. more research on potentially influencing factors, such as effective dosage and therapist competency within the more promising behavioural interventions
    iii. within-trial comparisons of interventions targeting specific syndromes with those targeting general somatic symptoms.

2. Testing the therapeutic effect of the general practitioner–patient relationship. This may be addressed by:

    i. increased awareness of likely general practitioner effects by researchers conducting trials of behavioural interventions for medically unexplained symptoms, with planned assessment of these as potential confounders
    ii. more research aimed at better understanding the therapeutic elements behind a successful therapeutic general practitioner–patient alliance, which are key to a successful outcome, and how these elements can be formalised as general practitioner (and health-care practitioner) skills.

3. Development of standardised measures of adverse effects in trials of behavioural interventions for medically unexplained symptoms.

Study registration

The study is registered as PROSPERO CRD42015025520.

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