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[Intervention Protocol]

Effects of changing practitioner empathy and patient expectations in healthcare consultations

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ABSTRACT

This is a protocol for a Cochrane Review (Intervention). The objectives are as follows:

The main aim of this review will be to assess the effects of changing practitioner empathy or patient expectations for all conditions. The main objective is to conduct a systematic review of randomised trials where the intervention involves manipulating either (a) practitioner empathy or (b) patient expectations, or (c) both.

BACKGROUND

Communication between patients and practitioners lies at the heart of medicine, being a component of every step in healthcare provision from initial diagnosis to follow up care. Unfortunately the administrative load of general practitioners (family practitioners) and other healthcare professionals can present a barrier to effective practitioner-patient communication. Some general practitioners claim that 25% of their time is spent filling out forms (Hoffmann 2014), while many healthcare practitioners report a need to improve their training in communication skills (Mondloch 2001). The potential for communication interventions to improve outcomes and reduce harms is also reflected in the National Institute for Health and Clinical Excellence (NICE, United Kingdom) recommendations to use psychological interventions for people with long-term conditions (Fellow-Smith 2012), and in the recent General Medical Council (GMC, United Kingdom) emphasis on the power and value of good communication (GMC 2014) as well as National Institutes of Health (NIH, United States) calls for improved communication and compassion (NIH 2014). Although medical student empathy seems to decline throughout medical school (Neumann 2011), communication skills can be taught and improved (Finset 2003; Kelm 2014).

Two aspects of patient-practitioner communication whose effects on patient outcomes are strongly supported by evidence, both from epidemiological and basic science studies, are practitioner empathy and the communication of expectations to patients (Benedetti 2009; Crow 1999; Derksen 2013; Di Blasi 2001; Fogarty 1999; Griffin 2004; Hojat 2011; Kelley 2014; Kelm 2014; Leloirain 2012; Levine 1984; Wartolowska 2014).

Specifically, patient expectancies about the response of a treatment have been theorised to directly impact patients' health outcomes (Kirsch 1985). Response expectancies are future-oriented cognitions about the occurrence of emotions such as anxiety or depression as well as symptoms such as pain (Kirsch 1985). For example the patients might be told that a treatment is effective and expect a positive response (Kaptchuk 2008). Positive response expectancies are believed to improve outcomes, and negative response expectancies are believed to make outcomes worse (Dutt-Gupta 2007; Varelmann 2010). Negative outcomes due to negative response expectancies are commonly referred to as 'nocebo' effects (Howick 2011). Positive (or negative) expectancies could also be induced without a treatment, for example after a healthcare practitioner informs them about a positive (or negative) prognosis.

Empathy has been conceptualised in diverse ways including as a behaviour, a personality trait, an affect and a cognition (Mercer 2002). In this review we will take a broader perspective that acknowledges clinical empathy as complex and multidimensional (Coulehan 2000; Decety 2014; Hojat 2009; Mercer 2002; Morse 1992; Neumann 2009). The broader definition of empathy is guided by Mercer 2002, and views empathy as an ability to

1. understand the patient's situation, perspective and feelings (and their attached meanings);
2. communicate that understanding and check its accuracy; and
3. act on that understanding with the patient in a helpful (therapeutic) way.

However, as Mercer 2002 argues, any single definition of clinical empathy is unlikely to incorporate all aspects of empathy relevant to all possible clinical encounters. Therefore studies will be included in this review if they attempt to alter any aspect of clinical empathy as defined above. This approach is similar to that of related empirical studies of empathy effects (Hojat 2011), which take empathy to mean generally engaging, sympathetic, attentive, warm, friendly, and supportive verbal and nonverbal communication.

Practitioner empathy and patient expectations are distinct, yet discussions with our patient representative lead us to suspect they are closely related. Patient representatives we have met pointed out that a non-empathetic practitioner attempting to induce positive expectations could make a patient feel as if they should feel better but at the same time make the patient feel alienated and not well cared for. Similarly, unrealistically positive expectations might not benefit patients, since evidence suggests that patients desire honesty, even about bad news (Parker 2007). Patients also desire hope (Parker 2007) so it may be important for empathy to be accompanied by somewhat positive messages. It follows from the likely connection between empathy and expectations that it is useful to study these two aspects of the patient/practitioner relationship in the context of the same review.

Description of the condition

We will examine the potential effects of modifying empathy and expectations in consultations with people regardless of their clinical condition(s). Investigating all clinical conditions is important because the mechanisms of action for empathy and expectations suggest they affect multiple conditions simultaneously (see [How the intervention might work](#)). For example, empathy and positive expectations are suspected to reduce anxiety and stress (Everly 2002) which in turn could reduce pain, depression, and various other conditions (Grossman 2004). Improving practitioner empathy and inducing positive patient expectations can also affect overall wellbeing (Thomas 1987). In fact, some of the studies we identified tested the combined effects of altering both empathy and expectations (Gryll 1978). In addition, patient satisfaction surveys (in patients with a variety of conditions) consistently show that patients consider 'emotional support, empathy, and respect' to be among the most important aspects of care, and at the same time note room for improvement in this area regardless of the condition (Coulter 2005).

Description of the intervention

We will consider two related but distinct patient/practitioner communication interventions in this review:

1. interventions aimed at changing practitioner empathy; and
2. interventions aimed at changing patient expectations.

We will also consider interventions aimed at changing both practitioner empathy and patient expectations together.

We will only include studies in which the communication between patients and practitioners occurs face-to-face. We will include simple and more complex interventions. A simple intervention might be one in which doctors are asked to vary a simple sentence. For example, a doctor might say that a treatment will certainly be very effective, compared with saying that the treatment might or might not work (Thomas 1987). More complex interventions involve

more extensive training programs such as three 60 minute empathy and relational skills training sessions (Riess 2012), or a semi-structured interview with a patient designed to empathetically induce positive expectations (Vangronsveld 2012). The more complex interventions sometimes involve comprehensive training and education about the neurobiological basis of empathy and expectations, aim to increase awareness of patients' emotions, improve understanding about the effects of various emotions, and teach specific skills to enhance empathy (Riess 2012). We have listed several examples of the types of interventions on which this review will focus in Table 1 and Table 2.

We will include studies where the comparison group was either neutral (standard care, sham intervention where practitioner empathy or patient expectations were not manipulated) or negative (designed to reduce practitioner empathy or produce negative patient expectations or where the comparison group received another intervention). Interventions that are compared with neutral or negative controls will be considered effective if they demonstrate superiority to the control, whereas interventions compared with other interventions need only demonstrate non-inferiority. This is because the active treatment itself has generally demonstrated additional benefits over and above a sham or no treatment control (Howick 2009; Howick 2011).

How the intervention might work

The mechanisms explaining how interventions for enhancing practitioner empathy and changing patient expectations may operate are complex.

Mechanisms explaining how positive expectations may improve healthcare outcomes

Inducing positive expectations has been shown in some studies to activate the brain's reward mechanisms (increased dopamine activity in the nucleus accumbens), as well as activate the endogenous opioid system to treat pain (Benedetti 2009; Colloca 2004). The effects of influencing patients' expectations on physiological outcomes has been most extensively documented in the field of pain research where an expectation of pain relief has been found to activate neurological systems involved in regulating pain (Hróbjartsson 2010; Price 2008). Conversely, negative expectations have been shown to adversely affect health, most notably by increasing pain (Bingel 2011; Varelmann 2010). In addition to conscious expectancy, expectation effects can be induced by classical conditioning. Classical conditioning is the body's subconscious reaction to a stimulus such as a visit to a healthcare practitioner whether or not the patient consciously expects a positive outcome. Numerous studies in animals and humans have demonstrated ways in which the immune system can be conditioned (Ader 2003). In one study subjects repeatedly consumed a flavoured coloured drink containing an immunosuppressant for three days. Then after five days off they were given the same flavoured drink, but with a placebo instead of the immunosuppressant. Because they had been conditioned to associate immunosuppressant with the flavoured drink, the placebo had a similar immunosuppressive effect to the actual drug when compared with control subjects (Goebel 2002). Hence if patients' immune systems are repeatedly activated after visiting their practitioner, their subconscious conditioning could lead to positive effects following any clinical encounter. This could partly explain the outcomes in the studies of changing patient

expectations. Some evidence suggests that positive expectations might reduce stress and anxiety (Nes 2006), which in turn appears to reduce pain, anxiety, depression, and a variety of other conditions (Grossman 2004). While some anxiety or stress is necessary to enhance performance and focus, about half of American working adults claim to be concerned that they have too much stress (APA 2013). Under stress, or the 'fight or flight' response (Cannon 1915), the body produces hormones such as adrenaline and cortisol (Jansen 1995), which, in turn, have numerous downstream affects on the body's immune system (Segerstrom 2004), pain (Hassett 2011), fatigue levels (Crofford 1998), neurodegenerative disorders (Esch 2002), cardiovascular disease (Stephoe 2012), wound healing (Gouin 2012), mental health (Jorm 2008), mortality (Russ 2012), and a variety of other disorders (Everly 2002). Evidence from the basic sciences (Benedetti 2009), as well as clinical trials indicates that physician empathy (Sarinopoulos 2013) and positive expectations (Brummett 2006) could reduce stress and anxiety, and thus are likely to help treat numerous stress-related conditions.

Mechanism of action of modifying practitioner empathy

Jani 2012 proposes that patients are more likely to provide accurate and sufficient information about their symptoms and concerns to empathetic practitioners. This, in turn, may allow the practitioner to make more accurate diagnoses and provide more appropriate treatment. An empathetic practitioner could also be better able to personalise and perhaps individualise care. Studies suggest that empathetic practitioners can reduce stress (Maier 2005) and thus possibly mitigate the negative health effects of stress (Rakel 2009).

Why it is important to do this review

The growing body of systematic review evidence showing that enhanced practitioner empathy and positive patient expectations can enhance treatment for a range of clinical conditions includes:

- Crow 1999 found that enhancing positive patient expectations improved symptoms.
- Di Blasi 2001 reported that 'context factors' (including practitioner empathy and patient expectations) enhanced patient care.
- Griffin 2004 and Kelley 2014 showed that empathy training for doctors improved healthcare outcomes.
- Derksen 2013 and Kelm 2014 found that empathy training for doctors within general practice (family medicine) and medical students could improve outcomes.

All of these studies included a variety of methods for changing practitioner expectations and patient expectations. None restricted their analysis to a specific condition, and all showed benefits across a range of conditions. The most recent systematic review investigated the effects of all context factors (including, but not limited to, practitioner empathy and positive patient expectations) for treating pain (Mistiaen 2015). The authors of the review concluded that context factors were beneficial for enhancing the care of pain. However, existing reviews have limitations. Some included non-randomised trials (Derksen 2013; Kelm 2014), making their results potentially more prone to bias than those of RCTs (Howick 2011). Others lacked focus on specific aspects of patient-practitioner communication (Griffin 2004; Kelley 2014; Crow 1999), or focused on specific ailments such as pain (Mistiaen 2015). Most importantly, the only review that studied the effects of both empathy and expectations within the same review is out of

date (Di Blasi 2001), being almost 15 years old. Our preliminary searches have identified several randomised trials of changing empathy and expectations published since the 2001 systematic review (Benedetti 2003; Colloca 2004; Dutt-Gupta 2007; Guo 2012; Knipschild 2005; Little 2015), meaning that a substantial recent evidence base exists in addition to what has been reviewed previously. The World Medical Association (WMA) notes that chronic diseases, many of which are accompanied by pain, anxiety, and depression, are the leading cause of death in developed and developing countries (WMA 2015). These problems become more acute if we consider that the population of the world is ageing, with 14% of the US and 17% of the UK population being over 65 (and this proportion is increasing) (World Bank 2014). Chronic pain, depression, and anxiety are very common in this multi-morbid population, almost 50% of the patients with three long-term conditions suffer from anxiety or depression while over 80% suffer from pain (Smith 2012). As a result there is a high demand for interventions to improve outcomes in these and other populations experiencing depression, anxiety and pain. This review is also important for reducing potential harms. Lack of focus on practitioner communication skills seems to cause practitioners to frequently fail to respond positively to subtle patient clues about their emotional state (Pollak 2007) and commonly misdiagnose anxiety and depression (Vermani 2011). Moreover, poor practitioner communication creates barriers to the potentially positive effects of the therapeutic relationship (Beck 2002; Benedetti 2009; Di Blasi 2001; Kelley 2014; Mistiaen 2015; Mondloch 2001) and increases the likelihood of litigation (Moore 2000). Based on this evidence it seems possible that for some mild conditions (such as mild to moderate pain, anxiety, or depression) empathy and positive expectations could either be used as a stand-alone treatment or to enhance the benefits of other drug and non-drug treatments, sometimes even allowing practitioners to reduce treatment doses, or improving quality of life. Studies also show that improving practitioner empathy can increase patient satisfaction (Eide 2002; Graugaard 2004).

However, not all of the evidence is positive. In some more recent, higher quality randomised trials positive expectations were not shown to produce any benefit. For example Dutt-Gupta 2007, and Petersen 2014 studied the effects of modifying empathy and expectations on the experience of pain. In these studies practitioners were randomised to either provide a positive suggestion (such as "this needle won't hurt") or a neutral control (where no positive or negative suggestions were provided). These studies failed to show statistically significant reductions in patient pain after healthcare practitioners gave patients positive suggestions. There is also insufficient evidence to be able to conclude whether modifying practitioner empathy or patient expectations affect some conditions more than others. Hence while a growing body of evidence suggests that changing expectations and empathy are beneficial for numerous conditions, many uncertainties remain and a definitive review is required of the evidence in this area.

This review is related but different from several other recent Cochrane reviews.

- Dwamena 2012 investigated randomised trials of patient-centred care. Their key criterion for including studies within their review was shared decision making about treatment decisions. While shared decision-making may be an effective

way of optimising patient expectations and improving patient perceptions of practitioner empathy, it is not the only way to increase empathy. Moreover for the group of patients who do not want to engage in a shared decision, the adoption of shared decision-making might not be an empathetic option. Some patients may prefer that a professional healthcare practitioner provide clear guidance. In these cases shared decision-making could reduce empathy because it disregards these patients' desires.

- Hróbjartsson 2010 investigated randomised trials comparing outcomes in placebo groups with outcomes in untreated groups. While it is likely that improvement in placebo groups is at least partly caused by enhanced practitioner empathy and patient expectations, placebo groups also receive a sham intervention. Our review does not require that a sham intervention be given as part of the treatment, and indeed many of the studies our preliminary analysis has identified do not involve a sham intervention.
- Akl 2011 investigated the effects of positive versus negative framing of messages about prognosis (for example "the chance of survival with cancer is 2/3" versus "the chance of mortality with cancer is 1/3"). While positive framing is one way of enhancing expectations, it is not the only way, and indeed the Akl 2011 review did not include any of the studies we identified in our preliminary analysis. There are also large differences between positive framing and empathy.

OBJECTIVES

The main aim of this review will be to assess the effects of changing practitioner empathy or patient expectations for all conditions. The main objective is to conduct a systematic review of randomised trials where the intervention involves manipulating either (a) practitioner empathy or (b) patient expectations, or (c) both.

METHODS

Criteria for considering studies for this review

Types of studies

We will include randomised trials (including cluster randomised trials) only.

Types of participants

We will include studies including participants who were aged 12 years or older, and were involved in a face-to-face interaction with a healthcare practitioner (such as a physician, nurse, or allied health professional). We will include studies of both conventional as well as complementary and alternative practices.

Types of interventions

To be considered for inclusion in this review an intervention must involve strategies designed to change practitioner empathy *and/or* strategies designed to modify patient expectations.

We will include studies in which the intervention was compared with:

- a neutral (usual care or sham) comparison group;
- a negative comparison group (receiving a strategy to reduce empathy and/or produce negative patient expectations); or

- another intervention to enhance empathy and/or encourage positive patient expectations.

The intervention could be very simple or more complex (see [Description of the intervention](#)). We will describe the complex interventions in detail in the results section of our review. We will include studies of both positive interventions (those designed to improve practitioner empathy or make patient expectations more positive) as well as negative interventions (those designed to reduce practitioner empathy or make patient expectations more negative). Since the direction of the effect in the negative expectations is likely to be the opposite of the direction of the effect in positive interventions, we will separate the positive and negative interventions in our analysis. Failing to separate the interventions could lead to the effects cancelling out in spite of the fact that positive interventions could have positive effects and negative interventions could have negative effects. To reflect the variety of communication styles within clinical practice, we will combine interventions that were compared with a neutral (standard care without attempting to manipulate practitioner empathy or patient expectations/sham intervention) or a negative intervention (designed to reduce practitioner empathy or produce negative patient expectations). However we will investigate the differential effects of these comparisons by excluding studies that compared positive interventions with negative control interventions in a subgroup analysis. We will consider and analyse separately studies in which the intervention involved attempts to induce negative expectations about outcomes in patients and (if we find such studies) interventions aimed at making practitioners less empathetic. This is because some studies indicate that negative patient expectations can cause 'nocebo' effects, which are negative outcomes produced by negative beliefs and expectations ([Dutt-Gupta 2007](#); [Varelmann 2010](#)). We will exclude studies where the communication is between a healthcare practitioner and a carer (for example because the patient has dementia). We will include clinical (where the intervention was introduced as part of routine care) but not laboratory (where the intervention was introduced in a more artificial environment, for example experimental pain) studies. We will exclude studies in which interpreters were used because the translator could have influenced the communication.

Types of outcome measures

Primary outcomes

1. Physical health outcomes.
2. Psychological outcomes.
3. Harms.

For all primary outcomes, we will choose the primary physical health outcome for the main clinical condition as reported by the study authors. In studies of more than one condition, we will report data on all conditions. We will select the primary physical health outcome which has been identified by the publication authors. Where no primary outcome has been identified, we will select the one specified in the sample size calculation. If there are no sample size calculations, we will select the outcome judged by two clinician authors (GL, PL) working independently to be most clinically relevant. For example longer-term follow up (weeks or months) is more likely to be clinically relevant than more immediate outcomes (hours or days). If there the two authors cannot reach agreement about the most clinically relevant physical health outcome, input from our patient representative will be sought.

For all primary outcomes, we will also assess the effects of positive and negative interventions in separate comparisons.

Secondary outcomes

In addition, since effective practitioner-patient communication could have global health effects (such as patient satisfaction, quality of life) we will also collect data about three secondary outcomes.

1. Patient satisfaction.
2. Quality of life.
3. Cost-effectiveness.

Timing of outcome assessment

Where outcomes were collected at more than one time point, we will choose the time point reported as primary by study authors. Where study authors did not state the primary time point we will choose the one most relevant to patients and provide a rationale. Longer-term follow up (months rather than weeks) is more likely to be clinically relevant.

Search methods for identification of studies

Searching for relevant studies in this area is challenging because of the absence of a common terminology for interventions that modify practitioner empathy or patient expectations. This comprehensive review is likely to represent a step forward in recognising the importance and contribution of these interventions that will help establish a common terminology. Eligible studies can be found in areas ranging from placebo research, patient-practitioner communication, and psychological interventions. This makes a search strategy with sufficient specificity challenging. Our search strategy was based on those used by [Di Blasi 2001](#) and [Mistiaen 2015](#), with the exception that we focused exclusively on randomised trials of expectancy and empathy manipulation whereas those authors included studies of all context effects and also included non-randomised trials. Yet because of the inherently fuzzy nature of the terminology used in the included trials a key component of our search strategy involves searching references of included studies and contacting experts.

The MEDLINE (OvidSP) search strategy is given in [Appendix 1](#) and will be adapted for other databases. The search strategy will consist of nine concepts, relating to different components of standard search strategies. These have been derived from:

- standard participants, intervention, comparison and outcome (PICO) components;
- patients;
- the practitioner;
- communication;
- suggestion;
- patient-practitioner communication;
- empathy;
- expectations;
- placebo and placebo effects.

We will identify randomised controlled trials by applying the Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE and adapting this strategy for other

databases: sensitivity- and precision-maximising version (Higgins 2011); Ovid format (Higgins 2011).

Electronic searches

We will search the following electronic databases from their start date:

- CINAHL;
- EMBASE;
- Database of Abstracts of Reviews of Effects (DARE) (*The Cochrane Library* via Wiley);
- LILACS;
- MEDLINE (OvidSP);
- PROQUEST Dissertations;
- PsycINFO;
- PubMed;
- Sociological Abstracts;
- The Cochrane Central Register of Controlled Trials (CENTRAL, *The Cochrane Library*), including Consumers and Communication Review Group Specialised Register;
- EED;
- Web of Knowledge.

We will also contact content-expert authors to identify all relevant trials. Searches will not be restricted in terms of the language. The results from all searches will be combined into a reference manager database and duplicate records will be removed.

Searching other resources

We will search reference lists of included studies, proceedings of placebo-specific conferences, and contact experts in the field and authors of included studies for advice about other studies. We will also perform a forward search in Web of Knowledge to find additional studies that cited one of the earlier identified relevant papers. For grey literature, we will do supplementary searches of OpenGREY (Open Grey 2015) and The Grey Literature Report (Grey Literature Report 2015). We will also search online trial registers for ongoing studies (ClinicalTrials.gov 2015) and WHO International Clinical Trials Registry Platform (WHO 2015).

Data collection and analysis

Selection of studies

Two review authors will independently screen all titles and abstracts identified from searches to determine those that meet the inclusion criteria. We will retrieve the full texts of any papers found to be potentially relevant by at least one author. Two review authors will independently screen full-text articles for inclusion or exclusion; discrepancies will be resolved by discussion and by consulting a third author, if necessary, to reach consensus. All potentially relevant papers rejected from the review at this stage will be listed as excluded studies, and the reasons provided in characteristics of excluded studies tables. We will also provide citation details and any available information about ongoing studies; we will collate and report details of duplicate publications, so that each study—rather than each report—becomes the unit of interest in the review. We will report the screening and selection process in an adapted PRISMA flow chart (Liberati 2009a).

Data extraction and management

Two review authors will independently extract data from included studies. Any discrepancies will be resolved by discussion until consensus is reached, or through consultation with a third author where necessary. We will develop and pilot a data extraction form using the *Cochrane Consumers and Communication Group 2015* data extraction template. Data to be extracted will include the following items: Details of the study (study design, types of participants, description of intervention and intervention components, study design, description of comparison group, completeness of outcome data, outcome measures, country, funding source). We will use the template for intervention description and replication (TIDieR) guidelines for describing interventions in the included studies (Hoffmann 2014). All extracted data will be entered into RevMan (Review Manager 2014) by one review author, and will be checked for accuracy against the data extraction sheets by a second review author working independently.

Assessment of risk of bias in included studies

We will assess and report on the methodological risk of bias of included studies in accordance with the *Cochrane Handbook* (Higgins 2011) and the guidelines of the Cochrane Consumers and Communication Group (Ryan 2011), which recommends the explicit reporting of the following individual elements for RCTs: random sequence generation; allocation sequence concealment; blinding (participants, personnel); blinding (outcome assessment); completeness of outcome data, and selective outcome reporting. We will consider blinding separately for different outcomes where appropriate (for example, blinding may have the potential to differently affect subjective versus objective outcome measures). For cluster-RCTs we will also assess and report the risk of bias associated with an additional domain: selective recruitment of cluster participants. We will judge each item as being at high, low or unclear risk of bias as set out in the criteria provided by Higgins 2011, and provide a quote from the study report and a justification for our judgement for each item in the risk of bias table.

Studies will be deemed to be at the highest risk of bias if they are scored as at unclear risk of bias for sequence generation or high or unclear risk of bias for allocation concealment domains, based on growing empirical evidence that these factors are particularly important potential sources of bias (Higgins 2011). We will therefore exclude all studies rated at a high risk of bias for the random sequence generation item of the risk of bias tool, since these studies are categorised as quasi-RCTs (Higgins 2011).

In all cases, two authors will independently assess the risk of bias of included studies, with any disagreements resolved by discussion to reach consensus. We will contact study authors for additional information about the included studies, or for clarification of the study methods as required. We will incorporate the results of the risk of bias assessment into the review through standard tables, and systematic narrative description and commentary about each of the elements, leading to an overall assessment the risk of bias of included studies and a judgment about the internal validity of the review's results.

We will perform sensitivity analyses based on the results of this bias assessment, as described below. If sufficient data are available, we will also investigate whether there is a dose-response effect: for example, whether inducing explicitly positive expectations

(telling a patient they will get better) is more effective than neutral expectations (telling a patient they may get better) compared with no treatment (such as putting a patient on a waiting list). We will also report whether the interventions and control treatments were described in sufficient detail to replicate, investigate most relevant causal factors, and report these factors.

Measures of treatment effect

For dichotomous outcomes, we will analyse data based on the number of events and number of individuals assessed in the intervention and comparison groups. We will use these to calculate the risk ratio and 95% confidence interval (CI) or extract summaries directly from the publication, if available. For continuous measures, we will analyse data based on the mean, standard deviation, and number of individuals assessed for both the intervention and comparison groups to calculate the mean difference (MD) and 95% CI. If the MD is reported without the data from each individual group, we will directly use the MD. If more than one study measures the same outcome using different tools, we will calculate the standardised mean difference (SMD) and 95% CI as the effect estimate.

Unit of analysis issues

If cluster-RCTs are included, we will check for unit of analysis errors—whether or not the analysis has adequately accounted for the presence of clustering. If errors are found and sufficient information is available, we will re-analyse the data using the appropriate unit of analysis by taking account of the intra-cluster correlation (ICC). We will obtain estimates of the ICC by contacting the authors of included studies or compute them using estimates from external sources. If it is not possible to obtain sufficient information to re-analyse the data in this way, we will use the reported effect estimates and annotate them as having a unit of analysis error.

Dealing with missing data

We will attempt to contact study authors to obtain missing data with respect to participants, outcomes, or summary data. For participant data, we will, where possible, conduct our analysis on an intention-to-treat basis; otherwise, data will be analysed as reported. We will report on the levels of loss to follow-up and assess this as a source of potential bias. For missing outcome or summary data, we will impute missing data, where possible, and report any assumptions made in doing this. We will investigate the effects of imputing data on pooled effect estimates in sensitivity analyses.

Assessment of heterogeneity

We anticipate heterogeneity in terms of intervention modalities, conditions, degree of bias, outcome measures, timing of outcome assessment and populations. Where studies are considered sufficiently similar, based on an assessment of the above factors, to allow pooling of data using meta-analysis, we will assess the degree of heterogeneity by visual inspection of forest plots and using the Chi^2 test for heterogeneity. We will quantify heterogeneity using the I^2 statistic, interpreting an I^2 value of 50% or more as representing a substantial level of heterogeneity. We will interpret the I^2 value in light of the size and direction of effects and the strength of evidence for heterogeneity based on the P value from the Chi^2 test and number of contributing studies (Higgins 2011). If too few trials are included in the meta-analysis, the Chi^2 test has little power to detect heterogeneity. In these cases we will interpret

non-significant results of the test of heterogeneity with care. Where heterogeneity is present in pooled effect estimates we will explore possible reasons for variability by conducting subgroup analysis.

Where we detect substantial clinical, methodological or statistical heterogeneity across included studies we will not report pooled results from meta-analysis but will instead use a narrative approach to data synthesis. In this event we will attempt to explore possible clinical or methodological reasons for this variation by grouping studies that are similar in terms of populations, intervention features, methodological features, or other factors to explore differences in intervention effects.

Assessment of reporting biases

We will assess reporting bias qualitatively based on the characteristics of the included studies (for example if only small studies that indicate positive findings are identified for inclusion), and if information that we obtain from contacting experts and authors or studies suggests that there are relevant unpublished studies. If we identify sufficient studies (at least 10) for inclusion in the review we will construct a funnel plot to investigate small study effects, which may indicate the presence of publication bias. If we identify at least 10 studies for inclusion in the review, we will construct a funnel plot to investigate the presence of publication bias. We will formally test for funnel plot asymmetry using the choice of test made based on Higgins and Green (Higgins 2011), bearing in mind that there may be several reasons for funnel plot asymmetry when interpreting the results.

Data synthesis

Our review is designed to be heterogeneous in terms of outcome measures because empathy and expectations are likely to be effective across inter-related outcomes. We will decide whether to meta-analyse data based on whether the interventions in the included trials are similar enough in terms of participants, settings, intervention, comparison and outcome measures to ensure meaningful conclusions from a statistically pooled result. If sufficient data are available, we will nevertheless consider conducting a random-effects meta-analysis in order to provide readers with an average effect size. We will obtain pooled estimates of the intervention effects with 95% CIs. With the exception of random sequence generation, where we will exclude studies with a high risk of bias, we will include in the meta-analysis all relevant studies, irrespective of risk of bias. However, we will conduct sensitivity analyses that exclude studies with unclear or high risk of bias in the random sequence generation of allocation concealment fields. We will include studies in which the intervention was compared with usual care or active control (other communication strategies).

If meta-analysis is possible, we will investigate possible sources of heterogeneity through subgroup analyses, and group the data based on the category that best explores the heterogeneity of studies and makes most sense to the reader (for example by interventions, populations or outcomes). We will present data in tables and narratively summarise the results for each category.

If we are unable to pool data using meta-analysis, we will group the data based on the category that best explores the heterogeneity of studies and makes most sense to the reader (i.e. by interventions, populations or outcomes). Within each category we will present the data in tables and narratively summarise the results.

Subgroup analysis and investigation of heterogeneity

If sufficient data are available, we will conduct three subgroup analyses.

1. Whenever there are three or more trials of a specific condition investigating the effects of modifying practitioner empathy / inducing patient expectations we will analyse these in separate subgroups. This is because empathy and expectations could affect these groups differently.
2. Trials in which placebo responsiveness was measured; we will study the subgroup of patients within these trials who were deemed to be placebo responsive, should this data be available.
3. Excluding trials in which a positive intervention was compared with a negative (rather than neutral) control group.

Sensitivity analysis

We anticipate performing four separate sensitivity analyses:

1. High risk of bias: excluding studies with high risk of bias, defined as trials with an unclear, or high or unclear risk of bias in the random sequence generation or allocation concealment fields respectively.
2. Imputation of data: excluding studies where assumptions about data had to be made because of missing data, for example, for continuous data the imputation of missing standard deviation values.
3. Subjective (patient-reported) versus objective (practitioner reported) primary outcomes.
4. Cluster-randomised trials: excluding trials where the intra-class correlation coefficients were assumed to impute study results.

Summary of findings table

Based on the methods described in Chapter 11 of the *Cochrane Handbook* (Schünemann 2011), we will prepare a summary of findings table to present the results of the meta-analysis. For each of the major primary outcomes, including potential harms, as outlined in the *Types of outcome measures* section we will present the results of the meta-analysis for the major comparisons of the review. We will provide a source and rationale for each assumed risk cited in the tables, and we will use the GRADE criteria to rank the quality of the evidence by means of GRADEpro software (Schünemann 2011). If meta-analysis is not feasible, we will present the results in a narrative summary of findings table format, such as that used by (Chan 2011a). We will not include duplicate outcomes—the same outcome using different measures.

Assessing the quality of the evidence

We will assess and report the quality of the evidence, using the GRADE system to assess the quality of the evidence for each outcome on each of the following domains: risk of bias, inconsistency, imprecision, indirectness and publication bias. Two authors will independently assess the quality of the evidence as implemented and described in the GRADEpro (GRADEpro) software (Schünemann 2011).

Patient and public involvement (ensuring relevance to decisions in healthcare)

The protocol has benefited from extensive comments from a patient representative. We have found the feedback from our patient and public involvement representative on our protocol to be enormously helpful in improving the relevance of our research to patients. In an extensive commentary on the draft protocol, that representative raised the following points.

1. Expectations and empathy are potentially distinct, though they are sometimes conflated in application. The representative cited the following personal experience: “The consultant... was much more cautious, pointing out that there was no real evidence available for this operation in cases like mine, and saying ‘I can’t promise that it will be better, only that it will be different.’ I felt that the doctor who gave a far less optimistic (that is, not inducing positive expectations)... took a far more empathetic approach and helped me to make a properly informed decision about my treatment... In the end I chose not to have the surgery.”
2. The representative emphasised the importance of quality-of-life outcomes over and above biological outcomes.

We modified our protocol in light of these comments by emphasising the differences and potential interactions between empathy and expectations. In addition, with guidance from the South Central Research Design Service (RDS; Southampton, UK), we are building a panel of three patient and public representatives (one who has already helped and two more that we have taken steps to identify), who will attend our monthly steering committee meetings, either in person or via teleconference. Patient and public involvement input will continue to benefit our project by:

- ensuring the outcomes we chose are relevant to patients;
- ensuring we report the results in ways that patients understand and are acceptable;
- disseminating the results to relevant groups;
- supporting translation of the results.

The main role of our patient and public involvement panel will be to provide input related to the design and conduct of our research. Our current representative has extensive experience as a patient representative and we do not anticipate that they will require training. We will, however, do a learning needs assessment of people, patients, and members of the public who end up involved in the review. We have included training costs in our budget. We will provide any required training through the Nuffield Department of Primary Care Health Sciences (University of Oxford) or the RDS (also within the University of Oxford). The principal investigator for this project will be the contact person for the patient and public involvement panel members.

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REFERENCES

Additional references

Ader 2003

Ader R. Conditioned immunomodulation: research needs and directions. *Brain Behavior and Immunity* 2003;**17**(Suppl 1):S51-7.

Akl 2011

Akl AE, Oxman AD, Herrin J, Vist GE, Terrenato I, Sperati F, et al. Framing of health information messages. *Cochrane Database of Systematic Reviews* 2011, Issue 12. [DOI: [10.1002/14651858.CD006777.pub2](https://doi.org/10.1002/14651858.CD006777.pub2)]

APA 2013

Stress in America. American Psychological Association 2013.

Beck 2002

Beck RS, Daughtridge R, Sloane PD. Physician-patient communication in the primary care office: a systematic review. *Journal of the American Board Family Practice* 2002;**15**(1):25-38.

Benedetti 2003

Benedetti F, Maggi G, Lopiano L, Lanotte M, Rainero I, Vighetti S, et al. Open vs. hidden medical treatments: The patient's knowledge about a therapy affects the therapy outcome. *Prevention and Treatment* 2003;**6**(1):-.

Benedetti 2009

Benedetti F. Placebo effects: understanding the mechanisms in health and disease. Oxford: Oxford University Press, 2009.

Bingel 2011

Bingel U, Wanigasekera V, Wiech K, Ni Mhuircheartaigh R, Lee MC, Ploner M, et al. The effect of treatment expectation on drug efficacy: imaging the analgesic benefit of the opioid remifentanyl. *Science Translational Medicine* 2011;**3**(70):70ra14.

Brummett 2006

Brummett BH, Helms MJ, Dahlstrom WG, Siegler IC. Prediction of all-cause mortality by the Minnesota Multiphasic Personality Inventory Optimism-Pessimism Scale scores: study of a college sample during a 40-year follow-up period. *Mayo Clin Proceedings* 2006;**81**(12):1541-4.

Cannon 1915

Cannon W. Bodily changes in pain, hunger, fear and rage: An account of recent researches into the function of emotional excitement. New York, London: D. Appleton and Company, 1915.

Chan 2011a

Chan RJ, Webster J, Marquart L. Information interventions for orienting patients and their carers to cancer care facilities. *Cochrane Database of Systematic Reviews* 2011, Issue 12. [DOI: [10.1002/14651858.CD008273.pub2](https://doi.org/10.1002/14651858.CD008273.pub2)]

ClinicalTrials.gov 2015

US National Institutes of Health. ClinicalTrials.gov. <https://www.clinicaltrials.gov/> (accessed 30 March 2015).

Cochrane Consumers and Communication Group 2015

Cochrane Consumers and Communication Group Data Extraction Template. <http://cccr.org/cochrane.org/author-resources> (accessed 30 March 2015).

Colloca 2004

Colloca L, Lopiano L, Lanotte M, Benedetti F. Overt versus covert treatment for pain, anxiety, and Parkinson's disease. *Lancet Neurology* 2004;**3**(11):679-84.

Coulehan 2000

Coulehan JL, Platt FW, Egener B, Frankel R, Lin CT, Lown B, et al. 'Let me see if I have this right...': Words that build empathy. *Annals of Internal Medicine* 2000;**135**(3):221-7.

Coulter 2005

Coulter A. Trends in patients' experience of the NHS. The Picker Institute 2005.

Crofford 1998

Crofford LJ. The hypothalamic-pituitary-adrenal stress axis in fibromyalgia and chronic fatigue syndrome. *Zeitschrift für Rheumatologie* 1998;**57**(Suppl 2):67-71.

Crow 1999

Crow R, Gage H, Hampson S, Hart J, Kimber A, Thomas H. The role of expectancies in the placebo effect and their use in the delivery of health care: A systematic review. *Health Technology Assessment* 1999;**3**(3):1-96.

de Craen 2001

de Craen AJ, Lampe-Schoenmaeckers AJEM, Kraal JW, Tijssen JG, Kleijnen J. Impact of experimentally induced expectancy on the analgesic effect of tramadol in chronic pain patients: a 2X2 factorial, randomised, placebo-controlled, double-blind trial. *Journal of Pain and Symptom Management* 2001;**21**(3):210-7.

Decety 2014

Decety J, Smith KE, Norman GJ, Halpern J. A social neuroscience perspective on clinical empathy. *World Psychiatry* 2014;**13**(3):233-237.

Derksen 2013

Derksen F, Bensing J, Lagro-Janssen A. Effectiveness of empathy in general practice: a systematic review. *British Journal of General Practice* 2013;**63**(606):e76-84.

Di Blasi 2001

Di Blasi Z, Harkness E, Ernst E, Georgiou A, Kleijnen J. Influence of context effects on health outcomes: a systematic review. *Lancet* 2001;**357**(9258):757-62.

Dutt-Gupta 2007

Dutt-Gupta J, Bown T, Cyna AM. Effect of communication on pain during intravenous cannulation: a randomised controlled trial. *British Journal of Anaesthesia* 2007;**99**(6):871-5.

Dwamena 2012

Dwamena F, Holmes-Rovner M, Gaulden C, Jorgenson S, Sadigh G, Sikorskii A, et al. Interventions for providers to promote a patient-centred approach in clinical consultations. *Cochrane Database of Systematic Reviews* 2012, Issue 12. [DOI: [10.1002/14651858.CD003267.pub2](https://doi.org/10.1002/14651858.CD003267.pub2)]

Eide 2002

Eide H, Graugaard P, Holgersen K, Finset A. Physician communication in different phases of a consultation at an oncology outpatient clinic related to patient satisfaction. *Patient Education and Counseling* 2002;**51**(3):259-66.

Esch 2002

Esch T, Stefano GB, Fricchione GL, Benson H. The role of stress in neurodegenerative diseases and mental disorders. *Neuroendocrinology Letters* 2002;**23**(3):199-208.

Everly 2002

Everly GS, Lating JM. A clinical guide to the treatment of the human stress response. 3. Kluwer Academic/Plenum Publishers, 2002.

Fellow-Smith 2012

Fellow-Smith E, Moss-Morriss R, Tylee A, Fossey M, Cohen A, Nixon T. Investing in emotional and psychological wellbeing. Mental Health Network, available on <http://mhinstitute.org.uk/publications-/working-papers-41/item/233-investing-in-emotional-and-psychological-wellbeing-a-guide-to-service-design-and-productivity-improvement-for-commissioners-clinicians-and-managers-in-primary-care-secondary-care-and-mental-health.html> (accessed 31 March 2015) 2012.

Finset 2003

Finset A, Ekeberg Ø, Eide H, Aspegren K. Long term benefits of communication skills training for cancer doctors. *Psychooncology* 2003;**12**(7):686-93.

Fogarty 1999

Fogarty LA, Curbow BA, Wingard JR, McDonnell K, Somerfield MR. Can 40 seconds of compassion reduce patient anxiety?. *Journal of Clinical Oncology* 1999;**17**(1):371-9.

GMC 2014

GMC. Consultation report: Making sure all licensed doctors have the necessary knowledge of English to practise safely in the UK. General Medical Council.

Goebel 2002

Goebel MU, Trebst AE, Steiner J, Xie YF, Exton MS, Frede S, et al. Behavioral conditioning of immunosuppression is possible in humans. *FASEB Journal* 2002;**16**(14):1869-73.

Gouin 2012

Gouin JP, Kiecolt-Glaser JK. The impact of psychological stress on wound healing: methods and mechanisms. *Critical Care Nursing Clinics of North America* 2012;**24**(2):201-13.

Graugaard 2004

Graugaard PK, Holgersen K, Finset A. Communicating with alexithymic and non-alexithymic patients: An experimental

study of the effect of psychosocial communication and empathy on patient satisfaction. *Psychotherapy and Psychosomatics* 2004;**73**(2):92-100.

Grey Literature Report 2015

New York Academy of Medicine. Grey Literature Report. <http://www.greylit.org/> (accessed 30 March 2015).

Griffin 2004

Griffin SJ, Kinmonth AL, Veltman MW, Gillard S, Grant J, Stewart M. Effect on health-related outcomes of interventions to alter the interaction between patients and practitioners: a systematic review of trials. *Annals of Family Medicine* 2004;**2**(6):595-608.

Grossman 2004

Grossman P, Niemann L, Schmidt S, Walach H. Mindfulness-based stress reduction and health benefits. A meta-analysis. *Journal of Psychosomatic Research* 2004;**57**(1):35-43.

Gryll 1978

Gryll SL, Katahn M. Situational factors contributing to the placebo effect. *Psychopharmacology* 1978;**57**(3):253-61.

Guo 2012

Guo P, East L, Arthur A. A preoperative education intervention to reduce anxiety and improve recovery among Chinese cardiac patients: a randomized controlled trial. *International Journal of Nursing Studies* 2012;**49**(2):129-37.

Hassett 2011

Hassett AL, Clauw DJ. Does psychological stress cause chronic pain?. *Psychiatric Clinics of North America* 2011;**34**(3):579-94.

Higgins 2011

Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011 Vol. Available from www.cochrane-handbook.org.

Hoffmann 2014

Hoffmann T, English T, Glasziou P. Reporting of interventions in randomised trials: an audit of journal instructions to authors. *Trials* 2014;**15**(-):20.

Hojat 2009

Hojat M, Vergare MJ, Maxwell K, Brainard G, Herrine SK, Isenberg GA, et al. The devil is in the third year: a longitudinal study of erosion of empathy in medical school. *Academic Medicine* 2009;**84**(9):1184-91.

Hojat 2011

Hojat M, Louis DZ, Markham FW, Wender R, Rabinowitz C, Gonnella JS. Physicians' empathy and clinical outcomes for diabetic patients. *Academic Medicine* 2011;**86**(3):359-64.

Howick 2009

Howick J. Reviewing the unsubstantiated claims for the methodological superiority of 'placebo' over 'active' controlled trials: Reply to open peer commentaries. *American Journal of Bioethics* 2009;**9**(9):W5-7.

Howick 2011

Howick J. *The Philosophy of Evidence-Based Medicine*. Wiley, 2011.

Hróbjartsson 2010

Hróbjartsson A, Gøtzsche P. Placebo interventions for all clinical conditions. *Cochrane Database of Systematic Reviews* 2010, Issue 1. [DOI: [10.1002/14651858.CD003974.pub3](https://doi.org/10.1002/14651858.CD003974.pub3)]

Jani 2012

Jani BD, Blane DN, Mercer SW. The role of empathy in therapy and the physician-patient relationship. *Forschende Komplementärmedizin* 2012;**19**(5):252-7.

Jansen 1995

Jansen AS, Nguyen XV, Karpitskiy V, Mettenleiter TC, Loewy AD. Central command neurons of the sympathetic nervous system: basis of the fight-or-flight response. *Science* 1995;**270**(5236):644-6.

Jorm 2008

Jorm AF, Morgan AJ, Hetrick SE. Relaxation for depression. *Cochrane Database of Systematic Reviews* 2008, Issue 4. [DOI: [10.1002/14651858.CD007142.pub2](https://doi.org/10.1002/14651858.CD007142.pub2)]

Kaptchuk 2008

Kaptchuk TJ, Kelley JM, Conboy LA, Davis RB, Kerr CE, Jacobson EE, et al. Components of placebo effect: randomised controlled trial in patients with irritable bowel syndrome. *British Medical Journal* 2008;**336**(7651):999-1003.

Kelley 2014

Kelley JM, Kraft-Todd G, Schapira L, Kossowsky J, Riess H. The influence of the patient-clinician relationship on healthcare outcomes: A systematic review and meta-analysis of randomized controlled trials. *PLoS One* 2014;**9**(4):e94207.

Kelm 2014

Kelm Z, Womer J, Walter JK, Feudtner C. Interventions to cultivate physician empathy: A systematic review. *BMC Medical Education* 2014;**14**:219.

Kirsch 1985

Kirsch I. Response expectancy as a determinant of experience and behaviour. *American Psychologist* 1985;**40**(11):1189-1202.

Knipschild 2005

Knipschild P, Arntz A. Pain patients in a randomized trial did not show a significant effect of a positive consultation. *Journal of Clinical Epidemiology* 2005;**58**(7):708.

Lelorain 2012

Lelorain S, Bredart A, Dolbeault S, Sultan S. A systematic review of the associations between empathy measures and patient outcomes in cancer care. *Psychooncology* 2012;**21**(12):1265-64.

Levine 1984

Levine JD, Gordon NC. Influence of the method of drug administration on analgesic response. *Nature* 1984;**312**(5996):755-6.

Liberati 2009a

Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: Explanation and elaboration. *PLoS Medicine* 2009;**6**:e1000100.

Little 2015

Little P, White P, Kelly J, Everitt H, Mercer SW. Randomised controlled cluster trial of a brief intervention to improve non-verbal communication in general practice consultations. *British Journal of General Practice* 2015;**65**(635):e351-6.

Maier 2005

Maier SF, Watkins LR. Stressor controllability and learned helplessness: the roles of the dorsal raphe nucleus, serotonin, and corticotropin-releasing factor. *Neuroscience and Biobehavioural Reviews* 2005;**29**(4-5):829-41.

Mercer 2002

Mercer SW, Reynolds WJ. Empathy and quality of care. *British Journal of General Practice* 2002;**52**(Suppl):S9-12.

Mistiaen 2015

Mistiaen P, van Osch M, Di Blasi Z, Bensing J, van Vliet L, van Dulmen S. The effect of patient-provider communication on pain: a systematic review. *Pain* 2015.

Mondloch 2001

Mondloch M, Cole DC, Frank JW. Does how you do depend on how you think you'll do? A systematic review of the evidence for a relation between patients' recovery expectations and health outcomes. *Canadian Medical Association Journal* 2001;**165**(2):174-9.

Moore 2000

Moore PJ, Adler NE, Robertson PA. Medical malpractice: the effect of doctor-patient relations on medical patient perceptions and malpractice intentions. *Western Journal of Medicine* 2000;**173**(4):244-50.

Morse 1992

Morse JM, Anderson G, Botorff JL, Yonge O, O'Brien B, Solberg SM, et al. Exploring empathy: a conceptual fit for nursing practice?. *Image - the Journal of Nursing Scholarship* 1992;**24**(4):273-80.

Nes 2006

Nes LS, Segerstrom SC. Dispositional optimism and coping: a meta-analytic review. *Personality and Social Psychology Review* 2006;**10**(3):235-51.

Neumann 2009

Neumann M, Bensing J, Mercer S, Ernstmann N, Ommen O, Pfaff H. Analyzing the "nature" and "specific effectiveness" of clinical empathy: a theoretical overview and contribution towards a theory-based research agenda. *Patient Education and Counseling* 2009;**74**(3):339-46.

Neumann 2011

Neumann M, Edelhauser F, Tauschel D, Fischer MR, Wirtz M, Woopen C, et al. Empathy decline and its reasons: a systematic review of studies with medical students and residents. *Academic Medicine* 2011;**86**(8):996-1009.

NIH 2014

Talking with your older patient. National Institutes of Health 2014.

Open Grey 2015

Open Grey. <http://www.opengrey.eu/about> (accessed 30 March 2015).

Parker 2007

Parker SM, Clayton JM, Hancock K, Walder S, Butow PN, Carrick S, et al. A systematic review of prognostic/end-of-life communication with adults in the advanced stages of a life-limiting illness: Patient/caregiver preferences for the content, style, and timing of information. *Journal of Pain and Symptom Management* 2007;**34**(1):81-93.

Petersen 2014

Petersen GL, Finnerup NB, Groesen K, Pilegaard HK, Tracey I, Benedetti F, et al. Expectations and positive emotional feelings accompany reductions in ongoing and evoked neuropathic pain following placebo interventions. *Pain* 2014;**155**(12):2687-98.

Pollak 2007

Pollak KI, Arnold RM, Jeffreys AS, Alexander SC, Olsen MK, Abernethy AP, et al. Oncologist communication about emotion during visits with patients with advanced cancer. *Journal of Clinical Oncology* 2007;**25**(36):5748-52.

Price 2008

Price DD, Finniss DG, Benedetti F. A comprehensive review of the placebo effect: recent advances and current thought. *Annual Review of Psychology* 2008;**59**:565-90.

Rakel 2009

Rakel DP, Hoelt TJ, Barrett BP, Chewnin BA, Craig BM, Niu M. Practitioner empathy and the duration of the common cold. *Family Medicine* 2009;**41**(7):494-501.

Review Manager 2014 [Computer program]

The Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan) [Computer program]. Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

Riess 2012

Riess H, Kelley JM, Bailey RW, Dunn EJ, Phillips M. Empathy training for resident physicians: a randomized controlled trial of a neuroscience-informed curriculum. *Journal of General Internal Medicine* 2012;**27**(10):1280-6.

Rose 1993

Rose S, Achkar E, Falk GW, Fleshler B, Revta R. Interaction between patient and test administrator may influence the results of edrophonium provocative testing in patients with

noncardiac chest pain. *American Journal of Gastroenterology* 1993;**88**(1):20-4.

Russ 2012

Russ TC, Stamatakis E, Hamer M, Starr JM, Kivimäki M, Batty GD. Association between psychological distress and mortality: individual participant pooled analysis of 10 prospective cohort studies. *British Medical Journal* 2012;**345**:e4933.

Ryan 2011

Rebecca R. Cochrane Consumers & Communication Review Group Study Quality Guide. The Cochrane Collaboration 2011.

Sarinopoulos 2013

Sarinopoulos I, Hesson AM, Gordon C, Lee SA, Wang L, Dwamena F, et al. Patient-centered interviewing is associated with decreased responses to painful stimuli: an initial fMRI study. *Patient Education and Counseling* 2013;**90**(2):220-5.

Schünemann 2011

Schünemann HJ, Oxman AD, Higgins JPT, Vist GE, Glasziou P, Guyatt GH. Chapter 11: Presenting results and 'Summary of findings' tables. In: Higgins JPT, Green S (editors), *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Seegerstrom 2004

Seegerstrom SC, Miller GE. Psychological stress and the human immune system: a meta-analytic study of 30 years of inquiry. *Psychological Bulletin* 2004;**130**(4):601-30.

Sjölin 1994

Sjölin M, Maerker M. [Effects of information on and reflection of women's pain experience during mammography] [Effekten av information om och spegling av kvinnors smärtupplevelse vid mammografiundersökning]. *Vard Nord Utveckl Forsk* 1994;**14**(1):11-15.

Smith 1995

Smith RC, Lyles JS, Mettler JA, Marshall AA, Van Egeren LF, Stoffelmayr BE, et al. A strategy for improving patient satisfaction by the intensive training of residents in psychosocial medicine: a controlled, randomized study. *Academic Medicine* 1995;**70**(8):729-32.

Smith 2012

Smith SM, Soubhi H, Fortin M, Hudon C, O'Dowd T. Managing patients with multimorbidity: systematic review of interventions in primary care and community settings. *British Medical Journal* 2012;**345**:e5205.

Steptoe 2012

Steptoe A, Kivimäki M. Stress and cardiovascular disease. *Nature Reviews. Cardiology* 2012;**9**(6):360-70.

Thomas 1987

Thomas KB. General practice consultations: is there any point in being positive?. *British Medical Journal* 1987;**294**(6581):1200-2.

Vangronsveld 2012

Vangronsveld KL, Linton SJ. The effect of validating and invalidating communication on satisfaction, pain and affect in nurses suffering from low back pain during a semi-structured interview. *European Journal of Pain* 2012;**16**(2):239-46.

Varelmann 2010

Varelmann D, Pancaro C, Cappiello EC, Camann WR. Nocebo-induced hyperalgesia during local anesthetic injection. *Anesthesia and Analgesia* 2010;**110**(3):868-70.

Vermani 2011

Vermani M, Marcus M, Katzman MA. Rates of detection of mood and anxiety disorders in primary care: a descriptive, cross-sectional study. *Primary Care Companion for CNS Disorders* 2011;**13**(2):ii.

Wartolowska 2014

Wartolowska K, Judge A, Hopewell S, Collins G, Dean BJF, Rombach, I, et al. Use of placebo controls in the evaluation

of surgery: systematic review. *British Medical Journal* 2014;**348**:g3253.

WHO 2015

World Health Organization. WHO International Clinical Trials Registry Platform. <http://www.who.int/ictrp/en/> (accessed 30 March 2015).

WMA 2015

World Medical Association. World Medical Association Statement on the Global Burden of Chronic Disease. <http://www.wma.net/en/30publications/10policies/c11/> (accessed 30 March 2015).

World Bank 2014

World Bank. Population ages 65 and above (% of total). <http://data.worldbank.org/indicator/SP.POP.65UP.TO.ZS> (accessed 30 March 2015).

ADDITIONAL TABLES
Table 1. Examples of interventions to change provider empathy

Study	Intervention	Main outcomes
Sjölin 1994	Empathetic, reflective feedback to patient	Pain during mammography
Vangronsveld 2012	Empathetic care (validation)	Back pain
Smith 1995	Intensive empathy training	Patient satisfaction
Riess 2012	Empathy training	Patient ratings of physician empathy
Little 2015	Non-verbal empathy training	Patient satisfaction

Table 2. Examples of interventions to change patient expectations

Study	Intervention	Main outcomes
de Craen 2001	Chronic pain patients were randomised to receive positive or neutral information	Pain
Kaptchuk 2008	Patients with irritable bowel syndrome (IBS) were treated with or without an 'augmented consultation' (increased time, warmth and confidence in a positive result)	Change in IBS symptoms (Global Improvement Scale)
Rose 1993	Non-cardiac chest pain patients were randomised to receive a provocative agent (edrophonium) by a physician who told them either that the intravenous medication was given for observing changes in the tracing or that it would elicit their usual pain	Pain
Thomas 1987	GP giving a clear diagnosis and providing positive statements about recovery compared with giving no clear diagnosis and ambivalent statements about the possibility of recovery	Speed of recovery (general)
Benedetti 2003	Open administration of analgesic more effective than hidden administration	Pain

APPENDICES

Appendix 1. MEDLINE search strategy

Search methods for MEDLINE (search strategy to be adapted for other databases)

MEDLINE (OvidSP)

1. patient care/
2. patient centered care/
3. ambulatory care/
4. preoperative care/
5. (preoperative education or (await* adj3 surg*)).ti,ab,kw.
6. exp perioperative care/ or anesthesia/
7. exp nursing care/
8. palliative care/
9. hospice care/
10. "referral and consultation"/
11. (consultation* or consult?).ti,ab,kw.
12. office visits/
13. (office visit* or (attend* adj5 clinic?)).ti,ab,kw.
14. interview psychological/
15. exp professional patient relations/
16. ((professional or physician or doctor or gp or surgeon or nurse or clinician or practitioner or provider or therapist) adj1 (patient or client)).ti,ab,kw.
17. exp professional role/
18. ((treatment or therapeutic) adj alliance).ti,ab,kw.
19. exp patients/
20. (patient? or subject? or client* or inpatient* or outpatient* or participant* or hospitali#ed or institutional#ed or survivor*).ti,ab,kw.
21. exp health personnel/
22. ((health* adj2 (personnel or practitioner* or provider*)) or doctor* or physician* or general practitioner* or gp or gps or nurse* or clinician* or dentist* or pharmacist* or an?esthetist* or midwi* or hospitalist* or surgeon* or oncologist* or obstetrician* or gyn?ecologist* or geriatrician* or gerontologist* or pediatrician* or radiologist* or therapist* or physiotherapist* or dietitian* or psychologist* or counsel? or*).ti,ab,kw.
23. (19 or 20) and (21 or 22)
24. interviews as topic/
25. (visit* or interview*).ti,ab,kw.
26. communication/ or interpersonal relations/
27. (communicat* or verbal* or interaction* or information or encounter* or interpersonal).ti,ab,kw.

28. 23 and (24 or 25 or 26 or 27)
29. or/1-18,28
30. attitude of health personnel/
31. (attitud* adj5 (health* personnel or health* practitioner* or health* provider* or doctor* or physician* or general practitioner* or gp or gps or nurse* or clinician* or dentist* or pharmacist* or an?esthetist* or midwi* or hospitalist* or surgeon* or oncologist* or obstetrician* or gyn?ecologist* or geriatrician* or gerontologist* or pediatrician* or radiologist* or therapist* or physiotherapist* or dietitian* or psychologist* or counsel?or*)).ti,ab,kw.
32. 30 or 31
33. (positiv* or negativ* or understanding or caring or engage* or disengage* or attentive* or inattentive* or interested or uninterested or disinterested or supportive* or warm or cold).ti,ab,kw.
34. 32 and 33
35. empathy/
36. (empath* or unempath* or sympath* or unsympath* or compassion* or dispassion* or uncaring or welcoming or enthusias* or kindness or warmth or warmly or friendl* or unfriendl* or coldness or coldly).ti,ab,kw.
37. exp facial expression/
38. (smiling or smile?).ti,ab,kw.
39. (emotional support or affective or reassur* or reduc* anxiety or comforting).ti,ab,kw.
40. ((positiv* or negativ*) adj (consultatation or information or attitude* or messag*)).ti,ab,kw.
41. suggestion/
42. persuasive communication/
43. (suggestion or suggestive or persuasion or persuasive or warn* or frame? or framing).ti,ab,kw.
44. hope/
45. trust/
46. (expectation* or expectanc* or hope? or hopeful* or optimism or optimist* or anticipat* or belief* or trust).ti,ab,kw.
47. negativism/
48. (doubt* or disbelief* or mistrust* or distrust* or pessimis* or skeptic* or negativism).ti,ab,kw.
49. (coach* or priming or conditioned or conditioning).ti,ab,kw.
50. placebo effect/
51. nocebo effect/
52. "set (psychology)"/
53. "unconscious (psychology)"/
54. or/34-53
55. 29 and 54
56. randomized controlled trial.pt.
57. controlled clinical trial.pt.
58. randomized.ab.
59. placebo.ab.

60. clinical trials as topic.sh.

61. randomly.ab.

62. trial.ti.

63. or/56-62

64. 55 and 63

65. (editorial or review).pt.

66. 64 not 65

CONTRIBUTIONS OF AUTHORS

JH wrote the first draft of the manuscript. All other authors contributed to the editing of the manuscript.

DECLARATIONS OF INTEREST

- Jeremy Howick: None known
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- Alexander Mebius: None known
- George Lewith: None known
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