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The effect of varying practitioner communication on patients' health status and treatment outcomes (Protocol)

Verheul W, Mistiaen P, Di Blasi Z, Kok L, van Dulmen S, Bensing J



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[Intervention Protocol]

The effect of varying practitioner communication on patients' health status and treatment outcomes

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ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:

To assess the effects of interventions in which healthcare practitioner communication in face-to-face consultations with patients is experimentally varied in comparison to usual care or contrasted active control interventions, on patient health and treatment outcomes.

A secondary aim is to investigate if the intervention effect is modified by intervention type, type of illness, length of follow-up, type of outcome and the way the subjects are exposed to communication in studies (real versus simulated).

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BACKGROUND

Communication between practitioners and patients lies at the heart of medicine, accompanying almost every step in health care (de Haes 2009). Communication is pivotal in establishing diagnoses and treatment plans, and inherent in giving advice and dealing with the patient's emotional reactions to the implications of disease. Nevertheless communication was, for a long time, taken for granted. In the last few decades, however, medical communication is increasingly addressed in the literature. Studies on patient-practitioner communication are often performed within theoretical frameworks. These include Roger's client-centred theory or the framework of patient-centred care (Bensing 2000; Bensing 2003); the biopsychosocial model (Engel 1988); and relationship-oriented care (Roter 2006) which all advocate an approach that does take patients, and not only their biomedical problems, into account. These are now favoured models for physician-patient communication because they connect to current ethical views on the physician-patient relationship and they also seem to be associated with beneficial patient outcomes (Michie 2003; Stewart 2000). However, the ideological base of communication in medicine seems more developed than its evidence base (Bensing 2000; de Haes 2009).

Intervention studies assessing the effects of manipulating healthcare practitioner-patient communication within these frameworks are often very complex. Furthermore such studies are few, lack methodological rigor or fail to specify the mechanisms through which communication influences outcomes (Griffin 2004). Instead, communication is used as a 'container concept', keeping us in the dark as to how it can be used as a tool to help reach desired outcomes.

In order to extend the evidence base of the effects of specified communication elements on patients, firstly potential mechanisms which can explain the influence of certain communication behaviours on patient outcomes should be defined, secondly these mechanisms should be operationalized in observable behaviours and thirdly these behaviours should be systematically varied in controlled experiments (de Haes 2009). In the proposed review we will seek to identify studies that do so in face-to-face patient-practitioner communication, with a focus on patients' health and treatment outcomes.

Practitioner-patient communication has to fulfil diverse criteria in order to be successful. In a systematic review (Di Blasi 2001), Di Blasi and colleagues used Leventhal's self-regulation theory (Cameron 2003) to explain how a person, threatened by signs and symptoms of illness, responds with cognitive and emotional reactions to a practitioner's communication. In consultations, healthcare practitioners influence the way patients think and feel about their illness or treatment. Di Blasi 2001 classified interventions into those varying either (or both) cognitive or emotional care by means of communication. Cognitive care aims to influence patients' expectations about the illness or the treatment, whereas emotional care refers to the style of the consultation (e.g. warm, empathic), and aims to reduce negative feelings such as anxiety and fear. Di Blasi 2001 found that patient-practitioner communication interventions using a combination of cognitive care and emotional care affected patients' health outcomes. Other reviews found similar results (Beck 2002; Griffin 2004).This closely connects to what Engel 1988 called the patient's double need: a need to know and understand, and a need to feel known and understood. For both needs, practitioner-patient communication has been shown to play an important role (Bensing 1992). The need to know and understand is a cognitive need for which cognitive care is important; this is achieved by communication targeting the transfer of information, such as the doctor telling the patient what is happening with their body and what they can expect. The second need is an emotional need for which emotional care is important. Emotional care is communication targeted at establishing a good therapeutic relationship between healthcare practitioner and patient. Examples are eye contact, empathic statements and leaving room for patients to tell their stories.

It is important to note that the difference between communication providing cognitive care and emotional care is not always clear-cut. For example, if a doctor tells a patient "I'm so relieved to tell you that your test results are all OK", the information offered about the test results is of an instrumental nature, while the expression of relief is affect-oriented. Nevertheless there is considerable evidence that such a distinction can be made in practice and that this distinction is useful in the sense that the amount of affect-oriented communication is related to patient outcomes (Bensing 1992; Hall 1987). The distinction between affect-oriented and instrumental communication is not always made, however, and their relative contribution has not been thoroughly assessed. For example, Kaptchuk 2008 found that healthcare practitioner communication with extra attention, warmth and confidence decreased problems in patients with irritable bowel syndrome in comparison to a control group in which the practitioner did not 'augment' the communication. However the extent to which these effects were the result of emotional care compared with cognitive care is unclear. This review will focus on disentangling these components of communication and will assess their separate and combined effects on patient outcomes.

Description of the intervention

We will review interventions which vary practitioner communication with patients. 'Communication' is defined as verbal and non-verbal interaction. We will only include studies in which the communication occurs face-to-face. By varying communication we refer to experimental manipulation of one or more elements in patient-practitioner communication. The manipulation might be to vary only a single sentence (for example, a doctor might say that a treatment will certainly have a positive effect, compared

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with saying that the treatment might or might not work) or to vary a practitioner's overall communication style (such as warm and friendly versus cold and formal).

As explained, communication can be classified as cognitive or emotional care or both; we will use these concepts throughout the review. Interventions in which the practitioner varies communication in terms of providing information about diagnosis, treatment and consequences for the patient will be classified as cognitive care. When communication is aimed at changing patients' emotions, for example by variations in the friendliness, trust, empathy or optimism conveyed, we will classify the intervention as emotional care. Communication providing information alongside optimism would be classified as both cognitive and emotional care (Di Blasi 2001). We have listed several examples of the intervention in Table 1.

Table 1. Examples of the intervention

Study	The manner in which communication was varied	Main outcomes	Cognitive or emotional care
Fogarty 1999	Breast cancer consultation with or without physician's statements of empathy	Patients' anxiety	Emotional
Gryll 1978	Dental patients were treated by a warm or neutral practitioner and practitioners raised positive, uncertain or no expectations regarding the effectiveness of sham-medication on tension, anxiety and sensitivity on pain.	Pain and anxiety	Cognitive and emotional
Kaptchuk 2008	Practitioner administering acupuncture to patients with irritable bowel syndrome (IBS) with or without extra communication conveying warmth, attention, and confidence	Change in IBS-symptoms	Cognitive and emotional
Rose 1993	Non-cardiac chest pain patients were administered a provocative agent by a physician who told that the intravenous medication was given to observe changes in the tracing or that it would elicit their usual pain.	Elicited pain	Cognitive
Thomas 1987	GP giving a clear diagnosis and raising positive recovery expectations versus giving no clear diagnosis and uncertain expectations about recovery	Patients' speed of recovery	Cognitive

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How the intervention might work

To establish how varying communication in the patient-practitioner relationship can influence patients' health outcomes, we need to look at the possible mechanisms involved. The division into cognitive and emotional care is a start. Different kinds of communication can lead to different cognitive responses (e.g. outcome expectancies) and emotional responses (e.g. stress), which in turn can directly or indirectly affect patients' health.

Research and theory on the placebo effect can guide us as to how cognitive and emotional care conveyed by communication can lead to changes in patients' health or treatment outcomes (Di Blasi 2001). Patients' responses are not only due to inherent characteristics of a certain treatment, such as the pain-relieving effect of an analgesic, but also to a range of unspecified factors. Placebo effects, sometimes called context effects, are effects on a patient's health caused by nonspecific factors of a treatment. This definition has a limited durability: once factors and their effects are specified, they are removed from the scope of this definition. Patient-practitioner communication is such a factor which is often left unspecified. While there are numerous studies assessing the specific effects of a certain pharmaceutical, surgical or other medical intervention, the effects of patient-practitioner communication on patients' health-related outcomes have received far less attention (Crow 1999; de Haes 2009; Di Blasi 2001; Griffin 2004). By making placebo effects and their causal factors an object of research, instead of something that needs to be controlled for in trials, our understanding of placebo effects' mechanisms has grown (Benedetti 2008; Harrington 1999). These mechanisms can help us understand the effects of patient practitioner communication on health-related outcomes.

Research on the placebo effect suggests that there are three important mechanisms involved: expectancy manipulation (Crow 1999; Di Blasi 2001; Kong 2007; Price 2008), conditioning (Price 2008; Benedetti 2003) and affect manipulation (Di Blasi 2001; Klossika 2006; Lieberman 2004; Price 2008; Staud 2004; Vase 2005; Villemure 2002).

Expectancy manipulation

Expectancies are cognitions, which can be manipulated by information and suggestion about medical procedures, treatment and the management of illness. The change in patients' self-efficacy and outcome expectations can lead to positive and negative health outcomes (Crow 1999). The direct effect of influencing patients' expectations on outcomes such as physiological status or pain has been extensively documented, perhaps most clearly in the field of pain research where an expectation of pain relief has been found to activate neurological systems involved in regulating pain (Price 2008). Studies have shown that where pain relief or anti-anxiety medication was administered by hidden compared with open means, their effectiveness was dramatically reduced. This highlights the importance of practitioner communication (Colloca 2004), as practitioners can influence patients' expectancies by means of their communication.

Conditioning

Placebo effects can also be attained by classical conditioning, especially when effects are not consciously experienced (such as hormone secretion (Benedetti 2003) or immuno-suppression (Ader 2003)). Conditioning occurs when a stimulus (such as a healthcare practitioner communicating in a certain way) coincides with an effect (such as recovery). A laboratory example of conditioning with health effects is provided in a study where subjects repeatedly consume a coloured drink containing an immunosuppressant, after which drinking an inert coloured drink will lead to immunosuppression (Goebel 2002). This means that previous experiences of patients not only shape their conscious expectations, but also can lead to conditioned responses. With regard to communication in the patient-practitioner relationship, this means that communication which matches patients' earlier experiences can act as a conditioned stimulus and elicit the same effects on health as effects which coincided with those earlier experiences.

Affect manipulation

Changes in negative affect or stress can have a direct influence on health status. For example, anxiety reduction can lead to positive health effects by mediation through decreased sympathetic activation (Drummond 2001). Neuroscientific research also offers clues that context effects on pain are influenced by negative affect (Benedetti 2007; Lieberman 2004; Vase 2005) by showing the activation of brain areas involved. Negative affect can also slow down wound healing (Vileikyte 2007). One could argue that reduction of negative affect is a mere by-product of positive expectations, but changes in negative affect can also be caused by a practitioner's emotional care. Such effects can be either beneficial (for example by being empathic) or detrimental (for example by acting in a rushed manner). Furthermore, a healthcare practitioner can be an important source of support when a person is confronted with an illness. The importance of social support and its relation to health outcomes is thoroughly established (Cacioppo 2003). Other examples of decreasing negative affect and/or increasing positive affect in patients is by increasing their trust (McKinstry 2006; Rosser 2001), hope (Clayton 2008; Schmid Mast 2005) and confidence (Thomas 1987), for instance by a practitioner's increased warmth (Kaptchuk 2008) or empathy (Fogarty 1999).

Apart from direct effects, cognitive and emotional care provided through communication can influence patients' health and quality of life outcomes by many mediating factors, including improvements in adherence to treatment plans (Robinson 2008), self-care, patient knowledge, patient understanding, patient empowerment, patient agency, the quality of medical decisions and emotional self-management, and attenuated negative social influences (Epstein 2007).

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Why it is important to do this review

Di Blasi 2001 reviewed the influence of contextual interventions related to the patient-practitioner relationship on patients' health outcomes. Other systematic reviews have sought studies in which the communication in the patient-practitioner relationship was manipulated, but their search or selection criteria were limited (Beck 2002; Stewart 1995) or their scope was narrower (Beck 2002; Crow 1999; Griffin 2004). Like Di Blasi 2001, Griffin 2004 concluded that there are few well-designed trials with communication-related contextual interventions. Di Blasi and colleagues' overall conclusion was that a warm, friendly, reassuring communication style showed the most consistent positive effect on patients' health outcomes. Griffin and colleagues found that interventions increasing patient participation, providing specific information about a disease and giving attention to emotion, showed the most promise in terms of promoting patients' health. However, most studies assessing the effects of manipulating practitioner-patient communication are very complex, or lack methodological rigor. Usually the trials do not specify the mechanisms through which communication influences outcomes. There is much heterogeneity in populations (such as setting, and patients' health problems) and the interaction with individual differences and demographic variables such as cultural context is unknown. In Di Blasi 2001 all of the 25 included studies were conducted in Europe and North America. We hope to identify relevant studies from other locations, in order to provide a more culturally-comprehensive review of how practitioner communication can influence patient outcomes.

Some studies (Ellington 2008; Fogarty 1999) have tried to tackle the complexity and ethical problems of researching the effects of varying communication, for instance by simulating a medical consultation by showing a video or using healthy subjects in a role-played medical situation. It is important to take such studies into account, because they allow a very high level of experimental control, and thus diminish the influence of confounding factors. Also, it might not be ethical to assign possibly vulnerable patients receiving actual medical care to, for instance, an unfriendly practitioner or practitioner raising negative outcome expectations. This is likely to be unpleasant for patients and might be detrimental to their health outcomes. However, the possibility that such 'negative' behaviours can have an effect on patient outcomes means they deserve further study. By using simulations it is possible to circumvent the ethical issues. Such simulations can indeed have an effect on some outcomes. A classic study using video simulation is Fogarty 1999 on breast cancer consultations. The same consultation was shown to all participants, but in the intervention group 40 seconds of empathic statements was incorporated in the healthcare practitioner's communication, resulting in significantly less anxiety amongst intervention group participants. Of course, the external validity of such studies has to be taken into account: it might be that in an actual clinical situation, patients will respond differently than in a simulation. However the added experimental control and the possibility of studying ethically-sensitive variations in communication through simulation studies might help this complex field to move forward.

We plan to conduct an extended follow up on Di Blasi 2001. The interventions in the 25 trials included in Di Blasi's review were targeted at cognitive care or a mix of cognitive and emotional care. No trials in which only emotional care was manipulated were found. Our review hopes to provide new knowledge about how patient-practitioner communication can be used to beneficially influence patients' health outcomes. A decade of communication research (both Di Blasi 2001 and Griffin 2004 searched up to 1999) is likely to have produced more well-designed trials assessing the effects of varying communication in the patient-practitioner relationship. The questions we want to answer in this review are:

1. What is the effect of varying communication in the patient-practitioner relationship on patients' health or health status?
2. Which kinds of communication interventions lead to changes in those outcomes?

OBJECTIVES

To assess the effects of interventions in which healthcare practitioner communication in face-to-face consultations with patients is experimentally varied in comparison to usual care or contrasted active control interventions, on patient health and treatment outcomes.

A secondary aim is to investigate if the intervention effect is modified by intervention type, type of illness, length of follow-up, type of outcome and the way the subjects are exposed to communication in studies (real versus simulated).

METHODS

Criteria for considering studies for this review

Types of studies

We will include randomised and quasi-randomised controlled trials.

We will exclude controlled before-and-after studies, interrupted time series studies, and all non-experimental studies, because of their higher risk of bias. We will not exclude studies on the basis of allocation concealment or blinding (Higgins 2008; Ryan 2007a).

Types of participants

Participants aged over 12 years involved in face-to-face communication with a healthcare practitioner (e.g. physician, nurse, allied staff).

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We will exclude studies of people with drug addiction, intellectual disability (people with a considerably lower than average intelligence combined with an inability to adapt to everyday life without help), or psychotic symptoms, because social functioning in these groups is probably markedly different than in other patient groups. We will also exclude studies in which participants use a translator to communicate with the healthcare practitioner, because the communication is influenced by the translator.

Types of interventions

Interventions in which face-to-face communication with a healthcare practitioner was manipulated. We will include simulation studies in which videos of patient-provider communication are shown to patients, or where healthy subjects were used instead of patients.
Intervention groups will be compared to usual care or other contrasted intervention groups (active control interventions).
We will exclude:

- interventions conducted via telephone, email or websites, as it is likely that such media change the dynamics of communication, for instance because many or all aspects of non-verbal communication are absent.
- interventions in which only biomedical treatment characteristics are varied, such as size and shape of medication.
- talking-therapy interventions such as psychotherapy, because in these the communication is the complete treatment rather than part of the context.

Types of outcome measures

Primary outcomes

Our primary outcome measures will be patients' physical and psychological health status, and treatment outcomes. The selected outcomes are described according to the Cochrane Consumers and Communication Review Group's taxonomy of relevant outcomes (Outcomes 2008). We will use the following subdivisions of this taxonomy to categorize outcomes: physical health, psychological health, psychosocial outcomes, adverse outcomes, clinical assessments, pain assessment or control and physiological measures.
We will exclude studies that do not report at least one of the primary outcomes. Any disagreement about whether or not study outcomes can be classified as primary outcomes for this review will be resolved by discussion among review authors.

Health Status

This outcome category includes:

- level of activities of daily living,
- level of dependency,
- self-care abilities,
- self efficacy,
- level of anxiety, depression, mood,
- well being,
- quality of life,
- self-esteem,
- level of confidence, and
- psychological or psycho-physiological stress.

Treatment Outcomes

This outcome category includes:

- complications,
- complication rate,
- need for medical intervention,
- morbidity,
- mortality,
- relapse,
- side effects of drugs,
- clinical assessments (e.g. wound healing, symptom resolution),
- pain assessment or control (e.g. use of medications or other means to reduce pain), and
- physiological measures (e.g. blood pressure, cell counts, blood glucose level).

Secondary outcomes

Secondary outcome measures will be all other reported consumer-oriented outcomes, for instance:

- adherence to treatment (self-reported adherence, refill rate),
- perceptions of coping,
- family functioning,
- social activity,
- recall of information.

Secondary outcomes do not form part of the criteria for including studies in this review. An extended list of these outcomes is available at Outcomes 2008 under the following subheadings: knowledge and understanding; communication; patient involvement in care process; evaluation of care, support; skills acquisition; health behavior.

Timing of outcome assessment

We will only include studies in which the first outcome assessment took place within one month after completion of the intervention, because effects of these interventions seem improbable after a longer period of time.

Search methods for identification of studies

Searching for relevant studies is challenging because of the absence of a common terminology for interventions in which communication in the patient-practitioner relationship is varied. Studies

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are scattered along different strains of research focused on mechanisms of the placebo effect, patient-provider communication and psychological variables in medical care, making it difficult to develop a search strategy that is sufficiently sensitive and precise.
Our search strategy is adapted from the search used by Di Blasi 2001. The rationale for the search strategy is described below. The PubMed 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 (derived from the standard PICO components: Participant or Population, Intervention, Comparison and Outcome): patients, the practitioner, communication, suggestion, patient-practitioner communication, relevant psychological constructs, the placebo effect, placebos and outcome assessment. We include sensitive filters to identify randomised controlled trials (Higgins 2008) and systematic reviews (Shojania 2001).

Electronic searches

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

- Consumers and Communication Review Group Specialised Register
- The Cochrane Central Register of Controlled Trials (CENTRAL, *The Cochrane Library*)
- EMBASE through Embase.com
- PubMed (incorporating MEDLINE and Old MEDLINE)
- PsycINFO
- CINAHL
- LILACS
- Controlled-trials.com
- ProQuest Dissertations & Theses (PQDT) database
- OpenSIGLE
- Sociological Abstracts

We will conduct a forward citation search in the following databases:

- Social Sciences Citation Index
- Sciences Citation Index

We will not restrict our searches in terms of the language in which studies are published or conducted, although the choice of electronic databases to be searched is a possible source of bias. We chose to search LILACS in order to find relevant Latin American and Caribbean reports. Search terms will be in English, which may be a source of bias if reports are not properly indexed with English search terms. We will take this into account in the discussion of possible bias in the review.

Searching other resources

We will seek relevant reviews and will examine all studies included in these reviews (backward search). We will also examine all studies citing these reviews (forward search), using the (Social) Sciences Citation Index. We will not conduct handsearches. Where possible we will contact authors of included studies to identify other potentially-relevant studies.

Data collection and analysis

Selection of studies

Given that we anticipate a large number of search results, all authors will be involved in the selection process, managed by WV and PM. Non-English language reports will be translated if necessary.

Phase 1

1.1 We will conduct the search for relevant reviews.
1.2 We will combine search results into a single database and remove duplicates.
1.3 We will screen titles and abstracts to remove obviously irrelevant reviews. Five per cent of the search output (up to 1000 items) will be screened by multiple authors to assess inter-rater reliability. If the percentage agreement is below 0.95, reasons for disagreement will be analysed and discussed to prevent further disagreement. This method is repeated until agreement above 0.95 is reached. Subsequently, titles and abstract will be screened by one rater per report (using multiple raters). Reviews of interest are reviews which potentially or actually include studies which meet the review's inclusion criteria (see also Appendix 2).
1.4 If all criteria are met or when it is unclear if all criteria are met, we will obtain the review in full text for further examination.
1.5 The reviews meeting all criteria form the set of reviews of interest.
1.6 We will add all studies referred to in these reviews to the database of potentially-eligible studies (backward search).
1.7 We will conduct a forward search for studies citing the relevant reviews, and add these studies to the database of potentially-eligible studies.

Phase 2

2 We will conduct the search for RCTs and quasi-RCTs.

Phase 3

3.1 We will combine the results from phases 1 and 2 into a RefWorks database and remove duplicate records.
3.2 We will screen the studies in the database against the review's inclusion criteria (see also Appendix 2). If all criteria are met or when it is unclear if all criteria are met, reports are included in the next stage of selection.

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3.3 We will retrieve potentially-relevant reports in full text and two authors will examine them independently for eligibility against the inclusion criteria (see also Appendix 3). In case of disagreement or doubt, a third author will arbitrate. If necessary information is missing we will contact the study authors to seek clarification.
3.4 We will scan the reference lists of included studies. Any possibly-relevant studies identified in this way are re-entered at step 3.1 and if not previously examined, screened on title and abstract and, if necessary, full text.
3.5 We will link multiple reports of the same study using all relevant information.
Studies excluded at any stage will be retained in a database. Any apparently relevant studies excluded on full text review will be listed in the table Characteristics of Excluded Studies in the review.

Data extraction and management

Using a data extraction form based on the Cochrane Consumers and Communication Review Group's data extraction template and the template used in Di Blasi 2001, we will extract the following information from included studies:

1. General information: title, authors, source, publication status, date published, language.
2. Study methods: aims of intervention, aim of study, study design, methods of participant recruitment, inclusion/exclusion criteria, informed consent and ethical approval, funding.
3. Risk of bias: see Assessment of risk of bias in included studies.
4. Patients: description, geographic location, setting, number, age, gender, ethnicity, socioeconomic status distribution, principal health problem or diagnosis, stage of illness, treatment received.
5. Providers: description (GP, specialist physician, nurse, physical therapist, etc), geographic location, setting, age, gender.
6. Interventions: description (which communication aspects are varied), frequency, timing, duration, purpose, initiator, details of control/usual or routine care, co-interventions.
7. Outcomes: principal and secondary outcomes as specified, methods of assessing outcomes, follow up for non-respondents, timing of outcome assessment, adverse events.
8. Results: for outcomes and times of assessment, control and intervention groups.

Two review authors will independently extract full descriptions of the interventions onto a standard form. The standard forms will then be checked by a third review author for discrepancies. If discrepancies between the two review authors' data extraction exist, then those will be discussed by the data extractors and other review authors until discrepancies are resolved. In the case of missing data, we will try to contact the authors of the studies to obtain the information.

Assessment of risk of bias in included studies

We will assess and report on the risk of bias in included studies in accordance with the guidelines of the Cochrane Consumers and Communication Review Group (Ryan 2007) and the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2008).
We will assess sequence generation, allocation concealment, blinding of participants, providers and outcome assessors, incomplete outcome data, selective outcome reporting and other sources of bias for RCTs and quasi-RCTs (Higgins 2008).
Two review authors will asses the risk of bias independently. Disagreements will be resolved in a team discussion. We will use a scoring sheet to assess bias and categorize studies for described sources of bias as having a low risk of bias, a high risk of bias or an uncertain risk of bias in the following categories: selection bias, performance bias, attrition bias, detection bias and other sources of bias (Ryan 2007). These forms of bias in the included studies will be assessed using the checklist provided by the Cochrane Consumers and Communication Review Group (Ryan 2007). We will contact study authors if necessary to obtain missing information. The risk of bias information will be in tables in the review. We will not provide overall quality scores to divide studies in into high and low quality (Herbison 2006). Instead we will address risk of bias by sensitivity analysis.

Measures of treatment effect

We will report standardised mean differences (SMDs) for continuous outcomes and risk ratios (RR) for dichotomous outcomes (Deeks 2001).

Unit of analysis issues

For cluster-randomised trials, repeated measurements or studies with more than two intervention groups, we will appropriately handle any unit-of-analysis issues, adhering to guidelines in Higgins 2008 if possible. More specifically, we will extract effect sizes from cluster-randomised trials if the analysis accounted for clustering. If not or if it is unclear, we will consult a statistician. For repeated measurements, we will use the measurement closest to the intervention to maximize available data (in studies in Di Blasi 2001 measurement often took place directly after the intervention; see also Subgroup analysis and investigation of heterogeneity).

Dealing with missing data

Where data are missing, we will try to obtain these data from study authors. The number screened, eligible and randomised patients will be examined. When outcome data are missing, for instance because of drop-outs, losses to follow-up and participant withdrawal, we will assess the risk of bias in accordance with Ryan 2007 and Higgins 2008. The numbers as well as the reasons for incomplete data will be reported. To this end, we will contact study authors if necessary.

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Assessment of heterogeneity

If clinical, methodological or statistical heterogeneity is large, we will not combine study results in quantitative meta-analysis. We will assess heterogeneity by inspection of the forest plots. Heterogeneity will be quantified using I^2 and interpreted according to Higgins 2008. Subgroup analyses will be undertaken to investigate heterogeneity, as outlined in Subgroup analysis and investigation of heterogeneity below.

Assessment of reporting biases

We will use funnel plots to assess reporting biases. Funnel plot asymmetry will be tested statistically when 10 or more studies with a continuous outcome or 10 or more studies with a dichotomous outcome are included (Higgins 2008). We will use a test based on linear regression of intervention effect estimates for continuous outcomes (Tang 2000) and dichotomous outcomes (Peters 2006). If funnel plot asymmetry exists, we will discuss its possible causes (Higgins 2008).

Data synthesis

We will provide a narrative overview of the included studies, structured according to similarity of interventions. We will list the exact communication behaviours which are varied. We will describe interventions as aimed at cognitive or emotional care, analogue or real patients, and provide the sample characteristics (also see Subgroup analysis and investigation of heterogeneity). Sample characteristics that will be used to structure the reporting of interventions, but are not mentioned under subgroup analysis, are variations in the gender and age of subjects or practitioners and the type of practitioner. Gender and age influences how patients and practitioners communicate, as well as how they perceive each other's communication (DeVoe 2009; Roter 2002). Types of healthcare practitioner can differ in communication style, available time for communication, and perceived status. This might impact the effects of interventions: for example, nurses generally have more time per patient compared to physicians. We will also address type of practitioner, because interventions seem to include physicians more often than other types of practitioners. We will also describe possible working mechanisms (expectancy manipulation, conditioning, affect manipulation; see Background). We will report the direction, size, consistency, strength of evidence of the effects of interventions and possible effect modifiers in included studies in tables. We will use graphs and box plots where we deem those will improve clarity of presentation.

The decision whether to perform a quantitative meta-analysis will be made after completion of the search, selection and extraction process. This decision will be based on homogeneity/heterogeneity of interventions and outcomes in the included studies. If a quantitative meta-analysis is undertaken, we will pool SMDs for continuous outcomes and RRs for dichotomous outcomes using random effect meta-analysis. In both cases we will report confidence intervals. Statistical analysis will be performed according to the Cochrane Handbook (Higgins 2008) using Review Manager 5 software.

Subgroup analysis and investigation of heterogeneity

If there are at least two trials from each subgroup, we will examine subgroups according to type. We will not analyse subsets of participants within studies because reports of studies seldom contain sufficient detail (Higgins 2008). Hence when more than one subgroup type is included in the study, we will not include it in the subgroup analysis. We will draw a distinction between 'qualitative interaction' (differences in the direction of the effect) and 'quantitative interaction' (differences in the size of the effect but not the direction) (Higgins 2008; Yusuf 1991). The subgroup analyses will be carried out with a random effects meta-regression model using the 'Metareg' macro with Stata. We will use P values of regression coefficients of dummy variables indicating subgroup to determine if statistically significant differences between subgroups exist. If significant effects exist, the regression coefficients will be used to investigate how the subgroups potentially affect the intervention estimate (Higgins 2008).

We will conduct the following subgroup analyses:

- Interventions targeting subjects' emotions, cognitions or both, since these may set off different mechanisms (see Background).
- The type of illness: patient's illness might enhance or limit the effectiveness of communication interventions. For example, non-specific low back pain might be more easily influenced than cancer-related pain, and acute irritable bowels might be more easily influenced than chronic irritable bowel syndrome (Harrington 1999). We will thus differentiate types of illness on both the specific illness and its chronicity. We will identify groups based on the International Statistical Classification of Diseases and Related Health Problems (WHO 2007). We will include a mixed group for mixed populations (e.g. patients in general practice). If information about duration is reported, we will differentiate between acute and chronic illnesses. We define an illness as chronic if the duration is equal or greater than six months.
- Studies of real versus simulated communication between patient and practitioner (see Background).
- Subgroup analysis for different outcomes: certain outcomes might be more easily influenced than others. For example, placebo effects on pain have been quite extensively documented, but influences on such outcomes as wound healing seem much less likely (Harrington 1999). Categorisation of outcomes will occur using the Cochrane Consumers and Communication Review Group's taxonomy of relevant outcomes (Outcomes 2008), in which the following subdivisions are made: physical health, psychological health, psychosocial outcomes, adverse

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outcomes, clinical assessments, pain assessment or control and physiological measures.

- We will also take into account differences in interval between intervention and outcome assessment. It is possible that many communication interventions have an effect which is diluted by other variables influencing the patient in everyday life. We will group studies measuring outcomes directly after the intervention (within one hour), more than 1 hour but within 24 hours after the intervention and more than 24 hours after the intervention. In case of repeated observations for several periods of follow up, we will perform separate analyses for outcomes measured at different times (Higgins 2008).

Other subgroups are of interest, but we are cautious about performing more subgroup analyses, as finding from multiple subgroups might be misleading (Higgins 2008). Subgroup analyses are observational by nature and are not based on randomised comparisons. The likelihood of false negative and false positive significance tests increases rapidly as more subgroup analyses are performed. We will therefore not perform more subgroup analyses, but we will present and discuss other subgroup characteristics in included studies without performing tests as described under Data synthesis. We will take care not to generate misleading recommendations by addressing possible misinterpretations of subgroup results.

Sensitivity analysis

If possible from the data sets, we will conduct multiple sensitivity analyses across the seven domains of risk of bias in which we will exclude studies with inadequate sequence generation, allocation concealment, blinding of participants, providers and outcome assessors, incomplete outcome data, selective outcome reporting or other sources of bias for RCTs and quasi-RCTs (see Assessment of risk of bias in included studies). We will perform separate sensitivity analyses excluding studies with high risk on a certain domain of risk of bias and we will also perform a sensitivity analysis that includes only trials deemed to be at a low or unclear risk of bias across the seven domains. During the review process individual peculiarities of the studies under investigation might be identified as suitable for sensitivity analysis, if so, we will carry out extra sensitivity analysis.

Consumer participation

We will report on the involvement of consumers in the design and implementation of each included study. The review protocol was discussed with four consumers (two patients and two practitioners) and their feedback was implemented in the final version of this protocol. These consumers were asked to pay attention to the applicability of interventions in clinical practice, both in a practical and an ethical sense. We intend to do so again in the discussion of the results. We will present our results to a consumer panel (consisting of both patients and practitioners who will be recruited after a first draft of the review is ready) in order to receive feedback for implementation of interventions or development of new interventions. As reported in several studies, patient-practitioner communication is a pivotal element of medical care for consumers. The results of this review could be used by consumers to inform themselves about the most adequate communication styles in medical care and use this as a measure of comparison for their care. Consumer organisations could use the review's findings to lobby for more attention to proper patient-practitioner communication as an element of care not only influencing patient satisfaction, but also health status.

Dissemination plans

In addition to publication in the *Cochrane Database of Systematic Reviews,* we aim to publish the review in a leading peer-reviewed medical journal. The review will also be published within the contact author's PhD thesis. We aim to present the findings of the proposed review at conferences and meetings for medical professionals, researchers and consumers. We also aim to publish a translation of the review in a Dutch medical journal.

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* *Indicates the major publication for the study*

APPENDICES

Appendix 1. PubMed search strategy

Medline AND Old-Medline through PubMed
#1. PATIENTS
(patient[MeSH] OR patient OR patients OR subject OR subjects OR participant* OR client* OR inpatient* OR outpatient* OR hospitalized* OR institutionalized* OR survivor*)

#2. PROVIDERS
(health personnel[MeSH] OR doctor* OR physician* OR provider* OR practitioner* OR gp OR gps OR health professional*OR nurse* OR carer* OR caregiver* OR clinician* OR health care professional* OR healthcare professional* OR health care worker* OR dentist* OR anaesthetist* OR anesthetist* OR midwi* OR hospitalist* NOT (veterinarian*))
#3. COMMUNICATION
(communication[MeSH] OR interact* OR communicat* OR relation* OR instruct* OR verbal* OR nonverbal OR smiling OR "facial expression" OR advis* OR Counsel* OR talk* OR contact* OR conversation* OR consult OR consultation)

#4. SUGGESTION
(suggestion[MeSH] OR suggest* OR frame* OR framing* OR label*)

#5. PATIENT-PROVIDER INTERACTION
("Professional-Patient Relations"[MeSH] OR "Patient-Centered Care"[MeSH] OR "Physician's Role"[MeSH] OR "nurse's role"[MeSH] OR "Professional Patient" OR "patient professional" OR therapeutic alliance OR "doctor-patient" OR "patient-doctor" OR "clinician-patient" OR "patient-clinician" OR "physician-patient" OR "patient-physician" OR "nurse-patient" OR "patient-nurse" OR "patient-practitioner" OR "practitioner-patient" OR patient-centered OR patient-centred OR patient-focused OR patient-focussed OR person-centered OR person-centred OR biopsychosocial*)

#6. RELEVANT PSYCHOLOGICAL CONSTRUCTS
("set (psychology)"[MeSH] OR "self concept"[MesH] OR anticipat* OR hope* OR expectanc* OR expectation* OR expect OR expected OR faith* OR wish* OR desir* OR (doubt* OR disbelie* OR mistrust* OR skeptic* OR sceptic* OR (attitude* AND (positive OR negative)) OR belief*[tiab] OR empath* OR compassion* OR warm OR warmly OR warmth OR friendly OR enthusias* OR humanistic OR attentive*) OR (trust* NOT (nhs*trust[tiab] OR service*trust[tiab] OR hospital*trust[tiab] OR research*trust[tiab] OR welcome?trust[tiab] OR centre?trust[tiab] OR heritage*trust[tiab] OR teaching*trust[tiab] OR community*trust[tiab] OR uni-

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versity*trust[tiab] OR healthcare*trust[tiab] OR trust*fund[tiab] OR trustees[tiab] OR health*trust[tiab] OR wellcome*trust[tiab] OR trust*headquarters[tiab] OR health*care*trust[tiab])) OR "anxiety"[MeSH] OR fear* OR "anxiety"[all fields] OR "anxious"[All Fields] OR stress[tiab] OR stressed OR negative-affect OR positive-affect OR relax* OR "conditioning (psychology)"[MeSH] OR conditioning OR conditioned)
#7. PLACEBO EFFECT
(Placebo effect[MeSH] OR context-action*[All Fields] OR contextual-action*[All Fields] OR context-effect*[All Fields] OR contextual-effect*[All Fields] OR context-influence*[All Fields] OR contextual-influence*[All Fields] OR context-intervention*[All Fields] OR contextual-intervention*[All Fields] OR context-response*[All Fields] OR contextual-response*[All Fields] OR context-result*[All Fields] OR contextual-result*[All Fields] OR nocebo-action*[All Fields] OR nocebo-effect*[All Fields] OR nocebo-influence*[All Fields] OR nocebo-intervention*[All Fields] OR nocebo-response*[All Fields] OR nocebo-result*[All Fields] OR non-drug-action*[All Fields] OR non-drug-effect*[All Fields] OR non-drug-influence*[All Fields] OR non-drug-intervention*[All Fields] OR non-drug-response*[All Fields] OR non-drug-result*[All Fields] OR nonpharmacological-action*[All Fields] OR non-pharmacological-action*[All Fields] OR nonpharmacological-effect*[All Fields] OR non-pharmacological-effect*[All Fields] OR nonpharmacological-influence*[All Fields] OR non-pharmacological-influence*[All Fields] OR nonpharmacological-intervention*[All Fields] OR non-pharmacological-intervention*[All Fields] OR nonpharmacological-response*[All Fields] OR non-pharmacological-response*[All Fields] OR nonpharmacological-result*[All Fields] OR non-pharmacological-result*[All Fields] OR nonspecific-action*[All Fields] OR non-specific-action*[All Fields] OR nonspecific-effect*[All Fields] OR non-specific-effect*[All Fields] OR nonspecific-influence*[All Fields] OR non-specific-influence*[All Fields] OR nonspecific-intervention*[All Fields] OR non-specific-intervention*[All Fields] OR nonspecific-response*[All Fields] OR non-specific-response*[All Fields] OR nonspecific-result*[All Fields] OR non-specific-result*[All Fields] OR placebo-action*[All Fields] OR placebo-effect*[All Fields] OR placebo-influence*[All Fields] OR placebo-intervention*[All Fields] OR placebo-response*[All Fields] OR placebo-result*[All Fields] OR situational-action*[All Fields] OR situational-effect*[All Fields] OR situational-influence*[All Fields] OR situational-intervention*[All Fields] OR situational-response*[All Fields] OR situational-result*[All Fields])

#8. PLACEBOS
(Placebos[MeSH] OR placebo effect[MeSH] OR placebo* OR nocebo)

#9. OUTCOME ASSESMENT
("Outcome AND Process Assessment (Health Care)"[MeSH])

#10. FILTER FOR IDENTIFYING RANDOMIZED CONTROLLED TRIALS
(randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR drug therapy [sh] OR randomly [tiab] OR trial [tiab] OR groups [tiab]) NOT (animals[mh] NOT (animals[mh] AND humans [mh]))

#11. SYSTEMATIC REVIEW FILTER
((meta-analysis [pt] OR meta-analysis [tw] OR metanalysis [tw]) OR ((review [pt] OR guideline [pt] OR consensus [ti] OR guideline* [ti] OR literature [ti] OR overview [ti] OR review [ti]) AND ((Cochrane [tw] OR Medline [tw] OR CINAHL [tw] OR (National [tw] AND Library [tw])) OR (handsearch* [tw] OR search* [tw] OR searching [tw]) AND (hand [tw] OR manual [tw] OR electronic [tw] OR bibliographi* [tw] OR database* OR (Cochrane [tw] OR Medline [tw] OR CINAHL [tw] OR (National [tw] AND Library [tw])))))) OR ((synthesis [ti] OR overview [ti] OR review [ti] OR survey [ti]) AND (systematic [ti] OR critical [ti] OR methodologic [ti] OR quantitative [ti] OR qualitative [ti] OR literature [ti] OR evidence [ti] OR evidence-based [ti])))) BUTNOT (case* [ti] OR report [ti] OR editorial [pt] OR comment [pt] OR letter [pt])

Search A:Studies on Patient-provider interaction (5) involving suggestion (4), relevant psychological constructs (6), placebo effects (7), placebos (8), OR outcome assessment (9).
#12 Combined as: ((#5 OR (1 AND 2 AND 3)) AND (#4 OR #6 OR #7 OR #8 OR #9)).

Search B:Studies on suggestive communication (4) in a clinical setting (1 AND 2) involving relevant psychological constructs (6).
#13 Combined as: (#1 AND #2 AND #4 AND #6).

Search C:Studies on Placebo effect(7) involving relevant psychological concepts(6) OR suggestion(4)
#14 Combined as: (#7 AND (#4 OR #6)).

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COMPLETE SEARCH for REVIEWS: (#12 OR #13 OR #14) AND #11

COMPLETE SEARCH for RCTs: (#12 OR #13 OR #14) AND #10

Appendix 2. Form for screening study reports on title and abstract

1. Reviewed by:	WV ZDB JB SvD PM LK
2. Full reference:	
3. Criteria:	
I. Communication in the patient-practitioner interaction is varied	No Not sure Yes
II. Study is a randomized controlled trial or a quasi randomized trial	No Not sure Yes
III. Study conducted on not mentally disabled, non psychiatric, non drug addict sample, age > 12 years	No Not sure Yes
IV. Outcome is physical, psychological or psychosocial health status or treatment outcome	No Not sure Yes
4. Recommendations:	
I. If any of the boxes are ticked 'No':	Exclude
II. If all boxes are ticked 'Not sure' OR Yes':	Preliminary include
Note: If you tick any of the criteria as 'No', do not continue to check the other criteria: exclude and move on to the next title & abstract	
Help: *I. There is a face-to-face communication between a patient and practitioners and this communication is varied. Not psychotherapy* *II. There is a control or comparison group and subjects are randomly or quasi randomly allocated to intervention or control/comparison groups* *IV. See outcome list for specified outcomes*	

Appendix 3. Form for screening full text reports of studies

1. Reviewed by:	WV ZDB JB SvD PM LK
2. Full reference:	
3. Criteria:	

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(*Continued*)

I. Communication in the patient-practitioner interaction is varied	No Not sure Yes
II. Study is a randomized controlled trial or a quasi randomized trial	No Not sure Yes
III. Study conducted on not mentally disabled, non psychiatric, non drug addict sample, age > 12 years	No Not sure Yes
IV. Outcome is physical, psychological or psychosocial health status or treatment outcome	No Not sure Yes
4. Recommendations:	
I. If any of the boxes are ticked 'No':	Exclude
II. If any of the boxes are ticked 'Not sure':	Discuss (AND/OR) Request info from study authors
III. If all boxes are ticked Yes':	Include
Summary and outcome of review authors' discussion:	
Additional information request to study authors study authors:	

HISTORY

Protocol first published: Issue 10, 2010

CONTRIBUTIONS OF AUTHORS

JB and WV conceived the idea for this review. WV wrote a first draft of the protocol. ZDB contributed by providing ideas, comments and documents of her earlier review. WV and PM developed the search strategies, which were reviewed by all other authors. PM, JB, ZDB, SvD & LK all commented on drafts of the protocol. WV wrote the final version which was approved by all co-authors.

DECLARATIONS OF INTEREST

WV, JB and SvD have been involved in the design, conduct or publication of potentially eligible studies for this Cochrane review. These authors will not be involved in the assessment of these studies for inclusion in the review, nor in their data extraction if they are included.

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