

Influence of context effects on health outcomes: a systematic review

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Summary

Background Throughout history, doctor–patient relationships have been acknowledged as having an important therapeutic effect, irrespective of any prescribed drug or treatment. We did a systematic review to determine whether there was any empirical evidence to support this theory.

Methods A comprehensive search strategy was developed to include 11 medical, psychological, and sociological electronic databases. The quality of eligible trials was objectively assessed by two reviewers, and the type of non-treatment care given in each trial was categorised as cognitive or emotional. Cognitive care aims to influence patients' expectations about the illness or the treatment, whereas emotional care refers to the style of the consultation (eg, warm, empathic), and aims to reduce negative feelings such as anxiety and fear.

Findings We identified 25 eligible randomised controlled trials. 19 examined the effects of influencing patients' expectations about treatment, half of which found significant effects. None of the studies examined the effects of emotional care alone, but four trials assessed a combination of both cognitive and emotional care. Three of these studies showed that enhancing patients' expectations through positive information about the treatment or the illness, while providing support or reassurance, significantly influenced health outcomes.

Interpretation There is much inconsistency regarding emotional and cognitive care, although one relatively consistent finding is that physicians who adopt a warm, friendly, and reassuring manner are more effective than those who keep consultations formal and do not offer reassurance.

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Introduction

As long ago as 400 BC, Hippocrates wrote of how “the patient, though conscious that his condition is perilous, may recover his health simply through his contentment with the goodness of the physician”.¹ Balint added that what mattered was “not only the medicine . . . or the pills . . . but the way the doctor gave them to the patient—in fact the whole atmosphere in which the drug was given”.² Although many have suggested that good doctor–patient relationships can have a therapeutic effect irrespective of any specific treatments provided by the practitioner, the extent to which this assumption is based on rigorous empirical evidence is not known. This lack of evidence is possibly a result of the focus of clinical research on the assessment of surgical and pharmacological interventions, and little emphasis on the effects of human care or “bedside manner” on health outcomes.

Nowadays, the influence of patients' expectations and the power of suggestion tend to be controlled for rather than investigated, and when noted, these effects are discounted as “non-specific” or “placebo” effects.³ However, given the proportion of patients who get better after receiving placebos,⁴ such effects are potentially of great value, and investigation of their healing properties is a worthwhile undertaking. In 1994, a series of articles^{5–7} and a review⁸ in *The Lancet* highlighted various aspects of the placebo effect, outlining how non-specific or “context” factors such as the method of treatment delivery interact with specific therapies (figure 1).

A systematic review by Turner and colleagues on pain and the placebo effect concluded that “The quality of the interaction between physician and patient can be extremely influential in patient outcomes, and . . . patient and provider expectations may be more important than specific treatment”.⁴ Effects originating from health-care interactions include factors common to all medical, alternative, and psychological therapies—eg, attention, bedside manner, empathy, positive regard, compassion, hope, and enthusiasm.⁹ Although a great deal of research has assessed the effects of training in communication skills,¹⁰ these

Treatment characteristics
(eg, colour, size, shape of drug)

Patient's characteristics
(eg, treatment and illness beliefs, anxiety, adherence)

Patient–practitioner relationship
(eg, suggestion, reassurance, compassion)

Health-care setting
(eg, home or hospital, room layout)

Practitioner's characteristics
(eg, status, sex, treatment, and illness beliefs)

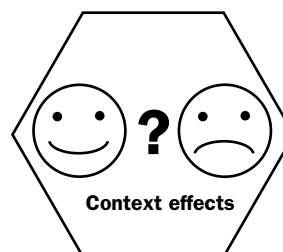


Figure 1: Factors that determine placebo or context effects

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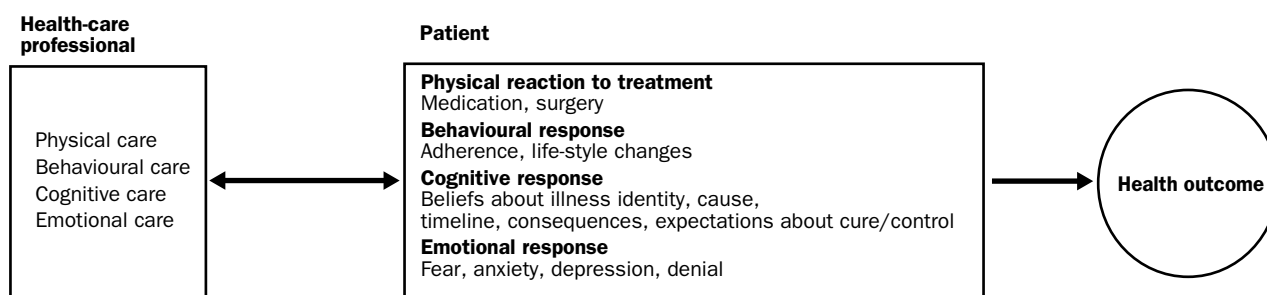


Figure 2: **Healing and the biopsychosocial consultation**

studies do little to highlight the mechanisms by which health professionals can influence patients' health. Interventions tend to be complex, and researchers have little control over what occurs during consultations. Establishment of any cause–effect relation between components of the intervention and changes in the physiological state of the patient is therefore difficult. To understand how health practitioners can influence disease processes it is important to examine pathways and possible mechanisms by focusing on context interventions.

A useful framework to understand how these factors may influence healing is Leventhal's self-regulatory theory.¹¹ This model suggests that when threatened by signs and symptoms of illness, individuals respond with cognitive and emotional reactions. For example, sudden pain may cause an individual to feel anxious and to try to make sense of the situation by thinking about what it might be, what caused it, whether it is curable, what the consequences could be, and how long these symptoms might last. In consultations, health professionals can be instrumental in shaping the way patients think and feel about their illness or their treatment, through the information and reassurance they provide. Alongside the use of appropriate diagnostic tests and treatment such as medication and surgery (physical care) and advice to practise a healthier lifestyle (behavioural care), practitioners can thus practise cognitive and emotional care as well (figure 2).

Cognitive care describes the ways by which practitioners can influence patients' beliefs about the effects of treatment or about the illness—eg, by giving a label to the condition or by giving a positive prognosis. Patients' expectations about a treatment can be made positive if they are told to expect the therapy to be “good”, “safe”, and “effective”; or negatively, if they are informed that the therapy they are about to receive is “dangerous”, “unsafe”, “ineffective”, “limited”, or has “potential side-effects”. Expectations can also be kept neutral, by withholding information or by giving unrelated information about the effects of a specific therapy. The term “emotional care” is used to refer to ways through which health professionals can lower unhelpful emotions such as fear or anxiety by providing support, empathy, reassurance, and warmth. Emotional and cognitive care are expected to work in an interactive manner, and to enhance substantially the effectiveness of therapy or physical care.

Some reviewers argue that the therapeutic influence of expectations and health-care interactions is real and powerful,¹² whereas others feel that this effect is simply the result of methodological bias.¹³ Such debates are understandable given the conceptual and operational difficulties associated with the term “placebo effect”.¹⁴ In this study, we use the neutral and broader term

“context effects” to refer to placebo effects deriving from patient–practitioner relationships. Since the assessment of therapeutic efficacy is best done by summarising evidence from randomised controlled trials, we did a systematic review of all such trials of the effects of patient–practitioner relationships on patients' health outcomes.

Methods

We designed comprehensive search strategies for a large number of medical, psychological, and sociological electronic databases (MEDLINE, Cochrane Controlled Trials Register, Cinahl, PsycLIT, Amed, Sociofile, Social Science Citation Index, Science Citation Index, EMBASE, SIGLE, and Dissertation Abstracts). These strategies are available from the authors. For MEDLINE alone, 183 search terms were used. These terms were related to the characteristics of practitioners, the patient–practitioner relationship, and placebo effects. In addition, we made requests from an internet discussion list (Evidence-Based-Health) and contacted experts in the field.

We included all randomised controlled trials in which at least one treatment was a contextual intervention related to the patient–practitioner relationship in a clinical population with a physical illness. We excluded studies examining contextual factors related to treatment characteristics (eg, size and shape of medication) and identified psychological interventions or those with a theoretical base such as psychotherapy, counselling, health education (including communication training), or interventions directed at drug addicts, psychiatric patients, or healthy volunteers.

Data were extracted by use of National Health Service Centre for Reviews and Dissemination Guidance¹⁵ and a standard data extraction sheet to assess the quality of clinical trials.⁸ Trials scoring 8·0–10·0 points were rated as very good, 7·0–7·9 as good, 5·0–6·9 as acceptable, and less than 5·0 as poor. To determine internal validity, the checklist also assessed the method of randomisation concealment, comparability of groups at baseline, masking, completeness of follow-ups, and intention-to-treat analysis.

Data were extracted and cross-checked by two assessors (ZDB and EH). Quality assessment was used for descriptive purposes and for underpinning recommendations for improving the quality of further research.

Our primary outcome measures were objective or subjective health status. Secondary outcome measures were health-service use, adherence to treatment, satisfaction with care, anxiety, treatment expectations, understanding of illness, and quality of patient–practitioner relationships.

Studies and context interventions	Country	Number of patients	Disorder
Cognitive care and diagnosis*			
Thomas, 1978 ¹⁹	UK	200	Ambiguous symptoms
Thomas, 1987 ¹⁷	UK	200	Ambiguous symptoms
Van Weel, 1985 ²⁸	Netherlands	124	Hypertension
Linden, 1989 ²⁷	Canada	60	Hypertension
Amigo, 1989 ²⁶	Spain	114	Hypertension
Rose, 1993 ²⁰	USA	51	Chest pain
Cognitive care and treatment†			
Butler, 1986 ³⁸	UK	12	Asthma
Luparello, 1970 ²¹	USA	20	Asthma
Neild, 1987 ³⁵	UK	25	Asthma
Agras, 1982 ²⁹	USA	30	Hypertension
Cooper, 1983 (study A) ²⁵	UK	570	Hypertension
Cooper, 1983 (study B) ²⁵	UK	342	Hypertension
Cooper, 1983 (study C) ²⁵	UK	558	Hypertension
Kaldor, 1973 ²⁶	Hungary	21	Hypertension
Dahan, 1986 ²²	France	60	Insomnia
Bergmann, 1994 ³⁰	France/UK	43	Cancer pain
Berk, 1977 ²³	USA	42	Shoulder pain
de Craen, 1998 ²⁴	Netherlands	112	Chronic pain
Gryll, 1978 ³³	USA	160	Dental pain
Kincheloe, 1991 ³⁴	USA	77	Dental pain
Wied, 1953 ¹⁸	Germany	120	Menopause
Freund, 1972 ³²	USA	64	Obesity
Lamb, 1994 ²¹	USA	53	Side-effects
O'Connor, 1996 ³⁷	Canada	292	Side-effects
Thomas, 1987 ¹⁷	UK	200	Ambiguous symptoms
Emotional care‡			
..
Positive consultations§			
Berk, 1977 ²³	USA	42	Shoulder pain
Gryll, 1978 ³³	USA	160	Dental pain
Olsson, 1989 ¹⁶	Sweden	100	Tonsillitis
Thomas, 1987 ¹⁷	UK	200	Ambiguous symptoms

*Patients with similar symptoms randomised to different diagnoses (eg, “hypertensive” or “normal BP”)²⁸ or to different suggestions about diagnostic testing (eg, “BP is higher when measured a second time” or “BP is lower when measured a second time, as people are more relaxed”).²⁶ †Patients with similar symptoms randomised to different suggestions regarding the effects of treatment (eg, “this will constrict your breathing” or “this will help your breathing”).³¹ ‡Style of consultation (eg, use of empathy, compassion). §Increasing treatment expectations^{22,33} or giving a positive prognosis.^{16,17} while being warm and friendly^{16,23,33} or confident and reassuring.¹⁷

Table 1: Overview of randomised controlled trials

Results

Data collection

The hit rate from electronic searches was 23 645, of which 624 were selected as potentially relevant to the review. 25 trials, with a total of 3611 patients, met our inclusion criteria.^{16–38}

Only 12 of the 25 studies presented enough information for a potential meta-analysis. Interventions in the eight trials with dichotomous outcomes were very different: they examined the effects of positive consultations,^{16,17} enhancing treatment expectations,¹⁸ giving a clear diagnosis and treatment,^{17,19} and presenting information about the side effects of treatment or of diagnostic tests.^{20–22} Outcomes were similar but recorded at different time-points—eg, “got better” at 1 month,¹⁹ 2 weeks,¹⁷ or 2 days.¹⁶ Since the level of heterogeneity was so high, the data were summarised qualitatively.

Of the 25 studies identified, 15 were done in Europe (mostly the UK) and ten were from the USA and Canada (table 1). The most frequently investigated clinical disorders were hypertension (n=8) and pain (n=6). None of the studies included an economic evaluation. 12 trials found patient–practitioner interactions to have a significant influence on health outcomes. Only two trials measured the quality of patient–practitioner relationships.^{17,23}

Five trials were rated as very good, six as good, ten as acceptable, and four as poor (table 2). More than half had fewer than 50 patients per group, the

Studies and quality	Quality score										
	A	B	C	D	E	F	G	H	I	J	Total
Very good											
de Craen ²⁴	1-0	1-0	1-0	1-0	1-0	1-0	0-5	1-0	1-0	1-0	9-5
Cooper B ²⁵	1-0	1-0	0	1-0	1-0	1-0	0-5	1-0	1-0	0-5	8-0
Cooper C ²⁵	1-0	1-0	0	1-0	1-0	1-0	0-5	1-0	1-0	0-5	8-0
Olsson ¹⁶	0	1-0	1-0	0-5	1-0	1-0	0-5	1-0	1-0	1-0	8-0
Rose ²⁰	1-0	0	1-0	0-5	1-0	1-0	0-5	1-0	1-0	1-0	8-0
Good											
Agras ²⁹	0	0	1-0	1-0	1-0	1-0	0-5	1-0	1-0	1-0	7-5
Bergmann ³⁰	0-5	0	1-0	1-0	0	1-0	1-0	1-0	1-0	1-0	7-5
O'Connor ³⁷	1-0	1-0	0	1-0	0-5	1-0	0-5	1-0	0-5	1-0	7-5
Cooper A ²⁵	1-0	1-0	0	1-0	0	1-0	0-5	1-0	1-0	0-5	7-0
Lamb ²¹	0-5	1-0	0	1-0	1-0	1-0	0-5	1-0	0	1-0	7-0
Luparello ²¹	1-0	0	1-0	0	1-0	1-0	1-0	1-0	1-0	0	7-0
Acceptable											
Thomas ¹⁹	0-5	1-0	0	0	1-0	0-5	0-5	1-0	1-0	1-0	6-5
Thomas ¹⁷	0-5	1-0	0	0-5	1-0	1-0	0-5	1-0	0	1-0	6-5
Amigo ²⁶	0	0	0	0-5	1-0	0-5	0-5	1-0	1-0	1-0	6-0
Gryll ³³	1-0	0	0	0	1-0	1-0	0-5	1-0	1-0	0-5	6-0
Linden ²⁷	0-5	0	0	0	1-0	1-0	0-5	1-0	1-0	1-0	6-0
Berk ²³	1-0	0	0	0	1-0	1-0	0-5	1-0	1-0	0	5-5
Kincheloe ³⁴	0-5	0	0	0	1-0	1-0	1-0	1-0	1-0	0	5-5
Neild ³⁵	0-5	0	0	0	1-0	1-0	1-0	1-0	1-0	0	5-5
Dahan ²²	1-0	0	0	1-0	0	1-0	0-5	1-0	0	1-0	5-5
Freund ³²	1-0	0	0	0	0-5	1-0	1-0	1-0	0	0-5	5-0
Poor											
Butler ³⁸	1-0	0	0	0-5	0	1-0	0-5	1-0	0	0	4-0
Van Weel ²⁸	1-0	1-0	0	0	0	0-5	0-5	1-0	0	0	4-0
Kaldor ²⁶	0	0	0	0	1-0	1-0	0-5	0	1-0	0	3-5
Wied ¹⁸	0	0	0	0	1-0	0-5	0	0	1-0	1-0	3-5

A=Well described inclusion criteria (diagnostic criteria, duration and severity of disease, previous treatment); B=At least 50 patients per group; C=Random allocation procedure described; D=Presentation of relevant baseline characteristics; E=Less than 10% dropouts and dropouts described; F=Interventions well described (nature, number, duration of treatments); G=Double-blinding; H=Effect of measurement relevant and well described; I=Intention-to-treat analysis; J=Presentation of results in such a manner that analysis can be checked. 1-0=yes; 0=no; 0-5=description was unclear or only some of several interventions, measurements of outcome, or data presentations met our requirements.

Table 2: Methodological assessment of studies reviewed

randomisation procedure was commonly not described, and baseline characteristics were often not defined. Many authors also failed to discuss whether patients dropped out of the trial and whether results were assessed by intention to treat.

Cognitive care and diagnosis

Six trials examined the effects of giving different diagnoses to patients presenting with similar symptoms^{17,19,28} or giving patients different information about diagnostic testing.^{20,26,27}

Thomas investigated the effects of giving a clear diagnosis to patients presenting with ambiguous symptoms such as a cough or fatigue in two trials.^{17,19} In his earlier trial,¹⁹ he found that patients who received a diagnosis and an active treatment did not feel different at 1 month from patients who had not received either a diagnosis or a treatment. A decade later,¹⁷ Thomas found that patients who had been given a firm diagnosis as well as a positive prognosis reported feeling significantly better at 2 weeks, than patients who were told “I cannot be certain what is the matter with you” (64% *vs* 39%). Van Weel²⁸ did not identify any difference in blood pressure at 1 year between patients with mild hypertension who were told that their blood pressure was “normal” and patients who were told that they were “hypertensive” and were prescribed medication. However, “hypertensive” patients paid significantly more health-care visits than “normal” patients during the year.

In a US study by Rose,²⁰ patients who were told to expect a test to reproduce their chest pain reported

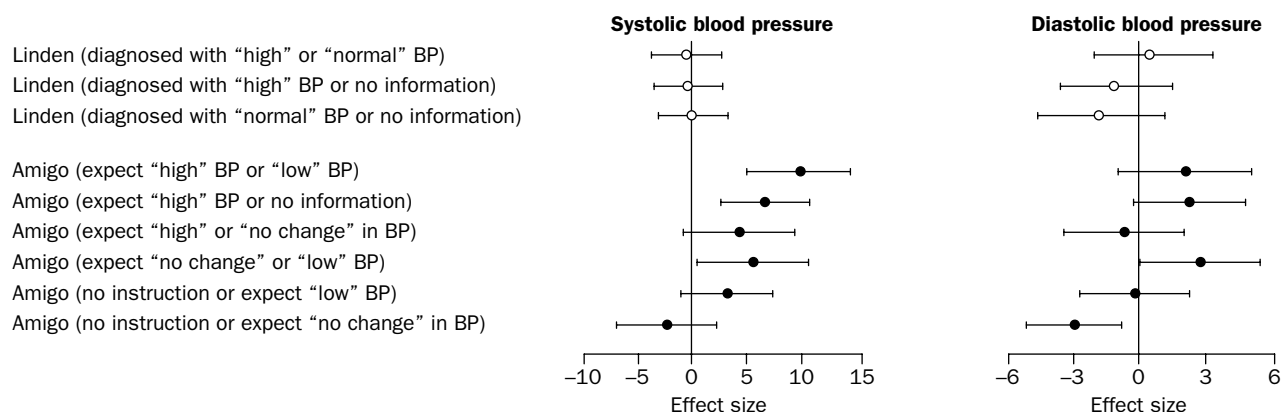


Figure 3: **Effect of cognitive care on blood pressure**

similar pain to those who expected the test to simply detect changes in their tracing. Amigo found systolic blood pressure to be higher in hypertensive patients who were told to expect a higher reading in a second assessment than patients who were informed that such a reading would be lower or that there would be no change.²⁶ The effect decreased with decreasing contrast between the two messages (figure 3). A similar but less pronounced gradient occurred for diastolic blood pressure. In randomly assigning patients with mild hypertension to receive three types of feedback about their blood pressure, Linden found no difference for systolic blood pressure, but similar effects to those of Amigo for diastolic blood pressure.²⁷

Cognitive care and treatment

We identified 19 studies (three of which were published in a single paper) that examined the impact of randomly assigning patients to different levels of treatment expectancy.^{17,18,21–25,29–38} Details of these studies were difficult to summarise because of heterogeneity. Data extraction tables will be available in the forthcoming report of the Centre for Reviews and Dissemination (www.york.ac.uk/inst/crd).

Ten of these studies found that practitioners who attempted to influence patients' beliefs about the effects of therapy had a significant impact on patients' health outcomes.^{17,18,29–33,35,37,38} In three of these studies, health was only partly influenced: in one, effects did not last until follow-up,³² and in the others, effects were limited to certain outcome measures.^{29,38} Of the ten studies that identified a significant effect after manipulation of treatment expectations, only two were rated as good;^{29,37} the rest were average or poor. However, in the nine trials that found no significant difference, three were rated as very good (ref 24 and studies B and C of ref 25) and two as good (ref 21 and study A of ref 25).²¹

Suggestion seemed to be more effective when treatment expectations were positively, rather than negatively, enhanced. In five trials, patients were given negative expectations about treatment, in the form of information about the likely side-effects of medication (study B of ref 25).^{21,22,37,38} Three of these studies found no significant difference in the number of reported adverse effects (study B of ref 25).^{21,22}

Cognitive and emotional care

None of the studies included in this review examined the effects of emotional care alone. Four trials examined the influence combining cognitive care—ie, giving patients a clear diagnosis, a positive prognosis, or

raising treatment expectations, with emotional care—ie, being warm and friendly^{16,23,33} or firm and reassuring¹⁷ (described by some of the authors as "positive consultations"). These consultations were found to be significantly more effective than neutral consultations in decreasing pain³³ and increasing the speed of recovery.^{16,17}

In 1978, Gryll and Katahn³³ allocated dental patients to three types of information about the effectiveness of a painkiller. Those who were told that they would receive a "new, fast acting drug, very effective in reducing tension, anxiety and pain", reported significantly less pain and anxiety than patients whose expectations about the drug had not been raised. The effect size was particularly strong when the message was delivered by a warm and friendly practitioner. Similarly, a Swedish team¹⁶ found that patients with tonsillitis recovered faster and were more satisfied when treated by a friendly practitioner who gave a positive prognosis, encouraged questions, and spent an extra 4 min with them.

Discussion

In reviewing context effects, we identified 25 trials that fulfilled our inclusion criteria. About half of these studies found positive effects on patients' health status after manipulation of patient–practitioner relationships. Conflicting findings are likely to have been influenced by the level of heterogeneity in the type of intervention, clinical sample, health outcomes, the methodological quality, and timing of the studies.

A combination of emotional and cognitive care (positive consultation) was found to produce the most consistent effect. Practitioners who attempted to form a warm and friendly relationship with their patients, and reassured them that they would soon be better, were found to be more effective than practitioners who kept their consultations impersonal, formal, or uncertain.^{16,17,33} One exception was a study by Berk and colleagues²³ in which there was no difference between the positive and negative consultation groups in the effects of acupuncture or placebo. There was also no variation in the ratings of perceived health-professional competence, enthusiasm, empathy, and friendliness between the two groups. This finding suggests that patients might interpret a formal consultation with little interaction as serious and professional.

Ten of the 19 studies that examined the effects of cognitive care by influencing patients' expectations about treatment were found to affect health outcomes, but these trials had lower methodological quality than those finding no effect after manipulations of treatment

expectations. Since these trials were older, poor quality was likely to have resulted from lack of reporting (eg, randomisation, drop-out rate), when such information was not always reported.

At the time, informed consent was not essential, and this might also have influenced the effects of the study, since participants who are unaware of a trial may react differently to patients who agree to be studied and know they have a 50% chance of receiving a placebo.^{22,30} Because context interventions commonly consisted of a single verbal statement (eg, "this is a very effective drug that will reduce your pain immediately after taking it"), it is possible that some might not have been strong enough to influence expectations, especially those of patients with chronic illnesses. This group might feel that the treatment is generally effective but might not believe that it will work for them, owing to previous experiences.³⁹ Because of the lack of data on the practitioners who delivered each intervention, it is difficult to establish the extent to which their beliefs about treatment or difficulty in assuming a "warm" and then "cold" interactive style contributed to the results.

Giving different diagnoses to patients presenting with similar symptoms had little or no effect, perhaps because the diagnoses given were for relatively mild conditions. For more serious illnesses, effects are possibly stronger, but ethical and practical reasons would obviously prevent researchers from doing such studies.

None of the studies examined the effects of emotional care. However, one trial, which failed to meet our inclusion criteria because of the lack of a health status outcome measure, found that patients who frequently attended emergency departments and who were assigned compassionate care had fewer repeated visits and increased satisfaction than patients receiving standard care.⁴⁰

In this review, we chose to focus on doctor-patient relationships because the area of context effects is very large. Some work on other context factors is available elsewhere.^{39,41,42} Since there are a number of related systematic reviews assessing the effectiveness of communication training,¹⁰ preparing patients for stressful medical procedures,⁴³ and changing patients' expectations,¹² these studies were excluded from our review.

Although extensive search strategies were done, this being a conceptually and operationally complex area, we might have missed some eligible randomised controlled trials. Research examining the effects of patient-practitioner interactions on health outcomes has often been based on healthy volunteers or psychiatric patients. A larger analysis that included these studies might have found different effects. However, these populations are likely to process context interventions differently, making the findings less generalisable to other patient groups.

Our findings suggest that studies could be too disparate to allow for any serious conclusions to be drawn, somewhat like comparing apples with oranges. Several aspects need to be considered. At one level, specific doctor-patient interactions are likely to be determined by individual factors, which vary substantially due to the unique nature of relationships. At another level, the effect of these interactions is likely to be modified by the specific disease and other interventions. Moreover, for most of the main conditions studied in this review (eg, hypertension), "specific" or established medical interventions might

not have been more effective. We feel that both aspects need further careful study, but on the basis of the current evidence, we speculate that there is an independent effect of doctor-patient interactions as well.

Vast amounts of energy and resources have been spent to advance diagnostic tools, and pharmacological and surgical treatment. The lack of attention to the more humane aspects of care, alongside increased specialisation and shortened consultation time, could have affected the patient-practitioner relationship and our understanding of its effects. To increase the effectiveness and quality of health services, it is important to study further the interactions between conventional or complementary medicine and context effects occurring during consultations. Our understanding of the therapeutic effectiveness of context effects in doctor-patient interactions could be advanced through an integration of rigorous qualitative and quantitative research, alongside assessments of changes in understanding (eg, treatment expectations, therapeutic alliance), and affect (eg, anxiety).

Contributors

Z Di Blasi developed the protocol; collected, analysed, and interpreted the data; and wrote the paper. E Harkness collaborated in data collection and analysis. E Ernst commented on the study process, the final written document, and supervised part of the data collection and analysis. A Georgiou helped in the conception and design of the study and commented on drafts. J Kleijnen coordinated and supported the study design, data analysis and interpretation, and commented on all revisions of the paper.

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