

Placebo interventions in practice: a questionnaire survey on the attitudes of patients and physicians

Margrit Fässler, Markus Gnädinger, Thomas Rosemann and Nikola Biller-Andorno

ABSTRACT

Background

Few studies have investigated whether patients and physicians differ in their attitudes regarding placebo interventions in medical practice.

Aim

To compare the proportions of patients and physicians who would accept therapies that do not work through specific pharmacological or physiological action but by enhancing self-healing capacities and by exploiting contextual factors.

Design of study

Survey of a random sample of GPs and patients consecutively attending in primary care practices.

Setting

Four hundred and seventy-seven patients and 300 GPs from primary care practices of the Canton Zurich of Switzerland were approached.

Method

Two questionnaires on responders' attitudes regarding non-specific therapies.

Results

The response rates were 87% for patients and 79% for GPs. Eighty-seven per cent of patients and 97% of GPs thought that physical complaints can get better by believing in the effectiveness of the therapy. Overall there was more support for placebo interventions among patients than among GPs, yet 90% of the physicians admitted to actively proposing treatments intended to take advantage of non-specific effects. Seventy per cent of the patients wanted to be explicitly informed when receiving a non-specific intervention, whereas physicians thought this was the case for only 33% of their patients. Fifty-four per cent of patients would be disappointed when learning they had unknowingly been treated with pure placebo ('sugar pill'), while only 44% would feel that way after treatment with impure placebo (for example, herbal medicine).

Conclusion

GPs rather underestimate the openness of their patients to non-specific therapies. However, patients want to be appropriately informed. Developing specific professional standards could help physicians to harness the 'power of the placebo', while remaining authentic and credible.

Keywords

attitude; ethics; general practice; patients; physician-patient relations; physicians; placebo effect; placebos; questionnaires.

INTRODUCTION

Despite ethical controversy,¹⁻⁴ empirical data from different countries show that placebo interventions are frequently used in medical practice. During the last 20 years, eight questionnaire studies have demonstrated a wide variety of physicians' attitudes and opinions on the use of placebo interventions in day-to-day practice.⁵⁻¹² Physicians are more hesitant to use pure placebos (for example, a sugar pill or an injection with saline solution) than impure placebos (substances or methods that do have a known pharmacological or physical action but that cannot be expected to have any direct therapeutic effects for the respective disease and in the chosen dosage).^{7,13} The published surveys suggest that many physicians are aware of beneficial placebo or context effects but are unsure how to use them in a non-deceptive manner.

To develop ways of fostering such effects, it is important to know the perspective of patients. So far there are very few studies on patients' attitudes and whether they differ from those of physicians regarding placebo interventions in medical practice.^{9,14,15} A Swedish study provided patients and physicians with three case examples of placebo use, revealing a broad variety of opinions across groups.⁹ A French study reported that most patients seem to

M Fässler, MD, research fellow; N Biller-Andorno, PhD, MD, professor, Institute of Biomedical Ethics, University of Zurich, Zurich, Switzerland. M Gnädinger, MD, research fellow; T Rosemann, MD, PhD, professor, Department of General Practice, University Hospital Zurich, Zurich, Switzerland.

Address for correspondence

Professor Nikola Biller-Andorno, Institute of Biomedical Ethics, University of Zurich, Pestalozzistrasse 24, 8032 Zurich, Switzerland. E-mail: biller-andorno@ethik.uzh.ch

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How this fits in

Few studies have investigated whether patients and physicians differ in their attitudes regarding placebo interventions in medical practice. Many patients seem to be more open to placebo interventions (non-specific therapies) than physicians. Most patients want to be informed about the mode of action when a non-specific therapy is proposed to them. Developing specific professional recommendations could help physicians to harness placebo effects, while remaining authentic and credible.

have a negative attitude towards placebo therapy and that less than one-third of patients would generally agree to take a placebo.¹⁴ These results have to be interpreted with caution, since it is not clear whether participants' understanding of the term 'placebo' was appropriate. In a patient questionnaire study from New Zealand, 'placebo' was defined as a sham intervention replacing 'a real pill', which may have led patients to believe that placebos had no effect at all and that a better treatment alternative was available. The authors concluded that many patients are amenable to the use of placebos, suggesting that the major issues of placebo use (deception and lack of informed consent) are tolerated by the patients surveyed.¹⁵

To date, it remains uncertain which proportion of patients would accept therapies that work not through specific pharmacological or physiological action but by enhancing self-healing capacities and by exploiting contextual factors. A questionnaire study was conducted with patients and GPs, to explore and compare their attitudes in relation to placebo interventions.

METHOD

Physicians

The researchers received a computer-generated random sample of 500 addresses of GPs in the Canton of Zurich from the Swiss Medical Association. This sample was randomly divided by

computer into two subsets: 300 addresses for the survey of physicians and 200 addresses to ask GPs to enrol patients. Anonymous physician questionnaires were sent to 300 addresses, including an incentive of CHF 20, followed by two reminders.

Patients

The GPs of the random sample of 200 were contacted, as were the 232 GPs who filled in the physician questionnaire. Altogether, 432 GPs were invited to enrol 20 consecutive adult patients into the study who were able to read and understand German language. The GPs were offered an incentive of CHF 200. For all eligible patients, the office staff had to run a screening list and note whether patients participated, their age, sex, and, if applicable, the reason for not participating.

Questionnaires

Two analogous questionnaires were developed, one for the patients and one for the physicians. The questionnaires were designed, based on the experience of the authors, to take into account the question of whether pure and impure placebos are considered differently. Both questionnaires consisted of 13 questions and a section on demographic data. Some items applied to both groups, such as: 'What would you administer to your patients?' for the physicians and 'What would you wish your doctor to administer to you?' for the patients. The results of questions 10 and 11 (patients) and 8–11 (physicians) are not included in this report. Pilot versions of the questionnaires were tested by 30 physicians and 50 patients. The questionnaires can be downloaded from <http://www.ethik.uzh.ch/ibme/team/mitarbeitende/margritfaessler.html> in their original German version and in an English translation.

Definitions of the two therapeutic modes of action were placed at the top of the questionnaire (Table 1). The questionnaires of the patient study were processed by optical-mechanical scanning (Readsoft FORMS 5). The physician questionnaires were manually coded. The study was carried out between May and August 2009.

Comparison with earlier data

From January to March 2008, the authors conducted a questionnaire study among GPs of the same geographic area.⁷ Its items on motives for the use of placebo interventions are compared to the patient data in the current study.

Statistical analysis

Data were processed using SPSS (version 17). Depending on variable scale level, differences were assessed by unpaired *t*-test (interval scaled), the

Table 1. Definitions of the two modes of action.

Mode of action	Definition
Pharmacological action	The pharmacological action is the interaction of compounds in the body via biochemical pathways. For example, individuals with diabetes inject insulin to regulate their blood levels of glucose
Non-specific action	Non-specific action is also known as the placebo effect. In this case, the caring attention of the physician, the desire of the patient to recover, and/or the associated circumstances of the therapy cause the patient to get better

Psychotherapies are excluded from these definitions because they cannot be assigned to either action.

Mann–Whitney *U* test, or Wilcoxon rank sum test (ordinal), or simple and McNemar's χ^2 test (nominal). The statistical significance level was 0.05 with a two-tailed hypothesis. Values are given as frequencies or mean (standard deviation [SD]).

RESULTS

Response rates

Patients. Twenty-four practices participated in administering the patient questionnaires. One physician failed to keep a screening log; four others had incomplete logs. Ten physicians reached the target of 20 complete questionnaires; the others returned between 5 and 19 questionnaires. Out of 477 eligible patients, 414 filled in the questionnaire (response rate 87%). The reasons given by the patients for not filling in the questionnaire were 'patient's refusal to participate' ($n = 34$), 'no return of the questionnaire' ($n = 9$), 'unclear reason' ($n = 8$), 'vision problems' ($n = 7$), 'lack of time' ($n = 4$), and 'patient deceased between screening and filling in the questionnaire' ($n = 1$).

Physicians. Out of 300 physicians contacted, eight mentioned that they were not GPs, leaving a sample of 292. Of these, 232 filled in the questionnaire (79% corrected response rate).

Demographic data. Table 2 shows the demographic data of the two samples. The mean age of the non-responder patients and physicians was older compared to the responder patients and physicians. There was no sex difference among either patient or physician responders and non-responders.

Placebo term and connotation. In an open question at the beginning of the questionnaire, patients participating in the study were asked to give an explanation of the term 'placebo'. Sixty-three per cent of the patients gave an appropriate explanation, 0.5% gave a wrong explanation, 36.5% did not know an explanation, and 0.5% did not answer the question. The most frequently used explanations were 'sham drug' and 'drug without active agent'. Among the patients who gave a nearly correct explanation, 24% perceived the term 'placebo' as positive, 63% as neutral, and 10% as negative; 3% did not know. Thirty per cent of the physician sample ($n = 232$) perceived the term 'placebo' as positive, 58% as neutral, and 13% as negative (not significant).

Effectiveness of placebo interventions. Among patients and physicians there was substantial agreement that physical complaints can get better simply by believing in the effectiveness of the

Table 2. Demographic data.

	Patients	Physicians
Mean age, years (SD)	55.9 (18.1) ^a	53.2 (8.6) ^b
Sex, <i>n</i> (%)		
Female	234 (57)	72 (31)
Male	180 (43)	159 (69)
Educational level, <i>n</i> (%)		
Did not complete 9 years at elementary school	3 (1)	
Completed 9 years at elementary school	29 (7)	
Completed an apprenticeship	234 (58)	
Advanced professional training (technical school/advanced technical college)	78 (19)	
General qualification for university entrance	16 (4)	
University academy or university degree	37 (9)	
Professional training not finished	7 (2)	
Self-assessed state of health		
Healthy	185 (46)	
Acute disease or disorder	81 (20)	
Slight or moderate chronic disease or disorder	124 (31)	
Severe chronic disease or disorder	13 (3)	

SD = standard deviation. $n = 414$ patients, 232 physicians. ^aAs compared to the non-responders 66.4 (26.7) years: $P < 0.001$ by t-test. ^bAs compared to the non-responders 56.3 (9.2) years: $P = 0.02$ by t-test.

therapy (Table 3). More physicians than patients were convinced of the effectiveness of placebo interventions.

Reasons for placebo treatment. The authors had explored different reasons for the use of placebos in their previous study with GPs.⁷ This multi-part question was not repeated in the current questionnaire to avoid the risk of a reduced response rate if the questionnaire had one more page. Patients were now asked these questions (Table 4). More patients than physicians responded affirmatively to all seven reasons given; the difference was highly significant ($P = 0.002$ to $P < 0.001$).

Information about non-specific treatment. Seventy

Table 3. Opinions on the effectiveness of placebo interventions: responses to the question 'Do you think that physical complaints can get better simply by believing in the effectiveness of the therapy?'

Response	Patients, <i>n</i> (%)	Physicians, <i>n</i> (%)
Yes	358 (87)	225 (97)
Quite often	231 (56)	178 (77)
Rarely	127 (31)	47 (20)
No	34 (8)	4 (2)
I do not know	21 (5)	2 (1)

Physicians were more convinced of the clinical effectiveness of placebo interventions than patients, $P < 0.001$, $z = 5.0$ by U test (difference remained significant when doing ordinal regression with sex and age as covariables). Patients: $n = 413$, physicians: $n = 231$.

Table 4. Reasons for the use of placebo interventions (odds^a): responses to the question 'In which of the following situations would you like your physician to give you a therapy that in his or her view only works via non-specific action (placebo effect)?'.

Response	Patients	Physicians (2008 study ^b)
Because it was my request to receive this therapy (χ^2 46 ^b , Cramer's V 0.28, $P < 0.001$)	2.6	0.8
To gain a therapeutic advantage for me through the placebo effect (χ^2 114, Cramer's V 0.43, $P < 0.001$)	7.4	0.9
To still be able to offer me a treatment option if I had an 'incurable' disease and there were no known substantial working therapy (χ^2 113, Cramer's V 0.44, $P < 0.001$)	3.0	0.4
To offer a treatment to me in situations in which standard treatments cannot be used (for example if I am hypersensitive or allergic), or that they have major side-effects (χ^2 135, Cramer's V 0.48, $P < 0.001$)	3.1	0.4
If my complaints and test results are not attributable to a certain disease (non-specific complaints) (χ^2 23, Cramer's V 0.20, $P < 0.001$)	1.9	0.8
If I were a difficult patient with psychological peculiarities, such as a sick person who has constant unwarranted complaints (χ^2 10, Cramer's V 0.14, $P = 0.002$)	1.0	0.6
To avoid addiction to my treatment medication (χ^2 176, Cramer's V 0.54, $P < 0.001$)	3.3	0.2

Patients: $n = 324$ to 380 , physicians: $n = 154$ to 162 . ^aOdds mean the proportion of 'yes' answers to 'no' answers (agreement to non-agreement). For analysis of this study's results, the GP answers 'I use pure and impure placebos' and 'I use only impure placebos' were pooled together into one binary category. ^bDegrees of freedom = 1.

per cent of the patients wanted to be informed about the fact that they received a drug that only has a non-specific action, 21% would leave it up to the physician about whether he or she told them, 7% found such information unnecessary, and 2% did not know (two missing answers). Conversely, the

physicians were asked about the percentage of patients they estimated would want to be informed about receiving a non-specifically acting drug. The mean estimated percentage was 33% (SD = 29%), $n = 164$, less than half of the value given by the patients.

Table 5. Attitudes to different information about placebo treatment and attitudes to using a homeopathic remedy depending on the physician's belief in homeopathy.

Different information about placebo treatment		Yes, %	No, %	I do not know, %
Agreement to pure placebo plus indirect information	Patients	62	29	9
	Physicians	37	61	2
Agreement to pure placebo plus direct lie	Patients	42	50	8
	Physicians	7	90	2
Use of a homeopathic remedy depending on physician's belief				
Agreement with use of a homeopathic remedy by a physician believing in its specific effects	Patients	79	12	9
	Physicians	82	10	8
Agreement with use of a homeopathic remedy by a physician not believing in its specific effects	Patients	46	40	13
	Physicians	43	49	8

Solid brackets $P < 0.001$ between groups by χ^2 test; dotted brackets $P < 0.001$ between both items within groups (McNemar's χ^2 test, 'yes' and 'no' answers only). Patients: $n = 405$ to 412 , physicians: $n = 231$. As for the homeopathy question, the patient and physician groups did not differ significantly. Patients: $n = 410$ to 412 , physicians: $n = 229$ to 230 . The total percentage may not equal 100 due to rounding.

Table 6. Patients' disappointment after finding out about receiving placebo treatment without adequate information in the past.

Response	Yes, %	No, %	Do not know, %
Disappointment after impure placebo (herbal remedy or multivitamin preparation)	44	46	10
Disappointment after pure placebo (sugar tablet)	54	35	11

$P < 0.001$, χ^2 21, degrees of freedom = 1, by McNemar's χ^2 test for the 'yes' and 'no' answers; $n = 338$.

Communication of pure placebo intervention. A case vignette was presented to the participants: a pregnant woman with heavy nausea persisting over a 2-week period was given sugar tablets. The accompanying information that the pregnant woman received differed. In the first version the physicians told her: 'Try this therapy, it has very few side-effects and can help with your nausea'. The second version contained an explicit lie: 'This is an effective new agent that works for nausea and has very few side-effects'. Table 5 shows that significantly more patients than physicians advocated for indirect information plus sugar tablets (62% versus 42%).

Influence of doctor's belief in specific action of treatment. In a subsequent variation of the case vignette, the aim was to explore the acceptance of placebos by study participants in relation to the beliefs of the prescribing physician. The two scenarios created were that the pregnant woman received homeopathic globules and that the prescribing physician either does or does not believe in homeopathy. Table 5 shows that the majority of both patients and physicians agree with the use of a homeopathic therapy by someone who believes in homeopathy (79% and 82%).

Patients' disappointment after finding out about placebo treatment without adequate information in the past. Table 6 also shows that significantly more patients responded that they would be disappointed with their physician if they found out they had been treated with a pure placebo (54%) compared to a treatment with impure placebo (44%). The pure placebo was described to the patient as a sugar tablet and the impure placebo as a herbal remedy or multivitamin preparation that was unlikely to have a significant specific effect on their complaints.

Intentional use of non-specific therapies. Ninety per cent of the physicians stated that they actively proposed therapies to patients that were intentionally used to take advantage of non-specific effects (31% quite often, 59% rarely), 10% replied 'no' (four missing answers). Moreover, 45% of the GPs stated that they already used a treatment for their own health problem where they thought it worked by non-specific action, while 55% did not use such treatment (two missing answers).

DISCUSSION

Summary of main findings

This study provides empirical information about patients' attitudes regarding placebo interventions in practice and compares them to the attitudes of GPs. The comparison of patients' and physicians' replies

suggests that patients tend to be more open to non-specific interventions than physicians. This was true for a range of reasons, from compliance with patient wishes to more paternalistic arguments for patient benefit. However, patients overall want to be informed about receiving such a non-specific treatment, and they want their physician to be authentic and convinced about the effectiveness of the treatment they recommend.

What does this greater openness of patients towards non-specific therapies mean for medical practice? The therapeutic ideal to treat specifically warrants that scientifically proven treatments are used to maximise the benefit for the patients.¹⁶ Many times, however, the diagnosis remains uncertain,^{17,18} or no specific treatment is available, particularly in general practice. Even when a treatment with a statistically proven effect is available, it may not work satisfactorily for an individual patient. Although a clear diagnosis and specific treatment remain important goals to be strived for, the authors think the role of non-specific interventions should not be underestimated: either as substitutes for non-existing specific interventions, signalling to patients they are not left alone with their problem, or as enhancers of specific therapies. The present results suggest that physicians should focus less on the distinction between 'real' medicine (which is good) and placebo (which is bad), and take into account that generally contextual healing¹⁹ is part of treatment processes.^{20,21} Patients are likely to appreciate the combination of specific and non-specific treatment components if this is communicated in an open, authentic way.

Strengths and limitations of the study

A major strength of this study was that it investigated the understanding and connotations of the term 'placebo' in patients. It also pointed out the different attitudes towards pure and impure placebos in a parallel survey of patients and physicians. Further strengths were the high response rates, the random sample of GPs, and the definition of the two therapeutic modes of action in an attempt to set up the same understanding for all participants.

Despite being given definitions of the pharmacological action and the non-specific action, participants could have understood questions differently because of the complicated topic. Furthermore, self-reporting is not always consistent with real behaviour. The results refer to a Swiss canton and might not reflect the situation of other countries. For the different reasons for placebo use, the comparability of the data of patients and physicians is limited because the response rate of the previous physician study was only 47% and the

physicians' 'I do not know' responses were not included in the list of potential answers.

Comparison with existing literature

Given that 70% of the patients in the study want to be informed about the fact that their treatment works non-specifically, the question arises as to how the physician can explain the mode of action to the patient. Finding an appropriate answer requires knowing patients' associations with the 'placebo'. To the authors' knowledge, this is the first study to address patients' understanding and connotations of the term 'placebo'. In the study sample, two-thirds of the patients gave an appropriate explanation of placebo. A French study with an unclear response rate found 59% of patients claimed they knew about the placebo effect, while it is uncertain whether the investigators verified these statements.¹⁴ Interestingly, and importantly for the issue of communicating the use of non-specific interventions, it was not possible to confirm an alleged negative attitude of patients towards the term 'placebo'. Nevertheless the term can be misunderstood as meaning ineffective or useless treatment. When explaining the treatment negatively — 'only non-specific effects', 'not scientifically proven mechanism', or 'via an unknown mechanism' — nocebo effects could result, driven by negative expectations of patients.²²⁻²⁷ Therefore, more positive wording of information should be considered, such as 'this treatment can support self-healing capacities and may help you recover'.

With regard to the communication of a non-specific therapy, the present results showed the inclusion of a lie clearly reduced the acceptance of a placebo treatment among patients and physicians. Explaining to patients the inert pharmacological action and the possible benefit through activated self-healing capabilities seems a difficult task. Particularly in the case of pure placebos like sugar tablets or saline solution, physicians may find it difficult to find appropriate ways of involving their patients without deception. This may in fact be an important reason for the reluctance of physicians to use pure placebos as shown in the authors' previous study.⁷ Applying the concept of pure and impure placebos to the examples given in other studies confirms that physicians hesitate to use pure placebos and tend to use impure placebos.^{5,6,8-13,28} However, no other studies were found that directly investigated attitudes towards pure versus impure placebos. Many treatments can be considered as impure placebos; for example, medications with proven benefit for another indication than the present one, or herbal medicines without evidence of pharmacological effectiveness. It is understandable

that physicians do not communicate such interventions as placebo because the majority of them might consider there is a possibility of an intrinsic effect.

Appropriate communication serves the partnership between the patient and physician and maintains patients' trust. Using placebo interventions in a deceptive way is likely to cause disappointment in the patient. In the authors' previous study, it was found that physicians were unsure if using placebos was appropriate and that many were afraid that patients would be disappointed if they found out they had been treated with a placebo.⁷ The patient survey data confirm this apprehension: more than half of patients stated they would be disappointed if they learned that they had unknowingly received a placebo, with numbers being somewhat lower for impure placebos.

Eighty-eight per cent of the GPs stated they actively propose therapies to patients where they intentionally use the advantage of non-specific effects. This finding contrasts with only 44% of the GPs agreeing with the physician in the case vignette where the GP uses a homeopathic remedy but does not believe in its pharmacological effects. This is an interesting disparity. Perhaps placing the question in a case vignette is closer to clinical practice and can lead to more reluctance towards non-specific therapies than an abstract general question, or the GP's degree of belief or disbelief in possible small, specific properties of the treatment played a role.

Implications for future research and clinical practice

Balint's metaphor of the doctor as drug arose from the notion that patients respond to the personal interaction with their physician.²⁹ This emphasises the importance of communication skills to enhance placebo effects. The awareness that every verbal or non-verbal comment can influence the therapeutic outcome provides a stimulus to avoid nocebo effects driven by ill-considered negative comments.

Qualitative interview studies of physicians and patients are needed to obtain a more detailed picture of their perceptions and experiences, especially to explore concrete examples of placebo interventions in-depth. The challenge seems to be to integrate non-specific therapies into practice in an ethical way. Developing general guidance pointing to possible pitfalls (for example in communicating the use of placebo interventions) might be useful. The recommendations should include clear definitions to avoid conceptual confusion and should relate to findings of placebo research to compensate for a possible lack of understanding of the placebo effect.^{11,14-15,28,30,31} Such professional standards could

increase the awareness of physicians that contextual healing factors are part of nearly every treatment, and could help physicians to harness the 'power of the placebo',³² while remaining authentic and credible.

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Ethics committee

The research ethics committee of the Canton of Zurich approved the study (KEK-StV-Nr. 69/09).

Competing interests

The authors have stated that there are none.

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