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Optimizing placebo effects in medical contexts: utilizing learning theories and exploring communication strategies

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5. Integrating placebo effects in general practice: A perspective from health care professionals.

Under review for publication

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ABSTRACT

Objectives: Placebo effects, beneficial treatment outcomes due to non-active treatment components, play an important role in the overall treatment response. To benefit from these effects, it is important to explore the perspectives of health care professionals (HCPs) on the integration of placebo effects in clinical care. Three themes were investigated: knowledge about placebo effects and factors that attribute to these, frequency of placebo use, and attitudes towards acceptability and transparency of placebo use in treatment.

Methods: A cross-sectional survey was conducted in two samples: a (nested) short survey in 78 nurses during working shifts (sample 1) and an extended online survey in 47 HCPs in general (i.e., medical psychologists, oncologists, surgeons; sample 2).

Results: Respondents were least knowledgeable about the adverse effects of expectations (nocebo effects) and the efficacy of open-label placebos. Mind-body interaction, positive expectations, and brain activity involved in placebo effects were rated as the most influential factors in placebo effects. The use of placebo effects was reported in 53.8% of the nurses (e.g. by inducing positive expectations), and 17.4% of the HCPs reported to make use of pure placebos and 30.4% of impure placebos. Attitudes towards placebo use in treatment were acceptant, and transparency was highly valued (both up to 51%).

Conclusions: The benefits of placebo effects were well understood, with the exception of adverse effects of nocebo and non-deceptive placebo use. Moreover, respondents indicated to be acceptant of the (transparent) use of placebo effects, and interested in learning more about this topic. These findings provide insights in how placebo effects can be integrated in clinical care, and potentially enhance treatment outcomes.

Keywords: placebo effects, expectations, clinician communication, attitudes and acceptability, cross-sectional survey

INTRODUCTION

Placebos are inert substances that inherently lack properties to induce any effect(1). Placebo effects, however, can induce beneficial treatment outcomes due to non-active treatment components, for example by learning mechanisms or contextual factors(2, 3). Frequency of placebo use in treatments has been reported to vary between 41% and 99% across countries (e.g. Switzerland, Canada, UK and the US)(4-7). Moreover, distinctions can be made between pure placebos (without active pharmacological properties, such as sugar pills) and impure placebos (with pharmacological properties but not for the specific symptoms, such as antibiotics for viral infections). To benefit from placebo effects, it is important to explore the perspectives of health care professionals (HCPs) on how these effects can be used for clinical practice and therapeutic benefit.

In the present study, perspectives on placebos and placebo effects were explored in HCPs by assessing three themes: knowledge about placebo effects and factors that attribute to this, frequency of placebo use, and attitudes towards acceptability and transparency for placebo use in treatment.

METHODS

Study design

A cross-sectional survey study was carried out in nurses at the Erasmus University Medical Center in Rotterdam, embedded in the WELCOME study, as approved by the Medical Ethics Review Committee (MEC -2017-1103). Due to the Covid-19 outbreak and its impact on the availability of nurses, a second sample was added to be more in line with sample sizes from previous studies (N=100)(5). This sample of HCPs received an extended version of the survey, as approved by the Psychology Research Ethics Committee of Leiden University (2020-04-07-A.W.M. Evers-V1-2368).

Recruitment and respondents

Respondents from the first sample represent a convenience sample of nurses from general wards and intensive care units, recruited during or at the end of a work shift and invited to fill in the survey on a tablet. The second sample consisted of a broader

range of HCPs recruited through social media platforms (LinkedIn) and the researchers' networks.

Measures

The short survey (sample 1) consisted of 7 items, and the extended survey (sample 2) of 14 items (see Table 1). The surveys were categorized in three themes. For current knowledge, respondents were asked about familiarity with placebo effects and how they would explain these effects. The influence of well-studied placebo factors in treatment (positive expectations, patient-practitioner relationship, mind-body interaction, social observational learning, brain activity related to positive expectations, and classical conditioning) were rated on a numerical slider (i.e., 0% not important, 50% somewhat important, 100% very important) (Smits et al., submitted). Second, respondents were asked about placebo use (sample 1) and the pure and impure placebo use (sample 2). A third theme was added in the extended survey to assess attitudes towards acceptability and transparency of placebo use with varying answer categories (i.e., in case of psychological complaints, a cold, chronic diseases, terminal diseases, never correct, or always correct). Multiple answers were possible(8).

Procedure

After providing informed consent, the respondents of sample 1 filled in background characteristics. All respondents then received introductory information about placebo and nocebo effects. In sample 2, a differentiation between pure and impure placebos was made and additionally explained (see Supplementary material for the provided descriptions). Subsequently, respondents were presented with the survey.

Statistical analysis

Data was analyzed using IBM SPSS Statistics (version 25). Data were summarized using percentages and cross-tabulations. Percentages of perceived influence of placebo factors were compared on a within-subject level in a repeated measures ANOVA. Pairwise comparisons were Bonferroni-corrected. Assumptions were checked, and corrections were made for sphericity violations (Huynh-Feldt correction)(9). Partial eta squared (η^2) was reported for effect size(10). A significance level of $<.05$ was set as statistically significant. Responses from free text entry fields were coded and most common examples are reported.

Table 1. Overview and results of survey questions (N=125)

						Sample 1 (N=78)	Sample 2 (N=47)
1 Current knowledge of placebo effects	Not at all	Slightly	Somewhat	Quite	Very much		
<i>How familiar are you with the placebo effect?</i>	0.8%	15.2%	24.0%	47.2%	12.8%	✓	✓
<i>How familiar are you with the nocebo effect?</i>	21.3%	31.9%	12.8%	27.7%	6.4%		✓
	Strongly disagree	Disagree	Neutral	Agree	Strongly agree		
<i>Do you believe that placebo effects can improve treatment outcomes?</i>	0.0%	0.8%	24.8%	55.2%	19.2%	✓	✓
<i>Do you believe that nocebo effects (negative expectations) can deteriorate treatment outcomes?</i>	0.8%	4.8%	46.4%	35.2%	12.8%	✓	✓
<i>Do you want to learn more about placebo effects?</i>	0.0%	4.9%	18.0%	67.2%	9.8%	✓	✓
<i>Can you describe an example of when you experienced a placebo effect in a patient?</i>			Free text entry ^a			✓	✓
<i>Can you describe an example of when you experienced a nocebo effect in a patient?</i>			Free text entry ^a				✓
<i>How would you explain the placebo effect to a patient?</i>			Free text entry ^a				✓
<i>How much do you think these factors influence treatment outcomes in %?</i>	M		SD		95%CI		
• <i>Positive expectations</i>	74.5		19.0		[71.4-77.6]	✓	✓
• <i>Good relationship between practitioner and patient</i>	73.5		17.4		[70.0-77.0]	✓	✓
• <i>Mind-body interaction</i>	75.1		15.1		[71.9-78.2]	✓	✓
• <i>Seeing or hearing positive experiences from other patients</i>	69.2		17.6		[66.0-72.4]	✓	✓
• <i>Brain activity related to positive expectations</i>	73.7		18.0		[71.0-76.4]	✓	✓
• <i>Classical conditioning (the body learns from medication)</i>	59.9		19.7		[56.5-63.3]	✓	✓
2 Frequency of placebo use	Yes	No					
<i>Have you ever made use of placebo effects?</i>	53.8%	46.2%				✓	
<i>Have you ever made use of pure placebos?</i>	17.4%	82.6%					✓
<i>Have you ever made use of impure placebos?</i>	30.4%	69.6%					✓
3 Acceptability of placebo use							
<i>Attitudes towards acceptability of placebo use</i>			See Figure 2				✓
<i>Attitudes towards transparency of placebo use</i>			See Figure 3				✓

^aAn example from the most common answers will be provided.

RESULTS

Sample characteristics

Depicted in Table 2.

Table 2. Sample characteristics^a			
	Nurses (N=78)	HCPs (N=47)	
Years of health care experience^b	14.2 (11.8)	17.3 (13.8)	
Age^b	33.8 (11.9)	41.0 (12.0)	
Gender (N M:F)	21:57	11:36	
Specialization	Frequency (%)	Specialization	Frequency (%)
Psychology ^c	11 (23.4)	Intensive care	42 (53.8)
Oncology ^{d,e}	8 (17.0)	Medium care internal medicine	25 (32.1)
Pediatrics ^{c,d,e}	4 (8.5)	Medium care surgery	11 (14.1)
Surgery ^{d,e}	3 (6.4)		
Medical doctor (unspecialized) ^d	3 (6.4)		
Geriatrics ^d	3 (6.4)		
Maternity care ^{d,e}	3 (6.4)		
General practitioner ^d	3 (6.4)		
Emergency room ^{d,e}	2 (4.3)		
Endocrinology ^e	2 (4.3)		
Unspecified ^d	2 (4.3)		
Phlebology ^d	1 (2.1)		
Anesthesia ^e	1 (2.1)		
Urology ^d	1 (2.1)		

Note: ^aOverall completion rate was 75.4%, ^bMean (SD), ^cPsychologist, ^dMedical doctor, ^eNurse. HCPs = Health care professionals.

Placebo knowledge: Likert scales

Percentages of familiarity with placebo and nocebo effects, treatment benefits, and interests in learning about placebo effects are summarized in Table 1.

Placebo knowledge: Mechanisms

A significant difference was found between perceived influence of the different placebo factors on treatment outcomes ($F(5, 119) = 20.921, p < .001, \eta^2 = .145$). Bonferroni-corrected pairwise comparisons indicated that conditioning was rated significantly lower than all other factors. Positive expectations, brain mechanisms and mind and body interaction were rated significantly more influential than social learning and conditioning. All factors were rated above 50% (Figure 1).

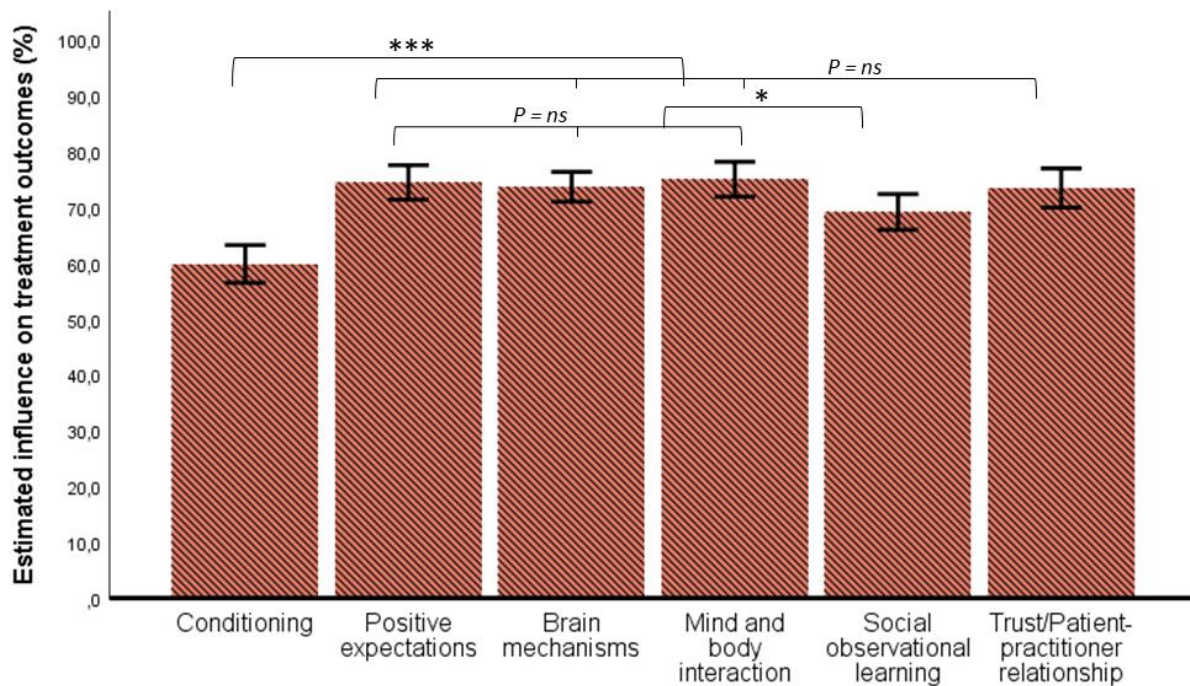


Figure 1. Ratings of perceived influence of placebo factors in treatment outcomes. Error bars: 95% CI, * $p < .05$, ** $p < .001$.

Placebo knowledge: Free text entry

Example of placebo use

The majority of the respondents (74 of 125; 59%) were able to provide an example. The most common example was the administration of paracetamol (acetaminophen) to induce sleep.

Example of nocebo use

Twenty-five out of 47 respondents (53%) were able to provide an example. The most common example described how negative expectations influence treatment outcomes adversely.

Explaining placebo effects to patients

Of the 47 HCPs, 43 (91%) were able to provide an example. The most common examples were based on mind and body interaction, positive expectations, and brain activity induced by placebo effects. Six respondents reported to restrain from explaining placebo effects, because they thought this would negate the positive effects.

Attitudes towards acceptability and transparency

For acceptability, we found high percentages for 'always correct' 'psychological

complaints' and 'mild health complaints'. For transparency, respondents indicated often that deception was 'never correct' (See Figures 2 and 3).

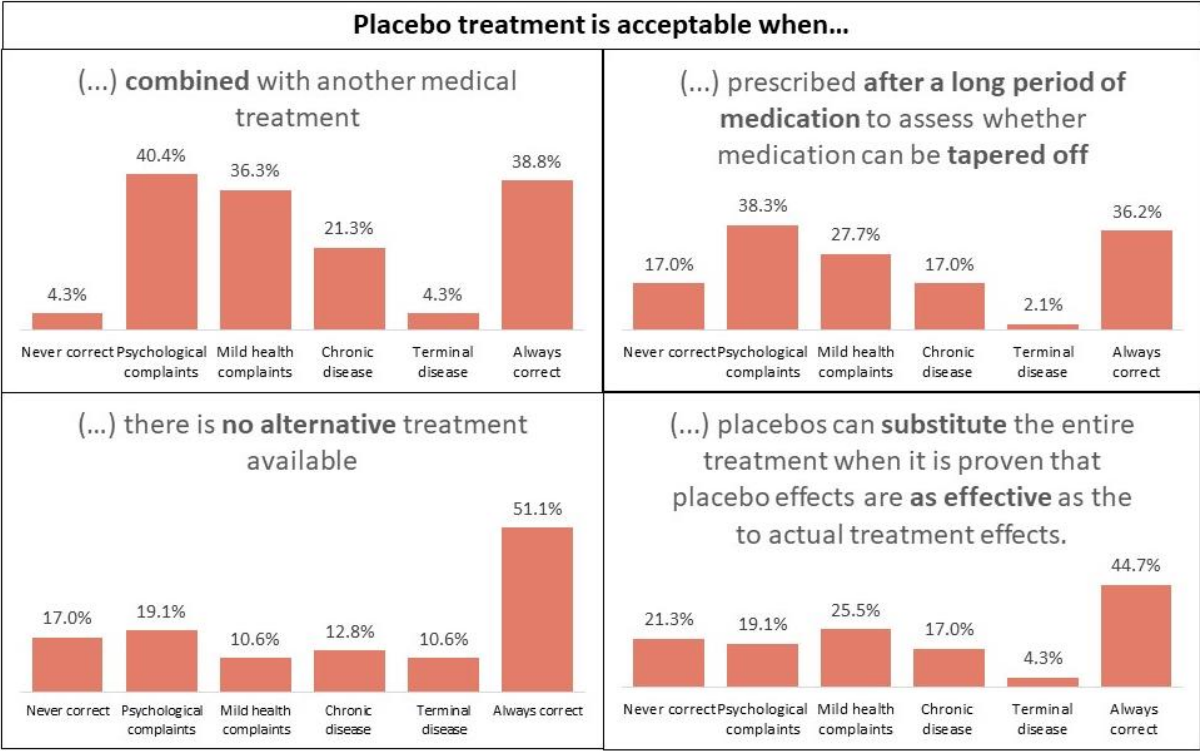


Figure 2. Outcomes of placebo acceptability scores in different scenarios.

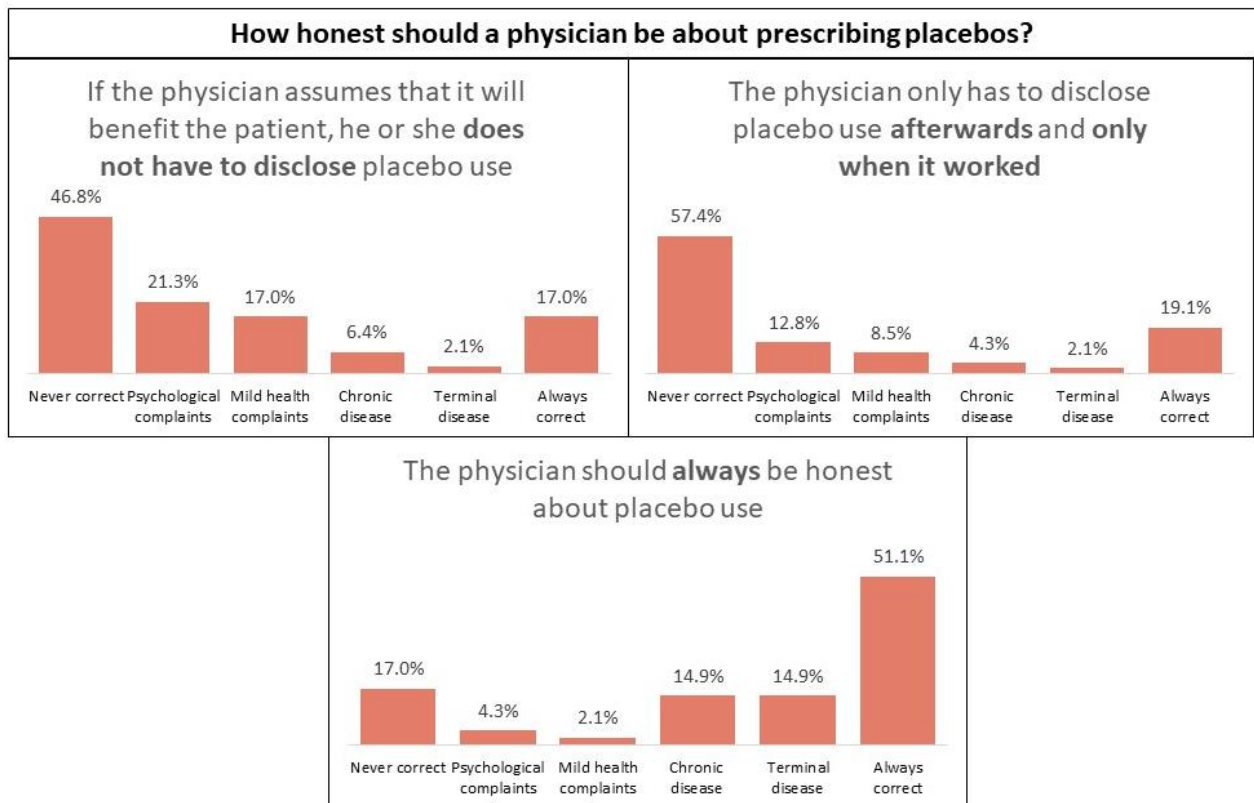


Figure 3. Outcomes of placebo transparency scores in different scenarios.

DISCUSSION

The present study explored perspectives of health care professionals (HCPs) on the integration of placebo effects in clinical care in a sample of HCPs based on three themes. Overall, the benefits of placebo effects and factors that contribute to treatment outcomes were well understood. The use of (impure and pure) placebos was reported in about half of respondents. Moreover, respondents indicated to be acceptant of the (transparent) use of placebo effects.

Results from the first theme, placebo knowledge, indicated that respondents were overall familiar with placebo effects. With regards to nocebo effects, respondents seemed to be less familiar, also supported by the finding that only half of the respondents could describe an example thereof in the free text entries. Moreover, results from the free text fields indicated a misconception about deception, namely that explaining placebo effects would negate their effects and respondents therefore refrained from explaining these. These findings are insightful since the current trend in placebo research is more leaning towards the direction of open-label