



Placebos in pediatrics: A cross-sectional survey investigating physicians' perspectives

Vanda Faria^{a,b,c,d,*}, Cameron Talbert^a, Nathan Goturi^a, David Borsook^e, Alyssa Lebel^f, Ted J. Kaptchuk^d, Irving Kirsch^d, John M. Kelley^{d,g}, Eric A. Moulton^{a,h}

^a Brain and Eye Pain Imaging Lab, Pain and Affective Neuroscience Center, Department of Anesthesiology, Critical Care and Pain Medicine, Boston Children's Hospital, Harvard Medical School, Boston, MA, USA

^b Department of Psychology, Uppsala University, Uppsala, Sweden

^c Department of Otorhinolaryngology, Smell & Taste Clinic, TU Dresden, Dresden, Germany

^d Program in Placebo Studies, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA

^e Departments of Psychiatry and Radiology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

^f Division of Pain Medicine, Department of Anesthesiology, Boston Children's Hospital, Boston, MA, USA

^g Department of Psychology, Endicott College, Beverly, MA, USA

^h Department of Ophthalmology, Boston Children's Hospital, Harvard Medical School, Boston, MA, USA

ARTICLE INFO

Keywords:

Children
Pediatric care
Placebo effect
Physicians
Survey

ABSTRACT

Objective: Placebo responses are significantly higher in children than in adults, suggesting a potential underused treatment option in pediatric care. To facilitate the clinical translation of these beneficial effects, we explored physicians' current practice, opinions, knowledge, and likelihood of recommending placebos in the future.

Methods: A cross-sectional web-based survey administered by REDCap was conducted at Boston Children's Hospital between October 2021 and March 2022. Physicians ($n = 1157$) were invited to participate through an email containing a link to a 23-item survey designed to assess physicians' attitudes and perceptions towards the clinical use of placebo in pediatrics.

Results: From 207 (18%) returned surveys, 109 (9%) were fully completed. Most respondents (79%) believed that enhancing the therapeutic components that contribute to the placebo response may be a way of improving pediatric care. However, whereas most (62%) found placebo treatments permissible, only one-third reported recommending them. In pediatrics, placebos are typically introduced as a medicine that "might help" (43%). The most common treatments recommended to enhance placebo effects are physical therapy, vitamins, and over-the-counter analgesics. Physicians most frequently recommend placebos for occasional pain, headaches, and anxiety disorders. Finally, the great majority of physicians (87%) stated they would be more likely to recommend placebo treatments if there were safety and ethical guidelines for open-label placebos.

Conclusions: Placebo treatments seem permissible to physicians in pediatric care, but the development of safety and ethical guidelines may be necessary before physicians systematically incorporate the benefits of the placebo effect in pediatrics.

1. Introduction

Placebo effects—beneficial therapeutic changes that can arise as part of active or inert interventions—are known to substantially increase the efficacy of virtually any clinical intervention [1–5]. These benefits may be as large as those observed with active medication in adult populations [5,6]. However, placebo response rates are often greater (in some conditions almost double) in children than in adults [7–9]. For

instance, in adult migraine trials, placebo effects have been estimated around 35% whereas pediatric migraine trials suggest placebo response rates of 50% or higher [8]. An inverse relation between age and placebo responsiveness has been suggested [9–11], implying that children may benefit from placebos even more than adults.

Nonetheless, the belief that deception is required and the common misconception that placebos lack efficacy have hindered their clinical implementation, particularly in pediatric care. Children are an

* Corresponding author at: Department of Psychology, Uppsala University, Von Kraemers allé 1A 1C, 752 37 Uppsala, Sweden.

E-mail address: vanda.faria@psyk.uu.se (V. Faria).

<https://doi.org/10.1016/j.jpsychores.2023.111421>

Received 21 March 2023; Received in revised form 7 June 2023; Accepted 18 June 2023

Available online 19 June 2023

0022-3999/© 2023 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

especially vulnerable population that requires additional obligations and protections. Most medical decisions in pediatrics involve surrogate decision makers, increasing the likelihood of ethical conflicts [12].

Over the past decade, however, accumulating work has consistently shown that clinically relevant placebo responses can be obtained in a non-deceptive, transparent manner (i.e., open-label placebo) [13–18]. During open-label placebo administration, patients are typically told that the treatment substance is inert, with no active drug component, but they are also informed that these treatments have sometimes been found to produce therapeutic benefits in patients with their condition [19]. In the pediatric field two studies have investigated the clinical efficacy of open-label placebos [20,21]. In children with ADHD, administration of open-label placebo paired with stimulant medication successfully reduced the intake of medication in affected children by 50%, minimizing side effects without compromising the therapeutic benefit [20,22]. Similar effects were observed in children with functional abdominal pain or irritable bowel syndrome who reported significantly reduced pain and reduced medication intake after open-label placebo treatment [14].

Taken together, these preliminary findings suggest that open-label placebo use may help clinicians improve therapeutic outcomes and decrease drug loads and side effects without violating the trust of children and parents or compromising the patient-physician relationship, as would be necessary with deceptive placebo administration. On the other hand, removing the placebo component from an active therapeutic intervention might reduce or even abolish therapeutic efficacy [23–25], further supporting the idea that placebo-related factors (patients' expectancies, anxiety, patient-physician relationship, and context) should be carefully considered in pediatric therapeutic settings.

Surveys across several countries have examined patients' and healthcare providers' perspectives regarding the use of placebo treatments in adult clinical practice [26–37]. Data suggest that a high proportion of physicians are aware of the benefits of placebos and prescribe them on a regular basis [35,36,38]. Generally, these placebo are not inert substances but rather physiological active interventions (e.g., vitamins) unlikely to change that specific condition. Physicians rarely reveal the true nature of the placebo intervention, typically introducing them as "potentially beneficial medicine". [35] Surveys of adult patients suggest that most patients value honesty, transparency, and shared decision-making [34,39]. The discrepancy between patients' values and physicians' practices may disturb the patient-physician relationship and affect treatment outcome.

To facilitate clinical translation of beneficial placebo effects in pediatric settings, the perspectives of the main players (patients, parents, and physicians) are important. A change in treatment outcome can arise, not only from patients' expectancies but also from the expectancies of proxies, such as parents and physicians. Placebo by proxy is a complex phenomenon that attempts to explain a change in treatment outcome arising from an interaction between a patient and an effect from proxies such as parents, caregivers or physicians [40]. Only two studies have been published on parents and patients' perspectives about the use of placebos in children [21,41]. Data suggest that both children and parents are interested in and accepting of open-label placebos as a treatment option. Parents' attitudes seem to depend on the physicians' certainty about benefits of the treatment, purpose of treatment, and transparency [41]. Parents tend to reject the use of deception in pediatric placebo treatments and endorse the creation of safety and ethical guidelines for placebo use [13].

When it comes to physicians' perspectives on the use of placebos in pediatric settings, there are no previous studies exploring this topic. Knowledge about physicians' attitudes and current practices is essential to develop clinical guidelines and effectively and ethically harness the beneficial effects of placebos in pediatric settings. Hence, the present study aims to explore, physicians' perspectives concerning the use of placebos in pediatric care.

2. Materials and methods

2.1. Survey development and piloting

We used REDCap, a secure online application for building and managing online surveys and databases, to administer the survey and collect the data [42,43]. The survey was developed in a focus group meeting composed of six participants with distinct backgrounds i.e. psychologists, placebo experts, and pediatric physicians, to assess four main areas: (1) physicians' current practices (frequency and rationale), (2) opinions about placebo-relevant factors, (3) placebo knowledge, and (4) likeliness of recommending placebos with the emergence of research findings. Some of the survey questions were based on previous studies [35,44]. To ensure face validity, the study was piloted in 10 physicians from the Headache Clinic of Boston Children's Hospital (BCH), and their expert feedback was incorporated into the final version. The final survey consisted of 23 questions (including demographics). The average time needed to complete the survey was 8 min (full survey and instructions in Supplementary Material). The study was reviewed and approved by the Boston Children's Hospital Institutional Review Board (IRB-P00037304). The study was granted an exemption from requiring ethics approval as it was determined by the IRB that it posed minimal risk. Participants were anonymous and provided their electronic written informed consent prior to starting the survey.

2.2. Participants

Participants were physicians, across all specialties, recruited from BCH through an email that contained a link to the REDCap survey. Data collection was from October 2021–March 2022. Physicians ($n = 1157$) were identified with the assistance of the Clinical Research Informatics Team at BCH using the following inclusion criteria: physicians (1) having an Doctor of Medicine (MD), Doctor of Osteopathic Medicine (DO), or Bachelor of medicine, Bachelor of Surgery (MBBS); and (2) working with patients between 0 and 18 years old. The contact email provided the content of the survey, purpose of the study, and participant's rights. No incentives were provided, and all responses were voluntary. After two reminder emails were sent, a total of 207 out of 1157 physicians (18%) returned their surveys—comparable to previous placebo survey response rates [36]. From the 207 returned surveys, 96 were excluded due to lack of completeness (as labeled by REDCap – for the survey to be labeled as complete by REDCap, participants had to advance through all the questions, if participants did not go through the entire survey their survey was labeled incomplete and participants were considered to quit responding to the survey) and 2 were excluded due to inconsistent information, leaving a final sample size of 109.

3. Results

3.1. Demographics and work-related characteristics

Of the 109 participants, 58% were female, 38% male, and 4% unspecified. The average age was 47.3 ± 14.2 years, and the average years of experience since graduating from medical school was 25.0 ± 10.4 . The top three specialties among the study participants were pediatric critical care and pain medicine (24%), pediatric gastroenterology (12%), and general pediatrics (10%). For other participant characteristics, see Table 1.

3.2. Current placebo practice

Almost two-thirds of surveyed physicians (61%) reported seeing an improvement due to placebo *sometimes*, and almost one-fourth (22%) reported seeing improvement *often*. Participants reported observing similar improvements for placebo by proxy (59% and 17%, respectively). However, when asked how frequently they recommend

Table 1
Demographics and work-related characteristics of physicians N = 109.

Characteristics	Value
Sex N (%)	
Male	42 (38%)
Female	63 (58%)
No answer	4 (4%)
Age, yrs., mean (SD) [range]	47.3 (14.2) [27–75]
Years of Experience, mean (SD) [range]	25.0 (10.4) [1.5–45]
Specialty N (%)	
Pediatric Critical Care and Pain Medicine	26 (24%)
Pediatric Gastroenterology	13 (12%)
General Pediatrics	11 (10%)
Adolescent Medicine	9 (8%)
Pediatric Ophthalmology	8 (7%)
Developmental Behavioral Pediatrics	7 (7%)
Pediatric Cardiology	6 (6%)
Pediatric Neurology	5 (4%)
Pediatric Endocrinology	5 (4%)
Pediatric Pulmonology, Allergy, Immunology, and Sleep Medicine	4 (4%)
Pediatric Hospitalist	3 (3%)
Genetics and Genomics	2 (2%)
Pediatric Infectious diseases	1 (1%)
Pediatric Hematology, Oncology and Stem Cell Transplantation	1 (1%)
Did not respond	8 (7%)

treatments primarily as a means to enhance the placebo effect, two-thirds of participants (67%) reported either *never* (28%) or *seldom* (39%), and only one-third (33%) reported recommending such treatments *sometimes* (29%) or *often* (4%). The majority who reported using placebos as a treatment option typically introduced it to their pediatric population as a medicine that “might help” (43%). Only 2% who use placebos prescribe them openly. In the past year, the most common treatments recommended to promote the placebo effect were physical therapy (28%), vitamins (24%), and over-the-counter analgesics (21%) (shown in Fig. 1). Thirty-two percent of physicians chose to write in

“other” treatments beyond the standard set of options provided. The top three (other) treatments that physicians reported using to promote the placebo effect were dietary recommendations, digestive aid, and melatonin. When participants recommended a treatment primarily to enhance the placebo effect, treatments were typically for occasional pain (36%), headaches (29%), anxiety disorders (29%), or discomfort due to irritable bowel syndrome (27%) (shown in Fig. 2). Finally, 9 of 10 participants stated that they tried to balance parents’ (94%) and children’s (82%) treatment expectations with realistic expectations. For participant’s placebo use in practice, see Table 2.

3.3. Placebo-related opinions

As shown in Fig. 3, the majority of surveyed physicians (62%) believed it is permissible to recommend treatments with the intention of eliciting the placebo effect, some (32%) believed it is permissible only in rare circumstances, and a small percentage (6%) believed it is never permissible. Many were optimistic that promoting therapeutic components that impact the placebo response could improve pediatric care in general. Regarding their opinions about placebo-relevant factors, such as clinicians’ characteristics and their contribution to treatment outcomes, participants reported “involvement of the patient and family in decision-making as being the largest contributor,” followed by doctor’s communication style and instilling positive treatment expectations. Regarding patients’ and parents’ characteristics, physicians reported “positive expectations of treatment” as being the largest contributor to pediatric treatment outcomes, followed by “readiness to change” and “optimism” (see Table 3).

3.4. Prior placebo-related knowledge

Although 59% of physicians stated they sometimes see improvement due to the placebo effect by proxy, almost one-third (32%) stated they were not aware of this term. Moreover, the majority reported being unaware of research regarding parental attitudes about placebos in pediatric care (73%), the effectiveness of placebos in controlling pediatric headaches/migraines (66%), or the effectiveness of placebos in

Percent of Physicians Who Recommended the Following Treatments to Enhance the Placebo Effect Within the Past Year

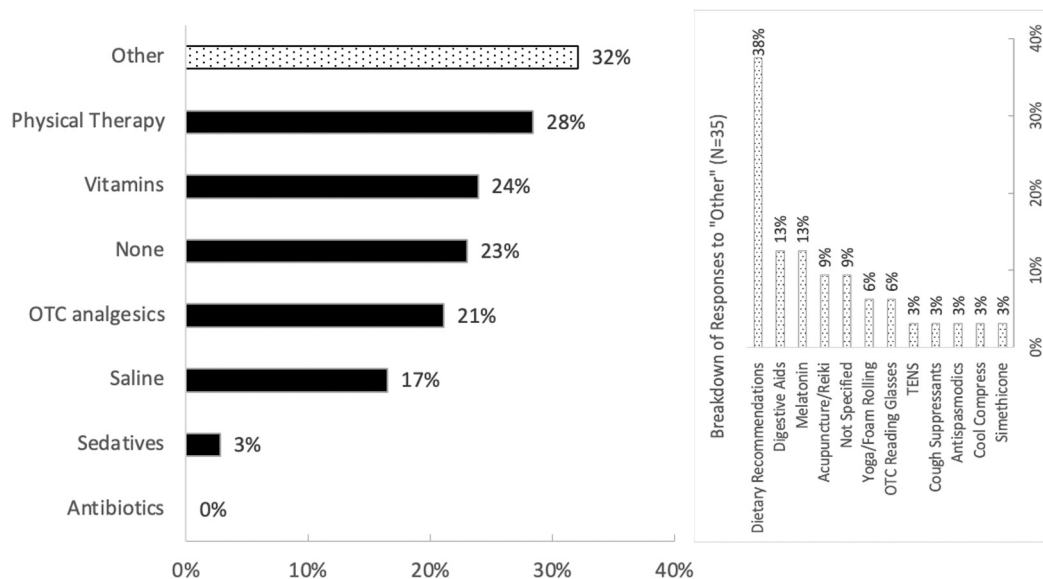


Fig. 1. Percent of physicians who would recommend placebo therapies listed on the survey with a subplot that breaks down the 35 responses to the “other” category. Note: Participants were allowed to check all that apply and input more than one answer in “other”.

Percent of Physicians Who Would Recommend Treatments to Enhance the Placebo Effect for the Following Conditions

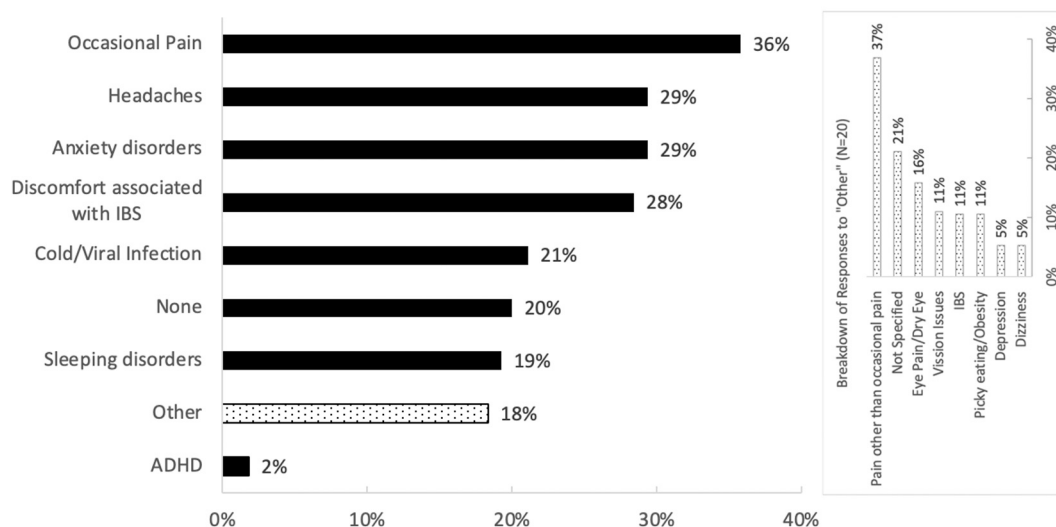


Fig. 2. Percent of physicians who would recommend placebo therapy for conditions listed on survey with a subplot that breaks down the 19 responses to the “other” category. Note: Participants were allowed to check all that apply and input more than one answer in “other”.

Table 2 Current practice (frequency and rationale) regarding placebos N = 109.

	N (%)					
	Never	Seldom	Sometimes	Often	Always	Blank
How often do you see improvement due to placebo effect?						
How often do you see improvement due to placebo by proxy?	7(6%)	11(10%)	67(62%)	24(22%)	0(0%)	0(0%)
How often do you recommend a treatment to enhance the placebo effect?	6(6%)	17(16%)	64(59%)	18(17%)	0 (0%)	4(4%)
How often do you recommend prophylactic migraine/headache treatments primarily to enhance the placebo effect?	Never 30(28%)	Seldom 43(39%)	Sometimes 32(29%)	Often 4(4%)	Always 0(0%)	Blank 0(0%)
Which statement best reflects how you typically introduce placebo treatments to children?	Never 32(29%)	Seldom 14(13%)	Sometimes 25(23%)	Often 9(8%)	Always 1(1%)	Blank 22(20%)
When you have recommended these treatments, it was mostly to:	Trigger the placebo effect 29(27%)	Placate patients 22(20%)	It is a medicine with no known effects for your condition 3(3%)	I have not recommended placebo treatments 24(22%)	Other 25(23%)	Not Applicable 6 (6%)
In your practice with children do you try to:	Enhance children's treatment expectations 20(18%)	Dampen children's treatment expectations 0 (0%)	It is a medicine not typically used for your condition but may benefit you 16(15%)	Balance children's expectations with realistic expectations 89(81%)	Not relevant - I never use this treatment approach 40(37%)	Blank 1(1%)
In your practice with children do you try to:	Enhance parents' treatment expectations 5(5%)	Dampen parents' treatment expectations 2(2%)	I have not recommended placebo treatments 24(22%)	Balance parents' expectations with realistic expectations 102(94%)	Blank 9(8%)	

controlling ADHD (77%). Notably, the 13% who were aware of placebo research in pediatric migraine reported that research findings changed their prescribing patterns in controlling headaches/migraines.

3.5. Likelihood of recommending placebo in the future

Notably, most participants (85%) stated they would prescribe placebos more often if there were safety and ethical guidelines regarding the open use of placebos. When specific questions were asked about

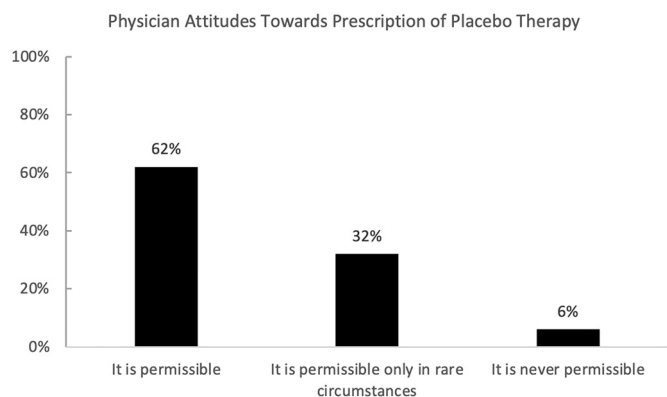


Fig. 3. Percentage of physician attitudes towards permissibility of prescribing placebo therapy.

prescribing placebos, with parental consent, in pediatric psychosomatic conditions, 78% of physicians said they would do so. Likewise, more than three-quarters of physicians (77%) were optimistic about recommending placebos for pediatric migraines, in line with scientific evidence. Furthermore, when it came to recommending conditioned placebo dose reduction to children with ADHD, only 6% of physicians were skeptical and reported being unlikely to do so.

4. Discussion

Our survey explored for the first time the perspectives of physicians on the use of placebos in pediatric settings, focusing on current practice (frequency and rationale regarding placebo usage), placebo-related opinions, placebo knowledge, and likelihood of recommending placebos in the future. Overall, physicians seem to welcome the use of placebos and placebo-related effects in pediatric settings. Regarding clinical practice, over 80% of respondents have seen improvements in

response to placebo—either sometimes or often—suggesting familiarity with the concepts, exposure to effects, and ability to detect such effects. This high recognition rate of beneficial placebo responses suggests a high occurrence of beneficial placebo effects in pediatric clinical settings, which is consistent with the large placebo response rates commonly reported in pediatric clinical trials [7,8].

4.1. Hesitation to prescribe placebo in pediatrics

When asked about the frequency with which they recommended treatments to enhance the placebo effect, only one-third of participants reported recommending these treatments in pediatric populations “sometimes” or “often”. This relatively low rate suggests that the surveyed physicians may not be comfortable with recommending placebos. This finding seemingly contradicts their given opinions on placebo. In fact, the majority felt favorably about recommending treatments to enhance the placebo effect and also considered enhancing the therapeutic components involved in placebo responses as a way of improving pediatric care in general. Physical therapy, vitamins, and over-the-counter analgesics were the most common treatments recommended to enhance the placebo effect. Prior studies of physicians treating adults indicate that vitamins are commonly prescribed as placebos [35,45], which is consistent with our findings. On the other hand, antibiotics have been previously reported as the most common active placebo prescribed to adults [36]. In sharp contrast, none of our surveyed physicians reported using antibiotics for their placeboogenic properties. This finding suggests that physicians are more cautious when prescribing unnecessary drugs to children.

When physicians recommend treatments primarily to promote the placebo effect in children, our data suggest that they typically do so for occasional pain, headaches, anxiety disorders, and discomfort due to irritable bowel syndrome. These results may reflect our participants’ specialties (largely pediatric pain medicine and gastroenterology). However, previous reports also suggest the highest clinical implementation of placebos in adults in the setting of affective and pain-

Table 3
Placebo-related opinions in pediatrics N = 109.

In your opinion, how much do the following clinician characteristics contribute to outcome? Rank 1–6 (Only largest contributor [1] displayed)	Attitude of prescriber	Prescriber communication style	Involvement of patient and their family in decision-making	Instillation of hope	Instillation of positive treatment expectancy	Contact frequency
In your opinion, how much do the following patient and parent characteristics contribute to pediatric treatment outcome? Rank 1–7 (Only largest contributor [1] displayed)	18(17%) Positive expectations of treatment	22(20%) Treatment preferences	43(39%) Ambivalence	17(16%) Optimism	20(18%) Personality	14(13%) Readiness to change
In your opinion, what are the relative contributions of the following factors on pediatric treatment outcome in oncological conditions? Rank 1–5 (Only largest contributor [1] displayed)	39(36%) Therapeutic alliance	14(13%) Active ingredient of drug	11(10%) Patient characteristics	13(12%) Parent characteristics	11(10%) Clinician characteristics	20(18%) 11 (10%)
In your opinion, what are the relative contributions of the following factors on pediatric treatment outcome in physical trauma? Rank 1–5 (Only largest contributor [1] displayed)	25(23%) Therapeutic alliance	47(43%) Active ingredient of drug	15(14%) Patient characteristics	8(7%) Parent characteristics	7(6%) Clinician characteristics	
In your opinion, what are the relative contributions of the following factors on pediatric treatment outcome in psychosomatic conditions? Rank 1–5 (Only largest contributor [1] displayed)	22(20%) Therapeutic alliance	26(24%) Active ingredient of drug	28(26%) Patient characteristics	6(6%) Parent characteristics	12(11%) Clinician characteristics	
	50(46%)	12(11%)	36(33%)	22(20%)	11(10%)	

Note: Participants were allowed to give the same ranking to all the characteristics/contributors, if they thought they are equally important. Hence, the sum could be above or below n = 109.

related disorders [45]. Among patients' and parents' characteristics most relevant in affecting pediatric treatment outcomes, our surveyed physicians emphasized "positive expectations", followed by "readiness to change" and "optimism". However, when it comes to managing parents and children expectations, similar to previous findings with adults [46], physicians also seem to favor realistic expectations as opposed to positive expectations in the pediatric field. Hence, promoting patients positive expectations, known to enhance the therapeutic benefits of most interventions, seems to be underused in both adult and pediatric clinic.

Overall, our data reflects the awareness that clinicians place on the role played by placebo-related components in pediatric settings. Similar data have been reported from our previous survey showing parents' positive opinions towards placebos and placebo-related components in pediatric settings [41]. Even though most of the surveyed physicians had positive attitudes towards placebos in pediatric clinical practice, more than two-thirds reported never or seldom recommending a treatment primarily for enhancing the placebo effect. Similar discrepancies regarding physicians' opinions and practices have been previously reported by US orthopedic surgeons. In particular, although orthopedic surgeons described open-label placebo treatments to be ethical and effective, they were unwilling to use them in their own practice [47]. Physicians may not be willing to prescribe placebos due to ethical constraints and lack of supporting guidelines in clinical settings, especially with children.

4.2. Solutions for systematic implementation of placebo

In our study, roughly nine of ten physicians stated they would prescribe placebo treatments more often if there were safety and ethical guidelines in place. However, the majority who use placebos as a treatment option typically introduce them as a medicine that "might help". Only two participants reported prescribing placebos openly. This is consistent with previous surveys reporting that, in clinical practice, physicians generally recommend hidden or deceptive placebo instead of open-label placebo [35,45]. This choice may be due to lack of knowledge regarding advances in placebo research. Historically, placebo administration has been associated with the use of deception, considered unethical by most medical societies. Nevertheless, accumulating evidence has shown that open-label placebos can be as effective as deceptive placebos [5,15,48]. Open-label placebos are also known to be beneficial as a dose reduction treatment, allowing patients to have the same therapeutic effect while reducing drug intake and associated side effects [20,49–51]. This becomes particularly compelling to parents and physicians who generally want to see children treated with the lowest effective drug doses. Accordingly, previous survey data show that more than two-thirds of parents were interested in having their children take placebo because they believed it would allow their children to take lower doses of medication and result in fewer medication side effects [21]. Open-label placebos, which are consistent with the values of informed consent and patient autonomy, may represent a powerful, safe and ethical new methodology to replace, augment, or extend the effects of drugs, thus reducing drug loads and decreasing side effects in pediatric patients [52].

Placebo researchers across interdisciplinary fields have developed clinical recommendations, and a preliminary taxonomy [53] has been proposed to guide ethical and effective clinical translation of placebo research [54,55]. These authors propose that placebos should be considered a standard treatment, open-label placebos should be used instead of hidden placebos, the patient-physician relationship should be built with trust and support to enhance the placebo effect, and training and education on placebo effects should be more common [54,55]. Since the majority of physicians in our survey were unaware of advances in placebo research, but were favorably inclined towards the implementation of placebos in pediatric clinical practice, the addition of training and guidelines with regards to, for instance, the promotion of

positive expectations in clinical practice has great potential for improving pediatric care. Because placebo responses are a part of virtually any therapeutic intervention, during the doctor-patient encounter, physicians hold the potential to optimize pediatric care by exerting a positive influence on the levels on the child and parents' anxiety and stress, and by promoting positive treatment expectations. Disregarding the clinicians' potential to maximize placebo responses can be considered suboptimal pediatric care. For detailed recommendations on how to optimize therapeutic effects by harnessing placebo responses in pediatric care, we direct the reader to our previous work [8].

4.3. Study limitations

Our findings must be interpreted in the context of the study limitations. Our survey was conducted solely at Boston's Children Hospital, which is likely not representative of US medical centers. Moreover, our response rate was relatively small. Although similarly low response rates were reported in previous surveys [36], this could indicate selection bias such that the physicians who are most interested and knowledgeable about placebo effects may be more likely to return a survey. This is in line with our surveyed physicians' specialties (Table 1), most of which treated conditions known for higher placebo responses. In addition, since we did not select our responders based on specialty and some of our survey questions mentioned specific conditions, these specific questions were not relevant to all responders' practices, which may have in turn influenced the results. Future surveys should be tailored to various pediatric specialties to determine whether there is variance across specialties in physicians' attitudes and opinions on the acceptability and effectiveness of placebo treatment with pediatric patients. Since previous research as shown that in clinical practice, pure placebos (ie., saline injections and sugar pills) are seldom used [45], our survey was not focused on pure placebos and did not provide definitions of pure or impure (ie., active interventions thought to have no specific activity on the condition being treated) placebos, which may have been helpful when answering question nr 8 of the survey. Notably, however, none of the participants mentioned that this question was unclear. On the contrary, many of our responders seemed to enjoy taking the survey and left positive comments about it.

5. Conclusion

Our data are the first to show that pediatric physicians are favorably inclined towards placebos and their beneficial effects; but they also show that physicians would feel more confident using placebos if they were more aware of the scientific data supporting open-label placebos and if relevant medical societies promulgated clinical practice guidelines regarding the appropriate and standard usage of placebos. In other research, parents and their children have also endorsed non-deceptive, open-label placebo as a method to potentially leverage placebo responses in pediatric patients [21,41]. Enhancing these effects may be an effective strategy for improving outcomes in pediatrics; and parents, patients, and physicians seem to be open to the possibility of harnessing the placebo effect to benefit pediatric patients. This general acceptance highlights the clinical relevance of open-label placebo research and the importance of developing, disseminating, and implementing specific guidelines to meet the current needs of patients and physicians alike.

Funding sources

Dr. Vanda Faria was supported by the Swedish Research council (grant number 437-2014-6767). The other authors received no additional funding. The Swedish Research Council had no role in the study design, data collection, analysis, or in the decision of writing and submitting this paper for publication.

Author contributions

Dr. Vanda Faria, Professor David Borsook, and Dr. Eric A Moulton conceptualized and designed the study, designed and developed the survey instrument, coordinated and supervised data collection, interpreted the data, drafted the initial manuscript and critically reviewed and revised the manuscript.

Dr. Alyssa Lebel, Professor Ted Kaptchuk, Professor Irving Kirsch, and Professor John M Kelley, conceptualized and designed the study, designed and developed the survey instrument, interpreted the data and critically reviewed and revised the manuscript.

Cameron Talbert and Nathan Goturi, designed the data collection instrument, collected the data, carried out the initial analysis, drafted the initial manuscript and critically reviewed and revised the manuscript.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Declaration of Competing Interest

Authors declare they have no conflicts of interest relevant to this article to disclose.

Data availability

The data that support the findings of this study are available within the article.

Acknowledgement

We thank the physicians at BCH for their participation, the Clinical Research Informatics Team at BCH for assistance with recruitment (participant selection), Dr. Scott Holmes at BCH for critical revision of the survey instrument, Robert Labadie for assistance with data collection and Jane Patrick at BCH for proofreading.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jpsychores.2023.111421>.

References

- T.J. Kaptchuk, F.G. Miller, Placebo effects in medicine, *N. Engl. J. Med.* 373 (1) (2015) 8–9.
- L. Colloca, A.J. Barsky, Placebo and nocebo effects, *N. Engl. J. Med.* 382 (6) (2020) 554–561.
- V. Faria, M. Fredrikson, T. Furmark, Imaging the placebo response: a neurofunctional review, *Eur. Neuropsychopharmacol.* 18 (7) (2008) 473–485.
- F. Benedetti, Placebo effects: from the neurobiological paradigm to translational implications, *Neuron.* 84 (3) (2014) 623–637.
- T.J. Kaptchuk, C.C. Hemond, F.G. Miller, Placebos in chronic pain: evidence, theory, ethics, and use in clinical practice, *Bmj.* 370 (2020), m1668.
- B.E. Wampold, T. Minami, S.C. Tierney, T.W. Baskin, K.S. Bhati, The placebo is powerful: estimating placebo effects in medicine and psychotherapy from randomized clinical trials, *J. Clin. Psychol.* 61 (7) (2005) 835–854.
- K. Weimer, M.D. Gulewitsch, A.A. Schlarb, J. Schwille-Kiuntke, S. Klosterhalfen, P. Enck, Placebo effects in children: a review, *Pediatr. Res.* 74 (1) (2013) 96–102.
- V. Faria, C. Linnman, A. Lebel, D. Borsook, Harnessing the placebo effect in pediatric migraine clinic, *J. Pediatr.* 165 (4) (2014) 659–665.
- S. Rheims, M. Cucherat, A. Arzimanoglou, P. Ryvlin, Greater response to placebo in children than in adults: a systematic review and meta-analysis in drug-resistant partial epilepsy, *PLoS Med.* 5 (8) (2008), e166.
- T.W. Ho, X. Fan, A. Rodgers, C.R. Lines, P. Winner, R.E. Shapiro, Age effects on placebo response rates in clinical trials of acute agents for migraine: pooled analysis of rizatriptan trials in adults, *Cephalalgia.* 29 (7) (2009) 711–718.
- H.J. Maas, M. Danhof, O.E. Della Pasqua, Analysis of the relationship between age and treatment response in migraine, *Cephalalgia.* 29 (7) (2009) 772–780.
- R.E. Shaddy, S.C. Denne, Clinical report—guidelines for the ethical conduct of studies to evaluate drugs in pediatric populations, *Pediatrics.* 125 (4) (2010) 850–860.
- B. Trogen, A. Caplan, P. Klass, The ethics of open-label placebos in pediatrics, *Pediatrics.* 140 (2) (2017).
- S. Nurko, M. Saps, J. Kossowsky, S.R. Zion, C. Di Lorenzo, K. Vaz, et al., Effect of open-label placebo on children and adolescents with functional abdominal pain or irritable bowel syndrome: a randomized clinical trial, *JAMA Pediatr.* 176 (4) (2022) 349–356.
- A. Lembo, J.M. Kelley, J. Nee, S. Ballou, J. Iturrino, V. Cheng, et al., Open-label placebo vs double-blind placebo for irritable bowel syndrome: a randomized clinical trial, *Pain.* 162 (9) (2021) 2428–2435.
- T.J. Kaptchuk, E. Friedlander, J.M. Kelley, M.N. Sanchez, E. Kokkotou, J.P. Singer, et al., Placebos without deception: a randomized controlled trial in irritable bowel syndrome, *PLoS One* 5 (12) (2010), e15591.
- C. Carvalho, J.M. Caetano, L. Cunha, P. Rebouta, T.J. Kaptchuk, I. Kirsch, Open-label placebo treatment in chronic low back pain: a randomized controlled trial, *Pain.* 157 (12) (2016) 2766–2772.
- M. von Wernsdorff, M. Loef, B. Tuschen-Caffier, S. Schmidt, Effects of open-label placebos in clinical trials: a systematic review and meta-analysis, *Sci. Rep.* 11 (1) (2021) 3855.
- C. Locher, A. Frey Nascimento, I. Kirsch, J. Kossowsky, A. Meyer, J. Gaab, Is the rationale more important than deception? A randomized controlled trial of open-label placebo analgesia, *Pain.* 158 (12) (2017) 2320–2328.
- A.D. Sandler, C.E. Glesne, J.W. Bodfish, Conditioned placebo dose reduction: a new treatment in attention-deficit hyperactivity disorder? *J. Dev. Behav. Pediatr.* 31 (5) (2010) 369–375.
- A. Sandler, C. Glesne, G. Geller, Children's and parents' perspectives on open-label use of placebos in the treatment of ADHD, *Child Care Health Dev.* 34 (1) (2008) 111–120.
- A.D. Sandler, J.W. Bodfish, Open-label use of placebos in the treatment of ADHD: a pilot study, *Child Care Health Dev.* 34 (1) (2008) 104–110.
- L. Colloca, L. Lopiano, M. Lanotte, F. Benedetti, Overt versus covert treatment for pain, anxiety, and Parkinson's disease, *Lancet Neurol.* 3 (11) (2004) 679–684.
- U. Bingel, V. Wanigasekera, K. Wiech, R. Ni Mhuiricheartaigh, M.C. Lee, M. Ploner, et al., The effect of treatment expectation on drug efficacy: imaging the analgesic benefit of the opioid remifentanyl, *Sci. Transl. Med.* 3 (70) (2011), 70ra14.
- V. Faria, M. Gingnell, J.M. Hoppe, O. Hjorth, I. Alaia, A. Frick, et al., Do you believe it? verbal suggestions influence the clinical and neural effects of escitalopram in social anxiety disorder: a randomized trial, *EBioMedicine.* 24 (2017) 179–188.
- R.M. Smits, D.S. Veldhuijzen, H. van Middendorp, M.J.E. van der Heijden, M. van Dijk, A.W.M. Evers, Integrating placebo effects in general practice: a cross-sectional survey to investigate perspectives from health care professionals in the Netherlands, *Front. Psychiatry.* 12 (2021), 768135.
- R.M. Smits, D.S. Veldhuijzen, T. Olde Hartman, K.J. Peerdeman, L.M. Van Vliet, H. Van Middendorp, et al., Explaining placebo effects in an online survey study: does 'Pavlov' ring a bell? *PLoS One* 16 (3) (2021), e0247103.
- A. Palese, L. Cadorin, M. Testa, T. Geri, L. Colloca, G. Rossetini, Contextual factors triggering placebo and nocebo effects in nursing practice: findings from a national cross-sectional study, *J. Clin. Nurs.* 28 (9–10) (2019) 1966–1978.
- G. Rossetini, A. Palese, T. Geri, M. Mirandola, F. Tortella, M. Testa, The knowledge of contextual factors as triggers of placebo and nocebo effects in patients with musculoskeletal pain: findings from a National Survey, *Front. Psychiatry.* 10 (2019) 478.
- G. Rossetini, A. Palese, T. Geri, M. Fiorio, L. Colloca, M. Testa, Physical therapists' perspectives on using contextual factors in clinical practice: findings from an Italian national survey, *PLoS One* 13 (11) (2018), e0208159.
- M.H. Bernstein, C. Locher, S. Stewart-Ferrer, S. Buergler, C.M. DesRoches, M. L. Dossett, et al., Primary care providers' use of and attitudes towards placebos: an exploratory focus group study with US physicians, *Br. J. Health Psychol.* 25 (3) (2020) 596–614.
- R. Fent, T. Rosemann, M. Fässler, O. Senn, C.A. Huber, The use of pure and impure placebo interventions in primary care - a qualitative approach, *BMC Fam. Pract.* 12 (2011) 11.
- K. Meissner, L. Höfner, M. Fässler, K. Linde, Widespread use of pure and impure placebo interventions by GPs in Germany, *Fam. Pract.* 29 (1) (2012) 79–85.
- S.C. Hull, L. Colloca, A. Avins, N.P. Gordon, C.P. Somkin, T.J. Kaptchuk, et al., Patients' attitudes about the use of placebo treatments: telephone survey, *Bmj.* 347 (2013), f3757.
- J.C. Tilburt, E.J. Emanuel, T.J. Kaptchuk, F.A. Curlin, F.G. Miller, Prescribing "placebo treatments": results of national survey of US internists and rheumatologists, *Bmj.* 337 (2008), a1938.
- K. Faasse, B. Colagiuri, Placebos in Australian general practice: a national survey of physician use, beliefs and attitudes, *Aust. J. Gen. Pract.* 48 (12) (2019) 876–882.
- A. Raz, N. Campbell, D. Guindi, C. Holcroft, C. Déry, O. Cukier, Placebos in clinical practice: comparing attitudes, beliefs, and patterns of use between academic psychiatrists and nonpsychiatrists, *Can. J. Psychiatr.* 56 (4) (2011) 198–208.
- R. Sherman, J. Hickner, Academic physicians use placebos in clinical practice and believe in the mind-body connection, *J. Gen. Intern. Med.* 23 (1) (2008) 7–10.
- R. Ortiz, S. Chandros Hull, L. Colloca, Patient attitudes about the clinical use of placebo: qualitative perspectives from a telephone survey, *BMJ Open* 6 (4) (2016), e011012.
- D.J. Grelotti, T.J. Kaptchuk, Placebo by proxy, *Bmj.* 343 (2011), d4345.
- V. Faria, J. Kossowsky, M.P. Petkov, T.J. Kaptchuk, I. Kirsch, A. Lebel, et al., Parental attitudes about placebo use in children, *J. Pediatr.* 181 (2017), 272–8.e10.
- P.A. Harris, R. Taylor, B.L. Minor, V. Elliott, M. Fernandez, L. O'Neal, et al., The REDCap consortium: building an international community of software platform partners, *J. Biomed. Inform.* 95 (2019), 103208.
- P.A. Harris, R. Taylor, R. Thielke, J. Payne, N. Gonzalez, J.G. Conde, Research electronic data capture (REDCap)—a metadata-driven methodology and workflow

- process for providing translational research informatics support, *J. Biomed. Inform.* 42 (2) (2009) 377–381.
- [44] S. Vijapura, J.A. Laferton, D. Mintz, T.J. Kaptchuk, D. Wolfe, Psychiatrists' attitudes toward non-pharmacologic factors within the context of antidepressant pharmacotherapy, *Acad. Psychiatry* 40 (5) (2016) 783–789.
- [45] K. Linde, O. Atmann, K. Meissner, A. Schneider, R. Meister, L. Kriston, et al., How often do general practitioners use placebos and non-specific interventions? Systematic review and meta-analysis of surveys, *PLoS One* 13 (8) (2018), e0202211.
- [46] G. Ongaro, S. Ballou, T. Kube, J. Haas, T.J. Kaptchuk, Doctors speak: a qualitative study of physicians' prescribing of antidepressants in functional bowel disorders, *Cult. Med. Psychiatry* (2022), <https://doi.org/10.1007/s11013-022-09795-0>. Epub ahead of print. PMID: 35764862.
- [47] M.H. Bernstein, M. Rosenfield, N. Fuchs, M. Magill, C.R. Blease, F.L. Beaudoin, et al., How orthopedic surgeons view open label placebo pills: ethical and effective, but opposed to personal use, *J. Psychosom. Res.* 151 (2021), 110638.
- [48] S. Kam-Hansen, M. Jakubowski, J.M. Kelley, I. Kirsch, D.C. Hoaglin, T.J. Kaptchuk, et al., Altered placebo and drug labeling changes the outcome of episodic migraine attacks, *Sci. Transl. Med.* 6 (218) (2014), 218ra5.
- [49] K.M. Flowers, M.E. Patton, V.J. Hruschak, K.G. Fields, E. Schwartz, J. Zeballos, et al., Conditioned open-label placebo for opioid reduction after spine surgery: a randomized controlled trial, *Pain*. 162 (6) (2021) 1828–1839.
- [50] L. Colloca, P. Enck, D. DeGrazia, Relieving pain using dose-extending placebos: a scoping review, *Pain*. 157 (8) (2016) 1590–1598.
- [51] B.K. Doering, W. Rief, Utilizing placebo mechanisms for dose reduction in pharmacotherapy, *Trends Pharmacol. Sci.* 33 (3) (2012) 165–172.
- [52] C. Blease, L. Colloca, T.J. Kaptchuk, Are open-label placebos ethical? Informed consent and ethical equivocations, *Bioethics*. 30 (6) (2016) 407–414.
- [53] F.L. Bishop, B. Coghlan, A.W. Geraghty, H. Everitt, P. Little, M.M. Holmes, et al., What techniques might be used to harness placebo effects in non-malignant pain? A literature review and survey to develop a taxonomy, *BMJ Open* 7 (6) (2017), e015516.
- [54] A.W.M. Evers, L. Colloca, C. Blease, M. Annoni, L.Y. Atlas, F. Benedetti, et al., Implications of placebo and nocebo effects for clinical practice: expert consensus, *Psychother. Psychosom.* 87 (4) (2018) 204–210.
- [55] A.W.M. Evers, L. Colloca, C. Blease, J. Gaab, K.B. Jensen, L.Y. Atlas, et al., What should clinicians tell patients about placebo and nocebo effects? Practical considerations based on expert consensus, *Psychother. Psychosom.* 90 (1) (2021) 49–56.