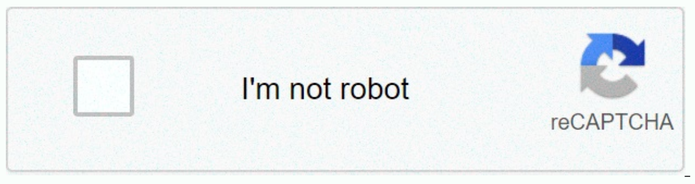

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Explain the difference between a single-blind and a double-blind experiment. chegg

When conducting clinical trials, the two main models one can use are single blind and double-blind trials. Choosing the right trial is important because it can affect the outcome of the trial or cause errors. The ideal model should be chosen based on the type of trial and other variables. In clinical trials, there are usually two groups of people conducting experiments. Members of one group are given a placebo, while members of another group are given treatments that are being studied. As this compares the effectiveness of the treatment to a placebo. In a single blind study, participants in clinical trials do not know if they are receiving a placebo or actual treatment. This is done to reduce the risk of error, because some participants may produce false results if they know they are taking a placebo or medication. In a double-blind study, both participants and experimenters did not know which group got a placebo and which received experimental treatment. This is considered to be an excellent model of clinical research because it eliminates the results produced due to the placebo effect, as well as observer bias by the experimenter. The fact that the experimenter does not know the group that received the placebo or experimental drug means that the risk of conscious and unconscious observer bias is reduced and makes the study more accurate. Jan M. Keppel Hesselinck, 1 David J. Kopsky, 2 Arun K. Bascal 3 1 Neuropathic Pain Institute, Bosch en Duyne, Netherlands; 2 Neuropathic Pain Institute, Amsterdam, Netherlands; 3Pain Management Center, Charing Cross Hospital Imperial Healthcare NHS Trust, London, U.K. Abstract: At our center in the Netherlands, patients who suffer from symmetrical peripheral neuropathic pain and very often receive treatment resistant to analgesics recommended in the guidelines are treated exclusively. For the treatment of neuropathic pain in treatment-resistant patients, we have developed a number of combined topical formulations, including classic analgesics such as ketamine, baclofen, amitriptyline and phenytoin. Single-blind and double-blind placebo-controlled response trials were developed to identify estimated responders and exclude (early) placebo responses. This test can be performed when the patient has a symmetrical multi-neurological disorder with a pain score difference of 1 point or less on the 11-point numerical evaluation scale (NRS) between bilateral pain regions. Placebo cream is applied to one area (e.g. left foot) and active cream to other areas (e.g. right foot). Within a 30-minute time frame, the patient is considered a responder if at least assessing the difference in painPoints on NRS between the bilateral areas to which the active cream and placebo cream are applied. You can easily conduct a response test at the first consultation. This paper explores the ethical context of using placebos in clinical settings in a single-blind and double-blind way to improve and personalize the treatment of neuropathic pain outside the context of formal clinical trials. Keywords: Ethics, trial, topic, treatment, enrichment neuropathic pain generally have an estimated morbidity rate of 7% to 10%. Patients with one neuropathic pain account for about a third of the patients seen in pain clinics. Often, they consulted neurologists, anesthesiologists, and other pain specialists without an effective treatment being successfully identified. Patients reported that the treatment was not effective enough to produce meaningful analgesity, or that the patient had suffered from undesirable adverse events, leading to discontinuation of treatment. The authors successfully developed a number of combined topical creams, including classic analgesics such as ketamine, baclofen, amitriptyline and phenytoin, for the treatment of pain in patients with indigentation and patients who cannot tolerate systemic medications. Formulations of these formulations can be classified as off-label use. Off-label use refers to the practice of prescribing or ordering drugs for use that are not recognized as official labeling by national licensing authorities. 2015.6 Patients suffering from peripheral neuropathic pain frequently complained of severe pain in both legs and/or lower limbs, with more than 5 million pharmacy composite products dispensed. Most patients noted that within 30 minutes of the application of topical analgesics there was a perceptible reduction in pain. This led us to initially develop an open response test, comparing the active cream applied to one foot to not applying the cream to the other. We then developed a single-blind, placebo-controlled response test to identify estimated responders and exclude (early) placebo responses. 7Th test can be performed when the patient has a symmetrical multiple neuropathy with a pain difference that is not >1 point on a numerical evaluation scale (NRS) between bilateral pain regions. In one area (for example, the left foot), a placebo cream is applied to the other area (e.g., the right foot).Active cream. Within a 30-minute time frame, the patient is considered a responder if they evaluate a pain difference of at least 2 points on NRS between the bilateral regions to which the active cream and placebo cream are applied (Figure 1). Figure 1 Initial and extended double-blind response test abbreviation: NRS, numerical evaluation scale. We are currently evaluating the use of double-blind, placebo-controlled response tests that can also be used in routine clinical settings when considering and evaluating a variety of topical analgesic options. We state that the essence of this new approach is to maximize the chances of finding the best treatment for patients while minimizing the risk of a placebo response. We present an approach, followed by a discussion about the clinical and ethical context in which these placebo-controlled blind response tests are used, and a therapeutic paradigm designed to distinguish responders on placebo or active creams in light of personalized pain therapy. After developing topical creams containing established co-analgesics for off-label use in test peripheral neuropathic pain using active creams and placebos to evaluate responders, our first approach was to start by prescribing one of those creams to patients. For example, amitriptyline 10% cream for the treatment of PDN. A follow-up consultation was held after a week or two, and the patient reported the following one - a considerable reduction in pain, sometimes a slight reduction in pain, or no response at all. We also checked and documented local or systemic adverse events. To avoid delays in effective treatment and to screen for local adverse events, we then began to test the effects of analgesic creams during consultation by applying one painkiller cream to one leg and different painkillers or no creams to the other. This was logical because most patients suffer from painful multi-neurological disorders with often equivalent pain intensity in both legs and/or lower limbs. Therefore, the left-right comparison was achievable compared to using only a single topical analgesic on one leg. Patients who responded to topical analgesics reported to us that there was a reduction in pain within 5-30 minutes. Our observation is that when patients reported a clear analgesic effect in this short period of time, they often showed confidence in treatment, which was especially high in those who had previously unders received various other treatments but had no good results. However, in the following consultation, many patients pointed out that the analgesic effect decreased after using the cream for several days or weeks; This caused us to develop an active, tested, single-blind, placebo-controlled response testCream. The essence of this new approach is to maximize the chances of finding the most suitable treatment for patients during their first visit, while reducing the incidence of true placebo response and treatment delays, including follow-up based on double-blind response tests. The use of placebo is generally unacceptable in clinical practices outside the context of clinical trials; Single-blind placebo-controlled response tests can be formally qualified as perhaps the simplest diversity of the N-of-1 treatment paradigm, since at least blind evaluation of results by patients is possible. Single-blind response tests can be performed when the patient has two similar, predominantly bilateral anatomical positions with similar pain intensity. In patients with peripheral neuropathic pain, the condition is almost always present in both the front of the foot, the entire area of the foot, or the more progressive conditions of both legs and lower limbs. The reason for ethnism is in peripheral neuropathy, in the longest nerves to reach the front of the foot due to toxicity (e.g., hyperglycemia, high alcohol consumption, chemotherapy, high vitamin B6 intake) or deficiency (vitamin B12 deficiency and hypothyroidism). A single-blind response test can be performed when the maximum difference in NRS in pain intensity between two anatomically similar regions (e.g., left and right legs) is 1 point. The doctor randomizes the active cream and placebo cream and explains to the patient that two different creams are applied to each foot. The test duration is up to 30 minutes, and after a response test, the doctor blinds the treatment and results, after which the implications of the test are discussed directly with the patient. The patient is considered an initial responder if the difference in pain is 2 points or more on the NRS between the two areas after active and placebo cream application. It is based on the recommendations of the European Medicines Agency, which is defined by responders as a two-point reduction in NRS in favor of aggressive treatment. They then received the observation that during the first two weeks of treatment, responders rarely complained of a reduced analgesic effect. So it seems that responders to the test remain as responders even with repeated use of analgesic creams. As a further development to challenge the therapeutic effects of blended creams, we are currently developing and evaluating a double-blind placebo-controlled trial design. The purpose of this test is to make a purposeMinimize the pharmacological effects of the compound, patient expectations and clinicians' effects of treatment. This increases the chances of choosing the best initial treatment for the patient. A double-blind response test is performed, but neither the doctor or the patient know which tube contains active cream or placebo cream, and for simplicity, we call these creams A and cream B, cream A is applied on one leg, and cream B is applied to the other. After 30 minutes, the tube is invisible and the results and results for future treatment are discussed (Figure 1). The second step is to observe the long-term effects in the initial responder on analgesic creams and use extended response tests between 1 and several weeks, in line with the more extended N-of-1 treatment paradigm. For example, in paradigm patients of such an extended N-of-1 treatment paradigm, two randomized blind creams (A and B) can be received, one of which is active and the other placebo cream. Cream A is applied during the first treatment period (for example, week 1), and cream B is applied to the second treatment period (for example, week 2). If sufficient analgesity does not result during the treatment period, cream C can be applied. Cream C includes the active cream evaluated during the initial response test. After a long test period (e.g., 2 weeks), the patient reports to the doctor the cream found to have the best analgesic effect, for example, using the impression of the patient's overall change after 2 weeks of our test. In all cases, in order to use a placebo in the clinic in the above way, a special context is required based on full informed consent and mutual trust that this step is included to reduce prejudice for the benefit of the patient. The ethical context is discussed here. Placebo use in clinical use Touwen and Enberts introduced an ethical debate about the use of placebos, both clinically as well as in the setting of the study .11 they presented an operational definition of placebo intervention, specific pharmacological of behavior according to current standards of knowledge as an intervention that doctors believe in. As they believe they do not have biochemical or physical mechanisms, to be treated states authors focused on two ethical issues when describing placebos in clinical practice. First, the prescription of a placebo in clinical practice is deceptive because the patient is not informed that non-efficacy therapy is being given, which can harm the doctor's trust and the patient's autonomy can be violated. Secondly, the prescription of placebo increases the risk during treatment.On the results of modern studies in the field of placebo, patients noted that they could not clearly distinguish between proven and effective treatments and treatments for which the mechanism of behavior is unknown. Therefore, they feel that there is limited room to prescribe a placebo in clinical practice. The key issue for Towen and Emberts is that it is supported by more literature using placebos in clinical settings, misleading patients and gaining transparent, reliable, informed consent. It seems important to understand that the effects of placebo and nocebo are always present in regular clinical care, even when no placebo is given. It is used to discuss in detail the clinical approach of Guyatt and his group at McMaster University in Ontario, Canada. In 1988, they published an important paper on the use of placebos in the context of N-of-1 randomized clinical trials (RCT): A clinician's guide to conducting randomized trials in individual patients. It is recognized as a milestone paper and as the first practical approach to encourage clinicians to conduct N-of-1 trials. The N-of-1 trial is now called a promising way to advance personalized medicine and a way to gain insight into comparative therapeutic effects among a wide variety of patients. A few years later, the authors tested an approach to repositioning the use of amitriptyline, a new off-label indication in chronic pain conditions, at which point they were diagnosed with fibrousitis (fibromyalgia), and in that paper defined the great value that N-of-1 RCT could have in the early stages of development designed for symptoms.For chronic diseases, who who who have biological effects ending immediately after withdrawal, in line with previous recommendations. This guideline (1988) defines many questions for entering the RCT, and those important questions are listed in Table 1. Table 1 N-of-1 Key Questions for RCT Abbreviations: RCT, Randomized Clinical Trials. The N-of-1 treatment paradigm has not yet been used in clinical settings, has not been widely explained, and is not practiced. However, such an approach is highly relevant by answering many practical questions, such as the field of chronic pain and attention deficit erring disorder, and in relation to estimated side effects, the N-of-1 clinical approach is considered compatible with the final end point of clinical practice. As well as a potential N-of-1 study, the McMaster Group's key questions followed step-by-step. There are two possible steps in adapting the single-blind and double-blind control N-of-1 treatment paradigm for active vs. placebo creams and evaluating responders to the realized anti-cream. The first step is to identify the initial responder in an initial single or double-blind response test. This will take at most 30 minutes. The second step is to provide the responder with an extended response test for at least one week for the first response test. We can think of our two first placebo-controlled response tests as being based on the simplest design of the N-of-1 treatment paradigm. In practice, the first and extended response tests have been shown to be achievable. The ethical question of whether such a placebo-controlled test paradigm is justified for patients without the approval of the Agency Review Board (IRB) can be answered based on a number of specific questions designed by the McMasters group. Six follow-up questions (2a-2f) are related to individual patient levels. Each question is followed by an answer related to the test modality. The last answer question (3a-3c) analyzes whether a trial is possible in clinical settings. 1a. Is the efficacy of the treatment really questionable? In the Netherlands, it is prescribed as a composite cream for off-label use in peripheral neuropathic pain. Therefore, the effectiveness of the treatment has not been proven. The same applies to other co-analgesics used in formulation topical formulations. 1b. If the treatment is effective, will it be long-term?The author gained experience in patent treatment and reporting of therapeutic effects. Already there are non-responders, our observation is that about 30% to 40% of patients suffering from peripheral neuropathic pain are responders, and most of the responders use creams in the long run. Currently, we have been documenting the long-term effects of patients for more than 3 years using phenytoin 10% cream. Are patients eager to work together in the design and implementation of N-of-1 RCT? We are currently looking for a willingness for patients to participate in double-blind N-of-1 RCT.2a. Does the treatment have a rapid onset? Most responders report feeling a clear and clinical effective reduction in pain, often early, within 20-30 minutes. 2b. Does the treatment stop acting immediately after discontinuation? As soon as the patient stops using the cream, the pain reappears after 3-72 hours according to our observations. 2c. Is the optimal duration of treatment possible? Peripheral neuropathic pain is a chronic disease, and Guyatt and others 19 authors mention the need for a treatment period of at least 10 days. In our case, the duration of treatment is much longer and the effect can be continuously evaluated repeatedly. In the case of a double-blind N-of-1 study, there can be at least two pairs of treatment periods before discontinuing the trial. 2d. Can clinically relevant targets be measured? Based on the scoring pain of patients with NRS.22 2e, there is consensus on the best way to measure pain. Can we establish sensible standards to stop trials? As soon as the clinical decline in pain is <30% or <2 points of NRS from baseline, we have patients decide whether pain relief is still relevant or whether stopping and trying a new cream is a better option. Since we have developed a number of analgesic creams, we may be able to offer potential options or explore other systemic alternatives. 2f. Is a blind run-in period necessary? The authors feel that an open run-in period can be used to determine the optimal concentration of side effects and topical analgesics. For an inacontable dose response to a .7 phenytoin 10% cream where tolerability is usually not an issue, we can rate high doses, for example, 30%.23 3a in the same session. Is there a pharmacist who can help me? 3b. Is there a strategy in place to interpret the data? The authors of the 1988 paper suggested many simple approaches to analyzing the data, and further noted that the use of N-of-1 RCT to improve patient care was not dependent on statisticsof the result. Strategies for randomizing, double-blinding, replicating, and quantifying results allow for better analysis of effects that are usually difficult in clinics. 3c. Is the trial ethical? This question is related to the question of whether N-of-1 RCT is clinical or research. According to the McMasters Group, such businesses are both, and argue that N-of-1 RCT can be part of routine clinical practice and should be (underlined by us). This approach is considered ethically correct if the patient is informed of the business, if there is no element of deception and the patient has the freedom to discontinue the trial at any time. This element of consent is so important and relevant that I'll go into a bit more detail. Patient Information during Informed Consent In 2008, a report by the American Medical Association's Council on Ethics and Justice Issues on placebo use in clinical settings was published. 24 The doctor may use the placebo for diagnosis or treatment only if the patient is informed and consents to its use. This is clearly consistent with the above literature, which requires transparency, trust and informed consent to avoid fraud. To achieve such transparency, Richtenberg and his team proposed the following wording for the use of a placebo during informed consent procedure 14: I would like to provide tablets that I believe will help alleviate your suffering. I don't know exactly how it works. Active comparator Richtenberg used the following wording: I have other drugs that provide the mechanism is clearer, but I'm not sure they work better for you, and they can also have more serious side effects. Another benefit of this description method involves its many definitions, associations and misconceptions placebo is avoided. At our center, we implemented Richtenberg's ethical approach and introduced a placebo-controlled response test to patients as follows: I would like to offer you a choice between two creams that I think will help reduce your pain. I don't know exactly how one of these creams works. And while I contain one other cream who has a clear mechanism, I'm not sure which cream works better for you. Therefore, apply both left and right foot creams so that you can compare the right and left effects. It is also pointed out that if there are doubts or adverse events later in the treatment phase, the patient can stop treatment directly and consider alternative options. And we can offer such options as we have a number of blended creams available for prescription. Richtenberg also noted that, in their opinion, placebo administration should be considered if the patient is indigestion.Suffering from adverse events or being in a situation where there is no specific standard treatment.14 It is exactly this situation and we are often seen in clinics, which led to the development of placebo-controlled response tests as described above. To implement the Institutional Review Board N-of-1 treatment paradigm, a key point of discussion is whether the trial must be reviewed by the IDB. Clearly, the McMasters Group pointed out that N-of-1 studies are part of routine clinical practice and therefore not scientific studies, and that IRB reviews are not required (vide infra). 16. The process of involving IRB also has several drawbacks: 1) creates a big time loss to start treatment. 2) Significantly increase the cost (e.g., the cost of an IRB review [€1,500], the cost of good manufacturing practices (GMP) creates topical analgesics [€10,000], making itself an unethical approach un feasible. There are some important arguments that do not include IRB reviews in short response tests or long N-of-1 treatment paradigms. 1.In, designing and conducting N-of-1 trials: One of usersGuide25's key statements is the introduction of an N-of-1 trial service to care for the sole purpose of providing individual clinicians with better tools to care for individual patients, and it may be reasonable to think that a larger research agenda will not be taken up and an external IDB review will not be required. According to Dutch law and regulations for medical scientific research with people, 2.In. (IRB approval is mandated when two criteria are met: 1) interventional medical scientific research. 2) Participants (reading patients) must be submitted to certain (e.g. blood test) actions or follow certain rules of behavior (e.g., strict diet). Whether a particular approach is defined as medical scientific research is medical scientific research is a study aimed at answering questions in the field of disease and health (etiology, etiology, symptoms/symptoms, diagnosis, prevention, results or treatment) by systematically collecting and studying data. Research is aimed at contributing to medical knowledge that applies directly to populations other than the research population. Obviously, our response tests have a different purpose: to identify the most optimal treatment for a particular, individual patient. In this respect, it is comparable to the diagnostic pain block. Answer tests are not intended to answer questions in the field of disease and health by systematically collecting and studying data, but should also contribute to medical knowledge that applies directly to populations outside the study population.the N-of-1 treatment paradigm, from which the results cannot be translated into the general population. In addition, according to Dutch law and regulations for medical scientific research with people, interventions can be defined as studies if they violate the physical or psychological integrity of subjects. This is not the case with response tests. On the contrary, both response tests and the N-of-1 treatment paradigm provide treatment physicians and patients with insights into the extent to which pain relief effects are attributed to active compounds, and help them quickly identify more specific personalized analgesic treatments. The use in the routine practice of single-blind and double-blind trial paradigms in the treatment of terminal neuropathic pain seems achievable and ethically justified. The use of double-blind trials in particular can then continue the more extended double-blind placebo-controlled N-of-1 treatment paradigm for 2-2 weeks. A fast response test (30 minutes), perhaps followed by an extended double-blind placebo-controlled N-of-1 crossover treatment paradigm, will lead to rapid identification of the best treatment for the patient. Both early and extended response tests are suitable for clinical use. The use of such paradigms is supported not only by McMasters standards, but also by the secondary medical

ethics literature on the use of placebos in clinical settings, and by the American Medical Association Council's formal standards on American ethics and judicial issues in 2008. In such a practical testing paradigm, there is no requirement for IRB approval, but on the contrary, as we have claimed, this will induce new ethical issues related to unnecessary delays in treatment and achievability issues. Therefore, the double-blind placebo-controlled trial paradigm can be seen as an essential part of our clinical practice, outside the context of formal clinical trials. Both single blind and double-bound test paradigms show the value of such an approach in clinics. Disclosure JMKH and DJK are holders of two patents: 1) topical phenytoin used in the treatment of peripheral neuropathic pain and 2) topical pharmaceutical compositions containing phenytoin and (co) analgesics used in the treatment of chronic pain. The authors do not report any other conflicts of interest in the study. See Also 1.van Hecke O, Austin SK, Khan RA, Smith BH, Torrance N. Neuropathic Pain in the General Population: A Systematic Review of Epidemiological Studies. 2014;155(4):654–662.2.High prevalence of neuropathic pain in pain clinics, confirmed by Perez C, Rivera MV, Galvez R, and others, but also believed to be a possibility. Yule J Payne. 2013;17(3):347–356.3.Hacovides A, Bogosi M,An epidemiological study evaluating the prevalence of diabetes peripheral neuropathic pain in diabetic patients attending private outpatient clinics in LA and other South Africa. J Int Med Res. 2014; 42 (4): 1018-1028.4.Abbott CA, Malik RA, Juan Ross ER, Kulkarni J, Boulton AJ. Prevalence and characteristics of painful diabetic neuropathy in large region-based diabetes populations in the UK. Diabetes care. 2011;34(10):2220–2224.5.Ruble J. Off-label prescription of drugs for pain: maintain optimal care at the intersection of law, public policy and ethics J-pain paria care fathers. 2012;26(2):146–152.6.Langedijk J. Patient Needs and Marketing Approvals for Continuous Innovation Medicinal Products in the Drug Lifecycle: Analysis of EU Law, Chapter 4.1. Utrecht: University of Utrecht;2016. 7.Kopsky D, Keppel Hesselink J. Phenytoin Cream for the treatment of neuropathic pain: Case Series.Pharmaceuticals. 2018; 11 (2): 53.8.Vavra MW, Rubin DI. Peripheral Neuropathy Assessment in Office-Based Neurology Semin Neurol 2011; 31 (1): 102-114.9.EMA. Guidelines for clinical medical products aimed at treating neuropathic pain. London: EMA;2007. Available: January 7, 2019. 10.Farrar JT, Young JP, Ramolow L, Wealth JL, Pool MR. The clinical importance of changes in chronic pain intensity as measured by the 11-point numerical pain rating scale. 2001;94(2):149–158.11.Towen DP, Emberts DP. These famous red pills - deliberation and hesitation. Ethics of placebo use in treatment and research settings.2012;22(11):775–781.12.Fässler M, Meissner K, Schneider A, Linde K. Frequency and situation of placebo use in clinical settings - A systematic review of experience studies. BMC Med 2010;8 (1): 1741–7015.13.Phinis DG, Kapchuk TJ, Miller F, Benedetti F. Ethical advances in biological, clinical, and placebo effects. Lancet. 2010; 375 (9715): 686–695.14.Richtenberg P, Hellesco Levy U, Hiyama U. Ethics of placebo in clinical practice. J Med Ethics .2004;30(6):551–554.15.Arnold MH, Finis DG, Kerridge I. Inconvenient Truths of Medicine: Placebo and Nocebo Effects.Intern Med J. 2014;44(4):398-405.16.Guyatt G, Saquette D, Adachi J. A clinician's guide to conducting randomized trials in other individual patients. CMAJ.1988; 139 (6): 497–503.17.Mirza RD, Punya S, Vola S, Guyat G. History and development of N-of-1 exams. J R Sock Med 2017; 110 (8): 330-340.18.Lily EO, Patey B, Diamant J, Issel B, Topor EJ, Scholk NJ. n-of-1 Clinical Trials: The Ultimate Strategy for Personalizing Medicine?2 per Day, January 8, 2011): 161–173.19.Guyatt GH, Haiting A, Yeshke R, Keller J,JD, Roberts RS. N in one randomized trial to investigate new drugs. Control clin trial. 1990; 11 (2): 88–100.20.Punya S, Schmidt CH, Hartling L, Yurichuk L, Nikles CJ, Vola S. Meta-analysis or not meta-analysis? J Clin Epidemeol.2016; 76:76–81.21.Balsky AJ, St. Fort R, Rogers MP, Borth JF. Nonspecific drug side effects and nocebo symptoms. Jama. 2002;287(5):622–627.22.Dwork-in RH, Turk DC, Perth Sandner S, and other considerations for improving assay susceptibility in chronic pain clinical trials: IMPACT Recommendations There is pain. 2012;153(6):1148–1158.23.Keppel Hesselink JM, Kopsky DJ. Personalized N-of-1 trials: dose response in monoblind crossover reaction trials of phenytoin 10% and 30% creams in neuropathic pain. EC anesthesia. 2018;4(6):1–6.24.Bostic NA, Sade R, Levine MA, Stewart DM; American Medical Association Ethics and Justice Council. Placebo use in clinical settings: The American Medical Association Council's report on ethics and judicial issues. J-Clin Ethics.2008;19(1):58–61.25.Panel tDMCN-o-G. Designing and Implementing the N-of-1 Trial: In the User's Guide: Kravitz RL, Duane N, Editor.Rockville, MD: Medical Research and Quality Agency: AHRQ Publishing No. 13 (14) - EHC122-EF; 2014. 2014.

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