

## **Exploring Patterns of Use and Attitudes Toward Placebo in Medical Practice**

**Purpose:** We aim to survey knowledge, beliefs, patterns of use, and attitudes among health care professionals concerning placebos. This large-scale survey will span multiple cities in multiple locales. Specifically, our research will constitute an effort to probe the way clinicians and pharmacists construe placebos and the extent to which these professionals use placebos in clinical practice. We will target health care professionals in major cities throughout North America, Europe, and Israel. These geographic locations seem to have similar “placebo practices.” We expect that our findings will elucidate the prevalence and impact of placebos in medical practice.

**Background:** Although scholarly definitions abound (1), most practitioners loosely regard the placebo effect as any treatment that improves a symptom or disease but is ineffective or is not specifically effective for the condition being treated (2). The placebo effect is both powerful and inherent in any clinical interaction (3). Placebos exemplify the link between psychosocial factors and physiological processes, and bind psychology to the techniques of neuroscience and medicine (4, 5). The psychosocial context that surrounds clinical treatment plays an important role in health outcome. As such, it is vital that health care practitioners appreciate these influences. The patient-practitioner relationship is a significant component of the psychosocial context of treatment, since health care workers transmit important information to the patient through their words, attitudes and demeanor (6).

Physicians before the 19<sup>th</sup> century commonly used placebos in the clinical setting, but placebos have fallen out of favor with the emergence of modern medicine (7). Over the past decade, however, our knowledge of placebo mechanisms has greatly increased, consequently rekindling the placebo “flame” (8). While bioethical issues shroud the use of placebos in evidence-based medicine (2), some clinicians, mostly academic physicians, appreciate the relative merits of placebos and capitalize on its mind-body therapeutics (9).

A survey of head nurses in a Connecticut health district evaluated the status of placebos within the hospital setting (10). Of 102 respondents, 45 reported that placebos were currently being used in their unit or that placebos had been used within the last 6 months. The ages of patients receiving placebos ranged from 9 to 90 years, with the majority of patients (91%) receiving placebos in order to relieve pain. In addition, the medical staff perceived most patients receiving placebos for pain as either anxious or emotional. Overall, respondents perceived placebos as eliciting positive initial responses in 81% of patients and as being effective in the long run for 68% of patients.

In another study aiming to determine knowledge and patterns of placebo use, researchers sent surveys to house officers and registered nurses (RNs) working in two university teaching hospitals in the USA (11). Sixty house officers working in internal medicine, family practice, psychiatry, and obstetrics and gynecology services responded to the

questionnaire. Thirty-nine RNs and 27 licensed practical nurses responded. Seventy-eight percent of physicians who responded had ordered at least one placebo for use as a painkiller, while 82% of RNs had administered at least one placebo as a painkiller. The majority of doctors and nurses ordered or administered placebos for the following reasons: “to help determine whether the pain was real,” “for a patient who was requiring more pain medication than they deemed necessary”, or for a “problem patient” (i.e., a patient about whom the nursing staff was complaining).

In Canada, researchers surveyed doctors and nurses from the Victoria General Hospital in Halifax to ascertain their knowledge of and attitudes towards placebo, as well as their patterns of placebo use (12). Analysis of 300 questionnaires (230 from RNs and 70 from physicians) revealed that 80% of both the RNs and physicians reported having administered a placebo during their time at the hospital, with 91% of the placebos consisting of saline injections. The data reveal that placebo use was more common on surgical wards compared to other clinical wards in the hospital, and that in nine out of ten cases placebo administration replaced analgesics.

Studying the frequency of placebo use within nursing clinical practice, researchers found that among 263 respondents, 178 (68%) had administered a placebo to patients; however, only 12% had done so within the last year (13). In 19% of the cases, the placebo had been administered to relieve pain, with the next most common reason (11.2%) being to treat insomnia. Two forms of placebos were most common: 40% of the nurses reported administering inert oral medication, while 32% reported using saline injections. Regarding knowledge of placebos, the majority of nurses in the sample (45%) thought that fewer than half of patients would demonstrate a placebo response. Interestingly, only 29% of the nurses believed that placebos would alter objectively measurable variables. Thus, although most nurses from this study administered placebos, many of them questioned whether placebos could influence a patient’s physiology.

A survey of 772 Danish physicians assessed the frequency of use of placebo interventions (14). Among the 503 respondents, 86% of the general practitioners, 54% of the hospital doctors, and 41% of the private specialists reported using placebo interventions at least once within the last year. Furthermore, 48% of general practitioners reported using placebo interventions over 10 times within the last year. In all three groups of physicians, the most common reason cited for administering placebos was “to avoid conflict and comply with the patients’ wishes”. Of all the physicians who responded, only 8% believe that placebo interventions have no real effect.

In a separate study studying the frequency of placebo administration among physicians and nurses, researchers found that 53 out of 89 respondents reported prescribing placebos, 33 of whom said they had prescribed them as often as once a month (15). Furthermore, of those prescribing placebos, 36 respondents reported telling the patient they were receiving medicine, while the remainder either indicated treatment was a placebo, referred to the pill as non-specific, or said nothing at all.

A more recent study found that academic physicians in the Chicago area used placebos in everyday clinical practice (9). Forty five percent of the physicians surveyed reported administering placebos, though 96% believed that placebos have a therapeutic effect. Among respondents who reported using placebos, 34% told the patient they were receiving a “substance that may help and will not hurt”, 19% said the placebo was medication, and 9% described the placebo as a “medicine with no specific effects.” Only 4% of physicians explicitly stated that they were administering a placebo. Overall, only 12% of all respondents believed that placebo use should be unconditionally prohibited. Despite reports suggesting that physicians are prescribing placebos (9, 15), no specific protocol currently governs their clinical use.

**Methods:** Using a survey, we will gather data by approaching health care professionals in hospitals, community and private clinics, pharmacies and infirmaries.

We will start this effort by running a pilot at one of the McGill-affiliated hospitals (e.g., we have obtained IRB permission from the Jewish General Hospital). There, we will circulate a web-based questionnaire to faculty physicians whose email addresses are publically available. (In most university-affiliated hospitals, such listings represent about 90% of the total clinical faculty.) We will use these results to refine and fine-tune our questionnaire and general survey approach. Next, we plan to distribute our questionnaire to McGill practitioners (e.g., the Interim Chair of the Department of Psychiatry at McGill, Dr. Mimi Israel, has agreed to circulate our survey to all staff psychiatrists in the McGill-affiliated hospitals). Thereafter, in order to collect data outside of McGill-affiliated hospitals, we will apply for permission to use our web-based approach in other academic institutions. In addition, we will tap potential participants by strategic phone calls. The advantage of phone surveys is that we can obtain a better statistic measure (e.g., we know the demographics of those who choose NOT to respond in addition to those who do). For the latter, we will generate a list of telephone numbers for health care professionals, and establishments throughout North America, Europe, and Israel. We will personally call select professionals for whom we have contact information and ask that they answer our survey questions over the telephone.

**Model:** Simple Random Sampling (SRS) is a basic design comparing the sampling variance of statistics using other sample designs. SRS assigns an equal probability of selection to each frame element, equal probability to all frames of pair elements, etc. Thus, one way to think about SRS is that we would first identify every possible sample of size  $n$  distinct elements within a frame population, and then select one of them at random (i.e., equal probability selection method (EPSEM)).

The vast majority of US surveys, for example, do not use SRS. They implement some stratification and/or some clustering.

**Stratified Probability Sampling:** On the one hand, some statisticians believe in separating the sampling frame into separate groups, different from one another, and then picking some units that “represent” the population. On the other hand, other statisticians advocate for random sampling giving each person an equal chance of selection through

randomization. Each design has relative merits, and it is possible to combine them using Stratified Random Sampling. Separating the population into strata, using different values for the key statistic of interest, could be done prior to random selection. By sampling for each stratum using random sampling, confidence limits can be derived. Furthermore, by using higher sampling fractions in strata with large internal variability on the key variables, the confidence limits of the statistic from the stratified sample could be minimized for any given sample size.

*Limitations:* optimal allocations could vary for different statistics from the same survey. Implementing the allocation requires knowledge of population variances within strata. Findings ignore nonresponse, coverage, and measurement errors in the survey.

### **How large should our sample be? How to Draw on a Representative Sample?**

Sample sizes are determined in different ways. One way is to find a sample size such that the confidence limits obtained from the subsequent sample will not exceed some value. No one sample size method, however, can tell us whether our sample is representative. For a representative sample we must sketch out the experimental design, rather than the sample size.

Let's assume that we want to find out whether US pharmacists prescribe placebos. We can get a list of all the pharmacists in the US and call a random subset. Given our resources, however, such an approach would be intractable. Cost is important because calling takes personnel, time, and a set of phones. Fortunately, we can do better.

One way to go about this question is to look up all the pharmacies in the US phonebook directories. We can estimate how many pharmacists work at each pharmacy and randomly sample a subset of those. The problem in this case is that pharmacists from small pharmacies (e.g., with just one pharmacist on staff) would count more than pharmacists at large pharmacies (e.g., with 20 pharmacists) because the one-pharmacist operations would have larger sampling probabilities for which we would have to adjust.

Calling pharmacies from phone books is an attractive possibility, however, because we can decide on a simple protocol where we ask to speak to the pharmacist, and if there is more than one, we ask for the head pharmacist. In this case, we would not get a representative sample of pharmacists, but we will obtain a representative sample of head pharmacists. For our purposes, however, this distinction is immaterial.

It will be critically important to have a wide sampling of pharmacists because we don't know who might fill placebo prescriptions. Furthermore, it is difficult to know whether filling placebos is a specialized activity uncommon to all pharmacies. We assume, however, that the numbers of pharmacists handing out placebos will be small. (We can hypothesize, for example, that placebo prescriptions are more common near large medical centers or in cities.) We would get a bias towards a "NO" response, if this is the case and if we do not consider this aspect (e.g., geography/proximity) in the selection process.

The most important thing is for the sampling to be random with respect to the population of interest. In case of a large degree of heterogeneity in the population, we can use a stratified design by targeting specific areas (e.g., 10 small areas and 90 large areas). If we choose these areas at random and weight them with respect to population of pharmacists, our results will be solid. One advantage of this approach is that if we need to, we can always re-weight the parameters later.

Another approach would be to pick, say 100 locations around the country, and count the number of listed pharmacies in the phone books for each of those locations. We could then sample a certain number of pharmacies from each location. This would be a valid method of sampling. However, we would want to be sure to weight the 100 locations appropriately to account for the different numbers of pharmacies in each area. For example, if we had 1 location with 10,000 pharmacists and 99 locations with 2 pharmacists, our sampling method, if not weighted properly, would not be representative of the whole population of pharmacists. The 10,000 pharmacists comprise 83% of the population, but they would have far less representation under our stratified design.

Thus, we want to stratify based on variables that we believe will be heterogeneous in the population in order to be sure that we get enough information to have a precise estimate of the population proportion. As we have shown, the weighting is important for adjusting for the stratification.

**Sample:** We expect to tap a large cohort of health care professionals. Our sample will consist of physicians (with special concentration on family doctors, psychiatrists, internists, dermatologists, pediatricians and general practitioners), nurses, nurse practitioners, physician assistants, and pharmacists. The McGill sampling frame will include professionals who publicly list their email contact information. Altogether, we expect to contact about 10,000 individuals. Based on previous response rates in similar studies, we anticipate a response from 20-45% of the individuals whom we contact.

**Procedure:** In a similar fashion to recent published efforts (9, 14, 15), we will use a short self-report questionnaire to assess beliefs, patterns of use and attitudes concerning placebos.

Initially, within a McGill-base pilot, we will administer our questionnaire online using the intranet (please see our pilot web-based survey <http://courseware.mcgill.ca/survey/index.php?sid=27474&lang=en>). This preliminary approach will ensure that our ultimate survey is as tight and as focused as possible. We may complement our initial efforts locally via email, phone, personal communications and mail, as we finalize the questionnaire items. (Enclosed with these materials, please find a hardcopy of the questionnaire draft). Once we finalize the English version, we will make a French version of the questionnaire available.

**Consent:** Professionals targeted for this study will be informed about the nature of this research. Potential participants from McGill-affiliated hospitals will receive an email invitation explaining the purpose of the study alongside two anonymous online links to

the research questionnaire, for an English and French version, respectively. In the event that the first email request yields no response, a maximum of 2 reminder emails will follow over the period of a month.

Once we finalize our questionnaire and begin to survey remote locations outside the McGill network, research assistants (RAs) will use publicly available phone numbers to get in touch with potential participants. RAs will begin each conversation by introducing this research project. Upon obtaining consent, they will proceed to either interview by phone or set up a convenient interview time. English-French-Hebrew speaking RAs will carry out all interviews, depending on the interviewee's preference. Data collection typically requires fewer than 5 minutes.

**Anonymity:** Both email and phone invitations will explain the purpose of the study and the guarantee of anonymity. For RA-based interviews, RAs will take special measures to protect a person's identity and will NOT record any identifying information.

**Data Storage:** An automated service provided by the Information & Computer Systems division at McGill University will collect web-based data. RA-based data (e.g., phone interviews) will use the same automated system whereby RAs key in the interviewee's selections during the interview.

All data will "live" off the web. We will store these data on magnetic and electromagnetic media and will lock them inside an unidentified room within the Raz Lab. We will use an encoding system that will prevent easy access to the raw data and store the decryption key separately in a location only accessible to Dr. Raz. Personal identification will not be possible.

**Data Analysis:** We will produce frequency distributions of responses and test associations among professionals' demographic variables, the frequency of placebo use, and beliefs regarding the therapeutic value of placebos (Pearson Correlation).

**Hypotheses:** We hypothesize that patterns of use and attitudes concerning placebos will be more lenient than the code commonly upheld by the medical community.

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