Special Section

Commentary: Harm, Truth, and the Nocebo Effect

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Introduction

Nocebo effects occur when an individual experiences undesirable physiological reactions caused by doxastic states that are not a treatment's core or characteristic features.[1] As Scott Gelfand[2] points out, there are numerous studies that have shown that the disclosure of a treatment's side effects to a patient increases the risk of the side effects. From an ethical point of view, nocebo effects caused by the disclosures of side effects present a challenging problem. On the one hand, clinicians' duty to inform patients of the consequences (including possible side effects) of their treatments is critical in ensuring that patients' autonomy is respected. Patients cannot act autonomously if relevant information is withheld from them (without their consent, perhaps). On the other hand, clinicians also ought to minimize harm to patients.

To be sure, medical interventions often involve injuring a patient; e.g., in the process of killing neoplastic cells, chemotherapeutic agents often destroy other healthy cells causing cancer patients to experience substantial discomfort and increased risks of comorbidities. The harm can be justified if a patient understands the trade-off and willingly accepts the harm associated with a treatment. The dilemma arises when the very act of truth disclosure (of side effects) causes an elevated risk of harm in a patient. It is here that we see a conflict between the two duties: a duty to respect autonomy and a duty to refrain from inflicting nonconsensual harm (nonmaleficence). Gelfand frames the problem as an exclusive choice between these two duties, and he suggests that the use of a visual analog scale for informational comfort can alleviate the tension between the two duties. I will argue in this paper that Gelfand's response is insufficient. To wit, I claim that his objections to the standard responses hold these responses to an unfair level of ethical and epistemic requirements. In the second half of this commentary, I argue that his proposal either falls prey to the very criticisms that he levels against the standard responses or it fails to be sufficiently different from authorized concealment—a response offered by Luana Colloca and Franklin Miller[3] to solve the problem of disclosure-induced nocebo effects.

Before we engage Gelfand's argument, it is worth clarifying two related issues: one technical and one philosophical. Firstly, throughout Gelfand's paper, he assumes that elicitation of nocebo effects must involve the patient's being aware of some undesirable side effects. "The nocebo effect," he writes, "is a phenomenon whereby learning about the possible side effects of a medical treatment increases the likelihood that one will suffer these side effects or that the side effects will be exacerbated." This is incorrect. If nocebo effect is defined as doxastic states (knowledge or belief) that are not core features of an intervention causing undesirable physiological reactions, then it is possible to induce nocebo effects without any disclosure of side effects. Karin Jensen et al.[4] cleverly induced hyperalgesic reactions in subjects by conditioning them to associate certain facial images with higher

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experience of pain. When the researchers applied moderate pain stimuli to subjects paired with the facial images that were associated with higher pain (from the earlier condition phase), subjects reported greater pain sensations. Since the hyperalgesia was brought about by a doxastic state (visual recognition of facial images), the patients had a nocebo experience without any anticipation of the unpleasant experience. As an aside, Jensen et al. were also able to induce the same hyperalgesia by flashing facial images for a length of time that was below our ability to consciously recognize them. It appears that nocebo effects (and placebo effects) can be elicited even if the individual is consciously unaware of the stimuli.

Secondly, although Gelfand's paper focuses on nocebo effects, the tension between a clinician's duty to truth disclosure and her duty to nonmaleficence obviously exists outside of the context of nocebos. Disclosing grim prognoses that could potentially cause a patient to become depressed (and, perhaps, to forgo promising treatments) is an old example that illustrates the tension.[5] In this respect, there is nothing ethically unique about nocebos—they do not present any specific ethical challenges that we have not encountered before. For brevity, let us refer to the tension between a clinician's duty to truth disclosure and her duty to avoid inflicting nonconsensual harm (nonmaleficence) within the nocebo context as the 'nocebic tension' and the same tension outside of the nocebo context as the 'conventional tension.' More than a mere editorial note, appreciating the nonuniqueness of the nocebic tension tells us that whatever solution Gelfand offers to resolve the nocebic tension should also apply to the conventional tension. In other words, it gives us a handy way to assess Gelfand's solution.

Gelfand's argument consists of two broad parts. In the first part, Gelfand argues that the three attempts that have been presented in the literature to resolve the nocebic tension fail. In the second part, he offers his positive solution. I will discuss these two parts in turn.

Gelfand's Objections Against Cohen's and Fortunato's Accounts

Shlomo Cohen[6] argues that the duty to respect patient's autonomy is not absolute. There are occasions in which clinicians are justified in relaxing "the rigid conception of informed consent," especially when respecting a patient's autonomy can cause her harm. Specifically, Cohen argues that clinicians are permitted to strike a careful balance between the duty to respect autonomy and the duty of nonmaleficence. He rightly points out that empirical factors such as a patient's likelihood to experience disclosure-induced nocebo effects and the potential magnitude of the harm should be taken into consideration when a clinician seeks to find the proper moral balance between competing duties. But these factors do not help us pick out the exact (or even approximately) correct resolution. Although Gelfand does not mention it, the perennial problem of *how* one should properly adjudicate competing duties also threatens Cohen's account. Without a more developed account, Cohen's proposal is at best a promissory note.

John Fortunato et al.[7] concur with Cohen that there are occasions when nondisclosure of side effects can be justified; e.g., a patient's manifestation of a disclosure-induced nocebo effect is certain. And, like Cohen, Fortunato et al. advocate a sort of balancing between the duty to respect autonomy (which, of course, includes the duty to truth disclosure) and the duty to nonmaleficence that is left up to physicians' discretion. The difference between these two accounts is that Fortunato et al.

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recommend the use of open-ended questions as a way to mitigate some of the moral cost of not disclosing potential side effects to patients. Fortunato et al. suggest that clinicians can ask questions such as "Tell me about what you have noticed since starting this medication" in follow-up meetings to determine if patients are suffering from side effects (that were previously not disclosed). Fortunato et al. write, "Nondisclosure of side effects for treatments with nocebogenic potential, particularly when executed in deference to nonmaleficence and with appropriate follow-up with the patient, fits the parameters of a caring, beneficent, and engaged practitioner."[8] In this sense, physicians can violate the duty to nondisclosure but limit its fallout by ensuring that if side effects did realize, physicians can address them quickly.

Similar to Cohen's account, Fortunato et al.'s proposal leaves it to clinicians to make the judgment call in terms of when violating patient's autonomy (such as the nondisclosure of side effects) is justified. Unfortunately, were the problem of competing moral duties resolvable by mere careful deliberation, we would not have the problem in the first place. The challenge of competing duties often involves cases where careful deliberation does not reveal obvious solutions. Perhaps there is no fact of the matter as to what the right course of action is in these penumbra cases, but even this more skeptical conclusion requires an argument. One thing is certain: thinking carefully about these cases is helpful, but it is likely not helpful enough. Rather than engaging Cohen's and Fortunato et al.'s accounts further, I will focus on Gelfand's objections and his proposal.

Gelfand's Objections

Gelfand presents four reasons for rejecting Cohen's and Fortunato et al.'s accounts, and they are:

(1) Their accounts are impractical;
(2) Their accounts decrease patients' trust in physicians;
(3) Their accounts permit a significant amount of implicit biases; and,
(4) Their accounts run the risk of medical paternalism.

These objections also serve as reasons in favor of the solution that he proposes on the ground that Gelfand believes his view avoids all of them.

The impractical objection concerns Gelfand's worry that in order to justify the nondisclosure of side effects, Cohen's and Fortunato et al.'s accounts require that clinicians know a sufficient amount about their patients to determine the likelihood that they would experience disclosure-induced nocebo effects. Gelfand argues that given how preciously few interactions physicians have with their patients, it is unrealistic to expect that clinicians can determine their patients' risks of nocebo effects.

In Cohen's case, he further suggests that we rely on some of the recent research on placebo responders—individuals who possess traits that make them more susceptible to placebo/nocebo responses. For instance, Leanne Wilson et al.[9] note that among patients with temporomandibular disorder, those with somatization tendency exhibited greater placebic/nocebic responses. Cohen suggests that clinicians could use these placebo/nocebo traits to help them identify likely responders and, in turn, this identification will assist clinicians in deciding when they should withhold information regarding potential side effects.

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The research on placebos and nocebos is still in its infancy, and their effects cannot be reliably induced. Although some studies have shown that placebo responders exist, the exact biomarkers or characteristics that distinguish them are largely unknown. Most of the evidence for placebo responders comes from older and less rigorous trials and more recent studies have provided contradictory results.[10] In this respect, Gelfand's skepticism about the practicality of clinicians making accurate determination of a patient's nocebo risks is well warranted.

For the second objection, Gelfand claims that Cohen's and Fortunato et al.'s views can undermine patients' trust in their physicians. When patients learn of clinicians' practice of withholding the disclosure of side effects (for patients' sakes), they might second-guess the truth of what clinicians say in general. The erosion of trust can lead to a host of therapeutic difficulties. Patients might look up information on their own and fail to understand the information within the proper clinical contexts (e.g., although the risk for X is doubled when one takes certain medication, the initial risk of X is so small that doubling it still does not warrant concerns). Likewise, savvy patients might 'game the system' by presenting themselves as less likely to have nocebo reactions so as to deceive clinicians and receive a full disclosure of information. This could expose patients to potential harm of nocebo effects.

Thirdly, Gelfand argues that Cohen's and Fortunato et al.'s views leave open ample opportunities for implicit biases to influence clinicians' behaviors. In assessing the relative risks of nocebo effects, both Cohen and Fortunato et al. rely on physician-patient interactions. Since implicit biases can cloud clinicians' judgments, unless a more regimented method is used to assess risks, implicit biases can shape inappropriate conclusions.

Gelfand's final objection claims that Cohen's and Fortunato et al.'s proposals do not include careful consideration of how much weight patients assign to their autonomy. In balancing the duty of truth disclosure against nonmaleficence, clinicians must have a clear grasp of the importance of these two values among a patient's preferences. Given the lack of explicit instructions in Cohen's and Fortunato et al.'s accounts, it is hard to see how clinicians can learn of their patients' preferences. Acting on assumed knowledge of patients' values risks turning medicine back to the days of rabid paternalism.

A Common Problem for Gelfand's Objections

All four of Gelfand's objections share a basic problem; that is, they seem to treat disclosure-induced nocebic risks as substantially different from other clinical practices. Take the worry that the assessment of nocebic risks is clinically impractical. Here, the worry is not so much the impracticality of the assessment; several diagnoses (e.g., identification of psychiatric pathologies) are cumbersome and time-consuming. The real worry is instead that clinicians cannot reliably assess nocebic risks, and acting on unreliable diagnoses is bad medicine. In making this argument, we ought to be mindful that we do not hold nocebic risks to a different epistemic threshold than those of conventional medicine. An individual's variability in achieving the same level of pain relief from morphine ranges from 15 mg/day to as much 15g/day—a 1,000-fold difference.[11] Yet, we do not think it is inappropriate for clinicians to prescribe a particular dose by using generalized clinical data. If we have good data from large-scale studies on the magnitudes of nocebo effects, the fact that individuals can vary in their responses does not mean that we are not justified in

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assessing the risks using generalized data. It is certainly true that we do not know nearly as much about placebo/nocebo actions as we do about analgesia. But the disanalogy means only that the unreliable nature of identifying placebo/nocebo responders is, at best, a temporary hurdle. Medicine routinely operates in a sea of uncertainties: from the use of off-label protocols to the typical trial-and-error approach to psychopharmaceutic dosages, clinicians act with incomplete information. It is paramount that we do not single out nocebos as somehow different in kind.

Similarly, withholding information from patients *can* undermine the trust patients have toward that care-providers. In conventional medicine, however, no one is under any illusion that *all* information is, or should be, conveyed when patients and physicians determine the proper therapeutic directions. Older classes of drugs are often left unmentioned because clinicians assume that no reasonable person would prefer a less effective or more toxic intervention. Likewise, clinicians do not disclose *every* possible diagnosis to their patients, regardless of its probability of being correct. Any patient who spends time reflecting on the nature of physician-patient relationship would conclude that physicians routinely leave out information and often do so for the perceived good of the patients. There is no need for any prior explicit consent from patients to justify this practice.[12] This rather typical form of paternalistic censorship does not erode trust (enough) such that patients' wellbeing and autonomy are seriously compromised. In claiming that the nondisclosure of risks undermines patients' trust in their care providers, we ought to ensure that we do not hold nocebic risks to a higher standard than those of conventional practice.

For the worry that implicit biases might seep into diagnostic assessments that lack more rigorous and algorithmic means, we once again must notice how diagnostics are conducted in conventional medicine. As much as Evidence-Based Medicine has advocated for a more algorithmic approach to diagnostics and treatment determinations, the reality of caring for a complex social organism virtually guarantees that in the foreseeable future, there is no diagnostic method that will be one-size-fits-all. Moreover, even if a pure algorithmic approach to diagnostics and treatment is available, it is not clear that patients and clinicians wish to be no more than 'values for variables.' People are not mere bundles of symptom presentations (as advocated by holistic approaches of medicine that see patients as whole persons). Like in any rich social interactions, in medicine, the parties bring their values to the table and these values shape what we see. A pediatrician might notice hesitation in a child's recollection of how she was injured when she is in the company of her parents. These subtle cues might lead the pediatrician to suspect child abuse. Judgments like this obviously involve observations that are tainted by the clinician's implicit and explicit biases. Yet, however worrisome these potential biases are, patients and physicians do not wish to eliminate these personal judgments in their clinical encounters. Indeed, one might argue that values will always play a role in healing relationships (and, really, any social interactions), and that the issue is not how clinicians can rid themselves of their personal values and biases in delivering care but how they determine which value and bias they should bring to the table. Like the two objections above, the threat of implicit biases in nocebic risk assessments seems to be exaggerated. At the very least, we have no reason to believe that these assessments pose any uniquely challenging problems.

Finally, it is certainly correct that unless a clinician knows the relative importance her patients assign to their values for autonomy and nonmaleficence, acting upon these values might entail an unacceptable level of medical paternalism.

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Conventional medicine regularly requires that clinicians make decisions about patients' care without the patients' explicit involvement. During an exploratory laparotomy performed to identify the source of a patient's abdomen's discomfort, a surgeon might spot clearly an inflamed appendix and proceed with an appendectomy. Whether or not her decision to proceed with the appendectomy is justified depends on a host of considerations including the urgency of the surgery, the likelihood that (were the patient conscious) he would consent to the procedure, and risks and benefits of the appendectomy. Surgeons rarely ever have extensive direct interactions with their patients; yet, they routinely make decisions that assume patients' value-rankings. A broad caveat "If immediate life-threatening events happen during the procedure, they will be treated based on my discussions with the doctor…"[13] included in a consent form does not guarantee that the patient would have consented to the additional procedure. The decision is left up to the discretion of the surgeon.

Gelfand's worry that nondisclosures of side effects border on an unacceptable level of medical paternalism depends on the actual risks of disclosure-induced nocebo effects. If conventional medicine gives clinicians enough leeway to make therapeutic decisions that they consider to be in the best interests of their patients, then the appropriate resolutions of nocebic tensions can follow suit.

To be fair, one might argue that being consistent with conventional practice is not good enough, especially if one deems the entire enterprise as being morally dubious. Being consistently wrong is arguably worse than being inconsistently wrong. I assume that Gelfand does not have such a bold claim in mind. A thorough evaluation of the ethics of the physician-patient relationship is obviously beyond the scope of this paper. My claim is the more modest one that Gelfand's objections appear to hold Cohen and Fortunato et al. to a standard far above that of conventional medicine. Unless there is some reason that warrants the discrimination, the objections would thus be unfair.

Gelfand's Solution

Assuming for the moment that Gelfand's objections successfully show that Cohen's and Fortunato et al.'s accounts are inadequate, does Gelfand's proposal avoid these pitfalls? Drawing on the work of Colloca and Miller[14] on authorized concealment and Donna Wong and Connie Baker's[15] research on the Pain Rating Scale—a widely used form of visual analog scale (VAS) for pain, Gelfand offers a solution to the nocebic tension. Colloca and Miller have argued that the nondisclosure of side effects can be justified if clinicians have obtained prior permissions from their patients that they could lie to them. A physician, for instance, would ask plainly "How much information regarding side effects would you like to know?" accompanied by an explanation of the potential increase in nocebic risks as a result of the disclosure. In a nutshell, Gelfand's proposal is that we obtain patients' consent to have information of side effects withheld (*à la* authorized concealment) by presenting to them a scale that is akin to the Wong-Baker Faces Pain Rating Scale. Gelfand's scale would consist of 10 numbers running from 0 to 10 and "[o]n the far left, just above the zero, there would be a picture of someone surrounded by books and looking at a computer with a smile on her face. On the far right, above the number ten, the same picture would appear, but the person would have a frown or an expression of pain or disapprobation." Patients can point to the degree to which

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they are comfortable with information prior to any clinical care. Once they have indicated the level of information they wish to receive, clinicians could then disclose as little as possible to avoid inducing nocebo effects. By antecedently indicating their levels of 'informational comfort,' Gelfand argues that patients have in fact consented to nondisclosure of certain side effects. Since the nocebic tension is a conflict between the duty to respect autonomy and the duty to nonmaleficence, Gelfand's proposal hopes to walk a fine line. In cases of nondisclosure of side effects, the informational chart would give physicians the moral cover to justify paternalism; thus, the respect for autonomy is left intact. On the other hand, if patients were to express their wishes to learn about all the side effects (and risk an increase in the odds of nocebo effects), whatever harm they might experience is consensual and hence consistent with the duty to nonmaleficence.

It is not entirely clear that Gelfand's proposal is an improvement over Colloca's and Miller's authorized concealment. The core of Gelfand criticism of authorized concealment is that in doing so, one could increase the odds of the nocebo effects. Unlike Colloca and Miller, Gelfand does not require that clinicians explain the rationale behind the nondisclosure of side effects; patients are left in the dark as to why they need to point to a chart to express the levels of their informational comfort. By skipping the explanation part of the exercise, Gelfand hopes that his proposal can avoid the nocebic risks that authorized concealment might induce. Whether authorized concealment in fact confers a sort of meta-nocebic risk is an empirical matter, and there is currently no evidence that it does. In that respect, the attractiveness of Gelfand's proposal turns on a worry that might not exist. Indeed, if Gelfand's entire worry with authorized concealment is only the possibility of meta-nocebic risks, then Colloca and Miller can simply eliminate the part of their proposal in which physicians explain the connection between risk-disclosure and nocebo effects. From the point of view of patient's autonomy, the failure to explain the rationale of nondisclosure is at worst a tie between these two views.

What distinguishes Gelfand's proposal from those he criticizes also depends on his concern that implicit biases might influence a clinician's assessment of a patient's degree of informational comfort. The use of a VAS to assess the degree of informational comfort is supposed to minimize the influence of implicit biases in a clinician's decision to withhold warning of possible side effects. This move, however, assumes that by quantifying informational comfort, implicit biases are less likely to creep into clinical care. The evidence of visual analog pain scales' ability to minimize implicit biases is unfortunately scant. Indeed, in a study on race and pain management, Miner et al.[16] note that physicians' opinions of whether their patients exaggerate their pain vary according to race. For Native American patients, on average, their physicians report that 50 percent of the patients exaggerated their pain reports in order to obtain analgesia. The difference appears to lead to Native American patients receiving less pain treatments and relief. Implicit biases play a role in the unequal treatment not because physicians had no way to quantify patients' pain—a visual analog pain scale was used in the study. Instead, the biases show up in how clinicians interpreted that piece of information. A similar problem lurks for a VAS for informational comfort; implicit biases will likely survive the quantification of patients' preferences and manifest at places where data are translated into treatment recommendations. It is entirely unclear whether a VAS for informational comfort would be of much (if any) help in combating implicit biases in clinical settings.

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In terms of Gelfand's other objections that Cohen's and Fortunato et al.'s recommendations are impractical, incongruent with patients' trust in their physicians, and border on medical paternalism, they seem to apply to Gelfand's solution as well. Recall that the impractical objection is really about the reliability of determining a patient's risks of disclosure-induced nocebo effects. How accurate is a visual analog scale in measuring a patient's level of informational comfort? Given the novelty of the idea, there is obviously no evidence to conclude one way or another. However, there are reasons to be skeptical of its reliability. Unlike pain, patients (and even seasoned physicians) have no subjective understanding of informational comfort. When does an amount of information become too much? For patients with chronic conditions, they often become expert in their ailments over the course of their prolonged care. Medical information that seemed utterly befuddling to a patient at the start might seem entirely basic not long into her treatment. For extended treatment, we are often surprised by how quickly we become comfortable with high level of informational detail.

When it comes to pain, we know when a level of pain hurts too much. We have had subjective experiences with pain for the better parts of our lives. But when it comes to informational comfort, it is not clear that we have the same level of privileged expertise. Since Gelfand's proposal does not actually disclose the rationale for the VAS for informational comfort, patients are even more confused as to what 'informational comfort' means. For the clinicians, the concern is to ensure that patients consent to the nondisclosure of side effects (in order to avoid nocebic responses). 'Comfort' is measured in terms of the risks patients are willing to assume. But because patients have no idea that their indicated levels of informational comfort are ultimately a way to justify paternalistic nondisclosure, they could very well have in mind a concept of informational comfort that differs widely from that of their care providers. Gelfand can avoid this worry by explaining the rationale of the VAS to patients. This response (along with the lack of evidence that VAS actually decreases implicit biases) would collapse the distinction between Gelfand's proposal and Colloca's and Miller's authorized concealment.

Finally, does a VAS for informational comfort safeguard patients' trust in their physicians? In his critique of Cohen's and Fortunato et al.'s proposals, Gelfand asks us to imagine the effects on trust if the general public learns of the routine practice of paternalistic nondisclosure of side effects. His conclusion is that their proposals threaten to erode patients' trust, leading to a plethora of potential clinical problems. It seems comparatively likely that when the general public learns of the real rationale behind the use of an informational VAS, patients would similarly harbor the same sort of suspicion. Unfortunately, just as there is little empirical evidence to support Gelfand's argument that Cohen's and Fortunato et al.'s proposals lead to an erosion of patients' trust, we also have no evidence to accurately anticipate the effects of Gelfand's VAS. His proposal includes a level of paternalism that is similarly hidden from patients; as such, the VAS for informational comfort is unlikely to provide a greater degree of protection for patients' trust in their physicians.

Conclusion

There are two main claims in this brief commentary: (1) Gelfand's reasons to reject Cohen's and Fortunato's views hold these views to epistemic and ethical levels

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that go far beyond what we accept in conventional medicine. Unless that is something fundamentally different between the risks within conventional medicine and the risks of disclosure-induced nocebo effects, Gelfand's objections would be unfair; (2) Although Gelfand claims that the use of a VAS for informational comfort is an improvement over authorized concealment, a closer examination challenges his claim. The dilemma is that if he opts to leave out the need for clinicians to explain the VAS' rationale to their patients, then his proposal runs the same risk of medical paternalism with which he charges Cohen and Fortunato. On the other hand, if he includes its rationale, then his proposal differs little from authorized concealment.

The question of how we should adjudicate conflicts between competing duties in medicine continues to be deeply puzzling. Nonetheless, it behooves us to keep in mind that nocebic tension and conventional tension are but the same beast with different coats. We should, of course, take into consideration the potential harm of disclosing the risks of side effects in our clinical interactions. But ultimately, disclosure-induced nocebo effects raise ethical challenges that we have long recognized and attempted to address. Drawing on the wealth of literature on the conventional tension might help us understand and better manage the nocebic tension.

Notes

1. This is a rough sketch of what constitutes a nocebo. See Howick J. The relativity of 'placebos': Defending a modified version of grünbaum's definition. *Synthese* 2017;194(4):1363–96 for some of the philosophical challenges that confront attempts to define 'placebo' and 'nocebo' properly.
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5. Pellegrino ED. Is truth telling to the patient a cultural artifact? *JAMA* 1992;268(13):1734–5, for example, mentions the example of disclosing poor prognoses that can cause a patient to become depressed. A negative emotional reaction to bad news is not typically thought of as a nocebic reaction.
6. Cohen S. The nocebo effect of informed consent. *Bioethics* 2014;28(3):147–54.
7. Fortunato JT, Wasserman JA, Menkes DL. When respecting autonomy is harmful: A clinically useful approach to the nocebo effect. *American Journal of Bioethics* 2017;17(6):36–42.
8. See note 7, Fortunato, et al., 2017, at 41.
9. Wilson L, Dworkin SF, Whitney C, LeResche L. Somatization and pain dispersion in chronic temporomandibular disorder pain. *Pain* 1994;57(1):55–61.
10. See, for instance, Kaptchuk TJ, Kelley JM, Deykin A, Wayne PM, Lasagna LC, Epstein IO, *et al.* Do "placebo responders" exist? *Contemporary Clinical Trials* 2008;29(4):587–95; Horing B, Weimer K, Muth ER, Enck P. Prediction of placebo responses: A systematic review of the literature. *Frontiers in Psychology* 2014;5(1079); and King BH, Dukes K, Donnelly CL, Sikich L, McCracken JT, Scahill L, *et al.* Baseline factors predicting placebo response to treatment in children and adolescents with autism spectrum disorders: A multisite randomized clinical trial. *JAMA Pediatrics* 2013;167(11):1045–52.
11. Hanks GW, Reid C. Contribution to variability in response to opioids. *Supportive Care in Cancer* 2005;13(3):145–52.
12. One might suggest that the institution of medicine is such that participants are largely aware of the implicit rules. As such, when a patient seeks help he assumes that his care-providers will behave

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(including the disclosure of risks) in a manner that is in his best interest while respecting his autonomy. Nondisclosure is not itself a sufficient reason to doubt clinicians' fidelity.
13. The State of Queensland. Consent form for laparotomy. Quesland Health. Queensland, Australia; 2018; available at https://www.health.qld.gov.au/__data/assets/pdf_file/0034/149497/shared_file_47.pdf (last accessed 9 Sept 2019).
14. See note 3, Colloca, Miller 2011.
15. Wong DL, Baker CM. Pain in children: Comparison of assessment scales. *Pediatric Nursing* 1988;14 (1):9–17.
16. Miner J, Biros MH, Trainor A, Hubbard D, Beltram M. Patient and physician perceptions as risk factors for oligoanalgesia: A prospective observational study of the relief of pain in the emergency department. *Society for Academic Emergency Medicine* 2006;13(2):140–6.

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