THE NOCEBO EFFECT OF INFORMED CONSENT

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Keywords
nocebo, informed consent, information disclosure, respect, autonomy, risk-benefit analysis

ABSTRACT
The nocebo effect, the mirror-phenomenon to the placebo effect, is when the expectation of a negative outcome precipitates the corresponding symptom or leads to its exacerbation. One of the basic ethical duties in health care is to obtain informed consent from patients before treatment; however, the disclosure of information regarding potential complications or side effects that this involves may precipitate a nocebo effect. While dilemmas between the principles of respect for patient autonomy and of nonmaleficence are recognized in medical ethics, there has not yet been an ethical discussion focused on the potential dilemma raised by the nocebo effect of informed consent (NEIC). This dilemma is especially pernicious, since it involves a direct causality of harm by the caregiver that is unparalleled by other potential harmful effects of information disclosure. This paper articulates the dilemma of the NEIC and offers a seminal ethical analysis.

The placebo effect is a well-documented phenomenon, whereby people experience improvement of symptoms in response to an intervention which is biologically inert with respect to their condition yet which they believe is helpful.\(^1\) The mirror-phenomenon to the placebo effect is the nocebo effect, where the expectation of a negative outcome precipitates the corresponding symptom or leads to its exacerbation.\(^2\) While much literature in medical ethics has dealt with the placebo effect, virtually nothing in philosophy has been written specifically on the ethics of the nocebo effect. (The search for ‘nocebo’ in the Philosopher’s Index yields a striking zero result.)\(^3\) The use of placebo in clinical practice raises moral concerns since it often involves a kind of deception which, as such, clashes with the principle of respect owed to patient autonomy. The well-known moral dilemma with regard to the placebo effect is therefore in cases where the positive effects on patient well-being may outweigh the harm to patient autonomy. The ethical problem with regard to producing the nocebo effect is obvious: the nocebo is in and of itself painful, stressful, or otherwise noxious to the patient. The relevant parallel dilemma is when the harmfulness of the nocebo effect may outweigh the good in proper disclosure of medical information to the patient, and where the duty to inform may therefore be suspended. This is of special importance with respect to the clinical practice of informed consent, where the very disclosure of potential side effects or complications can bring them about through a nocebo effect. I shall refer to this as the dilemma of the nocebo effect of informed consent (NEIC). While this was acknowledged as a problem mainly for the methodology of clinical trials,\(^4\) the moral dilemma of the NEIC has gone unnoticed in medical ethics. (This dilemma arises in both clinical research and clinical practice, but has different characteristics in each. The ethical analysis in this paper concentrates on clinical practice.) The first task of this paper is


the very articulation of this important yet unrecognized dilemma. Next, it will proceed to discuss its main ethical features.

The dilemma stemming from the potential for the NEIC is arguably more acute than the parallel dilemma with respect to the placebo effect, since the prevention of harm takes precedence over the enhancement of well-being, as indeed the supreme principle of clinical medicine reminds us. Contemporary views in medical ethics often hold that the principle of respect for patient autonomy trumps the principle of furthering patient well-being (paternalism is looked down upon); however, the balance of reasons may not point in the same direction when respect for autonomy is pitted against the stricter duty not to harm – as in nocebo cases.

The uniqueness of this dilemma should be clarified more precisely. The dilemma of the NEIC is more pernicious than the different, well-known dilemma regarding the nondisclosure of bad news to a patient about his condition, when this can be especially detrimental psychologically. Such is the case where, for instance, the caregiver decides to postpone the bad news about the patient’s exact diagnosis while the patient is suffering from depression, is therefore especially vulnerable, and the additional bad news may increase significantly his suicidal tendencies. The problem of the NEIC raises a special moral concern, since, in contrast to the above example, the caregiver is not called to refrain from reporting actual reality to the patient, but to refrain from describing hypothetical harmful possibilities (of potential side effects or other complications) – a description which could in and of itself be causal in turning them from mere potentialities to actualities. The causality of harm by the caregiver is therefore of a different magnitude altogether; his moral responsibility and the cautiousness he is required to exercise are hence of a correspondingly higher magnitude. The moral dilemma is thus distinct and unique, and a different balance of reasons is arguably called for.

After this basic articulation of the dilemma, let us proceed to examine it in more detail.

While the point of this paper is a philosophical one, a review of relevant biological evidence is mandatory background. The nocebo effects of negative expectations (secondary to suggestion) are well documented.\(^5\) Examples abound. When healthy subjects are made to believe falsely that electric current is being transmitted through their heads, more than two thirds experience a headache.\(^6\) Similarly, one quarter of patients with food allergies develop allergic symptoms when injected with saline that is described to them as an allergen.\(^7\) The nocebo effect of verbal suggestion was shown to be strong enough to reverse the placebo effect achieved by conditioning via pre-treatment with a potent analgesic.\(^8\) The nocebo effect demonstrates its greatest power, however, by the ability of verbal suggestion to completely reverse the biological effect of an agent, as in turning the analgesic effect of nitrous oxide into a hyperalgesic one.\(^9\)

The potential nocebo effect of verbal suggestion is no less relevant when the suggestion is part of the informed consent procedure. Before turning to discuss the ethical implications, let us review an example. The outcome of mentioning potential side effects in the consent form was examined in a trial of aspirin or sulfinpyrazone in the treatment of unstable angina.\(^10\) The consent form in two of the participating centers but not in the third included the mention of ‘occasional gastrointestinal irritation’ as a potential side effect. As a result, significantly more patients in the first two centers suffered from subjective gastrointestinal symptoms; with a striking sixfold increase (\(P < 0.001\)) in the relative number of patients who consequently discontinued their participation in the study. (There was no difference between the groups in the number of patients experiencing objective gastrointestinal complications or non-gastrointestinal symptoms.) The disclosure of information regarding potential adverse effects was instrumental in causing them. Just as this is seen in clinical trials, it is also pertinent to the therapeutic setting.

The special cautiousness that the caregiver is called upon to exercise due to her potential causal role in generating noxious symptoms in the patient is accentuated by the fact that the nocebo effect can cause actual clinical deterioration. This was illustrated in patients with Parkinson’s disease who had electrodes implanted into the subthalamic nuclei of their brains for ‘deep brain stimulation’ therapy. When the patients were tested for best motor performance, the false suggestion that the stimulator was turned off had similar negative effects on the velocity of hand movement – a nocebo effect – as when


\(^{4}\) Benedetti et al. 2003, op. cit. note 5.


the stimulator was indeed turned off.\textsuperscript{11} The traditional understanding of the difference between placebo/nocebo effects and real medical intervention was that while the latter works on the target tissue or organ, the former works ‘just psychologically’. (This provided the basis for rejection of placebo treatment on the grounds of deception.) This dichotomy (as opposed to a mere distinction) is in the process of deconstruction by accumulating scientific research, and at any event is untenable in its simple form. This is not the place to review the evidence for the \textit{objective biological effects} of placebos,\textsuperscript{12} but, to continue with the Parkinson example, PET scanning (a form of functional brain imaging) showed increased dopamine release in the striatum of parkinsonian patients in response to suggestion of motor improvement,\textsuperscript{13} which is precisely the biological response that real anti-Parkinson medications are designed to achieve. For obvious ethical reasons, research on patients designed to create nocebo effects in order to unravel their neurobiology is much more difficult to conduct, and so evidence is scarcer, but there is reason to believe that just as the placebo effect can at times mimic the actual physiologic action of real treatments, so does the nocebo effect. A possible example is the finding that proglumide – an antagonist of the pain mediator cholecystokinin – blocks the nocebo effect of pain suggestion,\textsuperscript{14} in parallel to the finding that naloxone – which antagonizes endogenous opioids – blocks the placebo effect of suggestion of pain relief.\textsuperscript{15} The important conclusion from all of this is the following. The emerging robustness of the nocebo effect and the potential objective harmful effects of nocebos – whether behavioral or physiological – underscore the significant moral liability of the caregiver when creating a nocebo effect in the patient and the gravity of the moral responsibility to prevent it.

The idea of the potential for harm in the mere disclosing of potential harms has often been criticized in recent decades as a rationalization used to justify the outdated paternalistic approach in medicine.\textsuperscript{16} It may be the case, however, that that criticism is to an extent a form of rationalization \textit{itself}, which in a parallel manner helps support the opposite, patient-centered, approach dominating current medical ethics. Much more importantly, the developing scientific understanding of the power of the nocebo was simply not available until a generation ago. Tom Beauchamp and James Childress, in their authoritative discussion of informed consent and specifically of intentional nondisclosure, make no mention of the nocebo phenomenon and – no doubt, partially as a consequence of this neglect – opine that: ‘empirical evidence indicates more often than not that physician-hypothesized negative effects [of information disclosure] . . . do not materialize.’\textsuperscript{17} One suspects that the paradigm of nocebo that ethicists (as everyone else) had in mind was something rather exotic, maybe along the lines of ‘tribal phenomena,’ such as ‘voodoo death.’ Although voodoo death may be a physiologic nocebo phenomenon in its own right,\textsuperscript{18} it is surely of anecdotal importance and prevalence compared with the robust evidence of the variety of nocebo effects, as discussed here. (On a larger scale, the central importance of top-down modulation of sensory experience in general was much less scientifically established a generation ago.)

Let us conclude: the traditional ethical problem regarding disclosure of information to the patient is raised in conditions of an existing or impending harm, and the dilemma involves the justification for the physician’s adding psychological harm to the patient by \textit{reporting} on it (i.e. disclosing the diagnosis or prognosis). In the dilemma of the NEIC, the harm in point does not exist; rather, as the evidence presented here suggests, the physician risks \textit{creating} it by merely mentioning its potentiality. Moreover, this harm can be biologically real and cannot be dismissed as ‘merely psychological.’ This raises a different, new moral dilemma, which demands a search for a new moral balance between respect for autonomy and paternalistic nonmaleficence, and which ethicists are called upon to investigate.

\textsuperscript{11} Benedetti et al. 2003, \textit{op. cit.} note 5.
\textsuperscript{14} Benedetti et al. 2007, \textit{op. cit.} note 2.
Ethics, Beuchamp and Childress argue accordingly that ‘the primary function and justification of informed consent is to enable and protect individual autonomous choice.’ In particular, the prominence of the autonomy paradigm tended to downplay the seriousness of perusal that considerations of nondisclosure merit.

Opposition to the above view has intensified in recent years, and has involved both a reevaluation of our understanding of informed consent and a more nuanced understanding of patient autonomy (these two factors are often connected). The relevant criticism may either reduce (even deny) the dependence of informed consent on respect for autonomy, or argue that even if autonomy is central, it should be understood in more complex ways, which, specifically, may diminish the duty to disclose medical information. I will review the basic relevant points, and then discuss considerations specific to the NEIC.

Despite the centrality of the notion of informed consent in medical ethics, the attempt to elucidate its philosophical foundation and rationale has led to persistent difficulties. As Onora O’Neill puts it, ‘informed consent has been supported by poor arguments and lumbered with exaggerated claims.’ The idea that the duty to procure informed consent is founded on respect for autonomous choice – as common wisdom in medical ethics has it – runs into the following intractable problem: ‘if an account makes autonomy sufficiently demanding that actions which meet it are worthy of respect for their own sake, then the account will be too demanding to allow the vast majority of the choices that patients make about their healthcare . . . to count as autonomous. However, if the account is sufficiently lax as to allow the ordinary choices of patients . . . to meet it, then we will no longer have reason to think of such choices as worthy of respect.’

The list of the myriad irrationalities that people ordinarily exhibit in decision-making defies repetition, and this contradicts the presumption that the practice of obtaining informed consent, in its common universal form, rests on a duty to respect people’s autonomous choice. This author has sharpened this dilemma by showing that the question of the nature of the connection between the information and the consent gives rise to a dilemma analogous to the Gettier problem in the concept of knowledge, and that this puts in great doubt the explanation of informed consent by respect for autonomous choice. Following her diagnosis and exposition of the problem with informed consent, O’Neill argues that its ethical point is indeed more elementary than respect for autonomous choice: it is to provide reasonable assurance that a patient has not been deceived or coerced. This necessitates the provision of some essential information (along with the liberty of the patient to request more information at any time), but the question of what should be disclosed – which nowhere has a precise answer – gets some degree of freedom from the straightjacket of the lofty articulations of autonomous decision making; the caregiver is consequently allowed more leeway in judging the limits of disclosure, in ways that preserve trust. Specifically, consideration of the harmfulness of the NEIC can then be legitimately assessed.

It would be impossible to provide here a comprehensive review of the criticisms of the justification of informed consent by respect for autonomous choice; the above, however, as well as other criticisms have led to alternative justifications. Alongside O’Neill’s solution, others justify informed consent by: caring for patient well-being – and then respect for autonomy is relegated to an instrumental value, alongside other considerations of beneficence; by respect for spontaneous free choice, where considerations of decisional rationality become marginal (this is the libertarian position, to which certain conceptions of ‘procedural autonomy’ come close); or by respect for a sphere of privacy, specifically in decisions that concern one’s body. Whatever the precise alternative justification, as long as it is not autonomous choice per se, we would be allowed to relax the almost reflexive reasoning against nondisclosure, as exemplified by the categorical statement in the AMA’s Code of Medical Ethics that ‘Withholding medical information from patients without their knowledge or consent is ethically unacceptable.’ Rather, the criticism provides enhanced legitimacy to factor potential harms – notably, the NEIC – into our considerations of information nondisclosure.

Another venue through which certain relaxation of the moral injunction against nondisclosure is justified involves more nuanced interpretations of the meaning of autonomous choice itself. This author has introduced the concept of ‘ironic autonomy’ to describe cases where a manipulation, such as nondisclosure of information, which would otherwise compromise patient autonomy, is in a given context necessary to uphold her autonomy. This characterizes situations where the nondisclosure is in

20 Beuchamp & Childress, op. cit, note 17, p. 142.
26 Cohen, op. cit. note 23.
complete consistency with the patient’s considered preferences and necessary for their achievement, as the patient cannot effect the self-ignorance necessary to advance her goal. Ironic autonomy describes the status of the patient in certain non-deceptive placebo interventions, allowing nondisclosure while preserving autonomy via an ironic process. This confers moral legitimacy to nondisclosure within a restricted domain. This legitimacy is in conditions that do not involve harm to the patient; a fortiori nondisclosure will be justified in situations that involve harm to patients, such as the NEIC.

A related yet different view was advanced by Bennett Foddy, who also claims that placebo treatments preserve patient autonomy when used judiciously, but argues that this happens despite their being deceptive. Deception is wrong when it injures the victim’s autonomy. But this is so only if, by camouflaging reality, it prevents her from making reasoned choices, thus thwarting her self-government. The judicious use of placebo, however, takes place only when no other acceptable treatment is available, and therefore no restriction of the patient’s choice range takes place. Nor does it prevent objecting to the treatment on grounds of preferring one’s symptoms to the side effects, since placebo treatment has no side effects. In addition, the concealment does not injure autonomy by coercing the physician’s decision on the unsuspecting patient, since the placebo is not really treatment, and in this respect not different from the beneficial effect of the physician’s reassuring smile; but it would be absurd to object to physicians smiling to patients on account that it coerces patients into a therapeutic set of mind, without informed consent.

The conclusion, again, is that nondisclosure does not automatically injure patient autonomy. Beauchamp and Childress acknowledge that ‘the meaning of informed consent . . . is better analyzed in terms of autonomous authorization, which has nothing to do with disclosure specifically.’ Our important insight is that respect for autonomy is not identical with full disclosure not only because ‘full disclosure’ is often impossible, and possibly meaningless, but also because autonomy can indeed be preserved in situations where its meaning and phenomenology are more nuanced – indeed, even ironic.

Since we can find ourselves in ironic situations where respect for autonomy involves nondisclosure, and since the disclosure of nondisclosure (to gain patient permission) would ordinarily defeat its purpose, determining the obligation to disclose must sometimes refer to the idea of the reasonable person and his interests in knowing. At this point, however, even those who argue that ‘medical information should never be permanently withheld from the patient’ admit that ‘little is known of the extent to which disclosure of alarming medical information may ultimately harm patients.’ Research into the nocebo effect is of course supremely relevant in this regard, and it must receive the close scrutiny that ethicists have so far neglected to give it. In view of the mounting evidence in this field, however, the conclusion that physicians should ‘think out loud’ with patients sounds at best premature and possibly outright reckless; words indeed can maim.

While it has been reported that most patients welcome accurate information, that this can reduce rather than augment anxiety levels and enhance healing and patient satisfaction, the relevant data refers to knowing one’s diagnosis, treatment and prognosis; it does not tell us to what extent patients want to know (let alone are better off knowing) details about certain side effects of treatments. In the absence of clear data, some caution is morally reasonable. To be sure, O’Neill’s principle of ‘extendable information’ must always be operative: whenever extra information is requested, it ought to be provided. We should remember, at the same time, that, as Foddy emphasized, the reliance of the duty to disclose on the principle of patient autonomy makes sense to the extent that the information is important for self-government, i.e. for patients’ ability to make optimal life decisions based on their individual needs and personal values. This, however, is much less the case with knowing certain side effects (see discussion below), as compared with knowing the diagnosis, prognosis, or basic treatment alternatives. The nocebo effect is hence a special kind of case, whose harmful potential caregivers must consider very cautiously in the practice of obtaining informed consent.

Can the advised caution be reconciled with the concern for patient autonomy by a prior pact between doctor and patient? It is not clear when and if discussing the nocebo effect with patients will help reduce the negative impact of disclosure (in some cases it might exacerbate the relevant unconscious processes and have the opposite effect). But even if the more optimistic possibility is indeed the rule – in which case discussing the nocebo effect should of course be a requirement – it is highly doubtful that this could eliminate the phenomenon and make nondisclosure unnecessary: some evidence in placebo research suggests

30 Beauchamp & Childress, op. cit, note 17, p. 145.
that overt placebo also works.\textsuperscript{35} It stands to reason that this is at least as true with the nocebo, if not truer (for it is simpler to scare patients than to reassure them).

Medical ethicists have tended to think that respect for autonomous choice is the justification for seeking informed consent and to understand the meaning of such choice in rather rigid ways. These assumptions, we saw, must be qualified. The conclusion that nondisclosure is essentially wrong is therefore in need of similar qualification and balancing. This sharpens the difficulty in the dilemmas that the NEIC cases often pose. The next section will review practical considerations in dealing with these dilemmas.

III

The various arguments for the relaxation of the rigid conception of informed consent as grounded in autonomous choice do not mean that considerations of autonomy are not important — they obviously are. These arguments allow us, however, to think more freely and fruitfully on the optimal balance between respect for autonomy and care for patient well-being in the practice of informed consent.

Some authors see balancing as secondary in importance, and rather endorse an order of priority with autonomy at the top.\textsuperscript{36} The uncompromising primacy of respect for autonomy, specifically with respect to the placebo, is expressed in the opposition by the AMA’s Code of Medical Ethics to the deceptive use of placebos in clinical practice. While it is a truism that ceteris paribus deception is morally bad, the great majority of moral thinkers agree that deception (and even straightforward lying) is sometimes justified in order to prevent harm to innocent persons. (Augustine and Kant are the luminary exceptions.) This view characterizes the consequentialist perspective almost by definition, but is common also among Kantians.\textsuperscript{37} A deontologist such as W. D. Ross views veracity as (only) prima facie obligating,\textsuperscript{38} and Sissela Bok’s seminal work on the ethics of lying similarly determines ‘the principle of veracity’ as (only) a presumption in favor of truthfulness.\textsuperscript{39} Virtue ethicists too find the goodness in truthfulness to be qualified in various ways\textsuperscript{40} and, as Bernard Williams in his masterpiece Truth and Truthfulness, argues: to know when not to say the truth ‘is part of what it is for someone’s disposition of Sincerity to be correctly shaped.’\textsuperscript{41}

In light of all this, one should not find it surprising that the view that the value of truthfulness always trumps the benefits of placebo treatment has been reexamined and contested recently.\textsuperscript{42} But if indeed deception can sometimes be ethically justified in placebo treatment, then a fortiori the prevention of the nocebo effect can be justified too. This follows from two important reasons. (1) The nature of the manipulation of the patient is significantly milder in the nocebo case: while ethical objection to placebo treatment is based on the fact that it involves (when it does) a deceptive message, the problem presented by the NEIC stems from the element of nondisclosure of information; and it is widely agreed that ceteris paribus nondisclosure is the least morally problematic of all kinds of deceptive manipulation.\textsuperscript{43} (2) The prevention of harm is ceteris paribus of greater moral weight compared with improving well-being.

Moral dilemmas force us to assess the relative claims of opposing moral duties. In medical ethics, one of the most oft discussed is the dilemma between respect for patients’ autonomy and care for their well-being. This dilemma has usually been recognized as one between autonomy and paternalistic beneficence, while the parallel dilemma between autonomy and nonmaleficence has received far less attention (Beauchamp and Childress, for example, dedicate a 20 page discussion to the former, while the latter can only be gleaned from between the lines).\textsuperscript{44} The dilemma of the NEIC brings this important but relatively neglected topic to front stage. Miller and Colloca have recently sounded an important seminal call to rethink the traditional separateness of two duties: risk-benefit assessment of treatments before they are recommended to patients and the obligation to obtain informed consent, arguing that information disclosure can by itself produce or shape the risks and benefits. They also rightly claim that this calls for a reevaluation of the dominant,


\textsuperscript{39} Bok, op. cit. note 16.

\textsuperscript{40} A. Baier. 1990. Why Honesty is a Hard Virtue? In Identity, Character, and Morality. O. Flanagan and A. Okensgerge Rorty, eds. Cambridge MA: MIT Press.


\textsuperscript{44} Beauchamp & Childress, op. cit. note 17.
autonomy-based justification of informed consent. The present articulation of the NEIC and its analysis support this perspective, provide it with ethical substance, and focus attention specifically on assessing the strength of the duty not to harm, as pitted against the duty to respect patient autonomy – both integral to the obligation to obtain informed consent.

With any serious moral dilemma, it is often the details of the case that tip the balance of reasons in favor of one argument or the other. In the case of the NEIC, we should assess the nature and degree of manipulation in nondisclosure and its effect on autonomy versus the chances and magnitude of the harm it can prevent. Particular cases will present important idiosyncratic details, which will influence our consideration; here, we can do no more than review some preliminary general considerations. The advancement of empirical research on nocebos (and related subjects) will enable more precise distinctions to be made and thus enrich our tools for decision making.

It would seem that the most obvious first consideration ought to be the level of harm to the patient: the greater the harm of the nocebo effect, the weaker the obligation to disclose. But it is unlikely in fact that this should make a difference, since just as it is worse to cause greater harm via the NEIC, it is equally worse to hide a more serious potential harm from the patient. Since these opposing considerations increase simultaneously, they seem to cancel each other out. (The one exception would be if recognizing a side effect were important for seeking immediate medical evaluation – then disclosure would be mandatory.) What we can say instead is that nondisclosure should be directly related to the degree of sensitivity of the particular side effect or complication to suggestion. For example, not all symptoms of Parkinson’s disease are equally sensitive to suggestion: while bradykinesia is sensitive, tremor and rigidity apparently are not. The more the potential side effect is sensitive to suggestion, the more caution should be applied in disclosing it. In contrast, the rarer a side effect or complication, the lesser is the duty to disclose it (this is true in general and is not unique to the NEIC). With the dilemma of the NEIC in mind, therefore, the duty to disclose should be directly correlated to the ratio between the probability of a specific side effect to occur after suggestion and the rarity of its occurrence as a result of the real drug or intervention. For example, in a study on the efficacy of placebo versus anti-hypertensive drugs for the treatment of stage 1 and stage 2 hypertension, at least as many subjects (proportionally) had to discontinue treatment due to adverse drug effects in the placebo group (i.e. a nocebo effect) as in the treatment group. This shows an unacceptably high ratio between the prevalence of suggestion-induced symptoms and symptoms due to real drugs. (The interpretation of those results is more complicated, in fact, but that discussion does not change the conclusion and thus irrelevant here.) Since side effects reduce compliance to treatment, and since hypertension is responsible for much mortality (and in patients with other conditions, such as cardiac or pulmonary insufficiency, even low-level hypertension may be dangerous), it is very clear why doctors must recognize the serious moral dilemma they potentially face when disclosing information about side effects to patients.

The more a specific nocebo effect is empirically validated, the more weight it should get in our ethical calculation. If or when we have well defined cases where evidence of the creation of specific nocebo effects is robust and compelling, we may have no choice but to begin thinking of the full disclosure of information in those cases as if coupled with a real and actual harm (say, painful electrocution of the patient), and think whether this kind of treatment of the patient is indeed the necessary price for the respect owed to her autonomy.

The above considerations concerning the nature of the intervention should be supplemented with consideration of the nature of the patient. The need for personal tailoring of informed consent is under-developed in medical ethics. Here, however, I am not speaking of tailoring the amount, timing or character of disclosure to the values and interests of the individual patient – an important thing in itself – but of fitting the level of disclosure to the personality type of the patient and its susceptibility to nocebo effects. This seems to be recognized as a moral concern virtually nowhere in the informed consent literature, at least not in any systematic manner. It was found, for example, that, among patients with temporomandibular disorder, those suffering from somatization disorder or tendency (high values on the Somatization Scale) are three times more susceptible to suffer pain secondary to placebo examination and treatment. A tendency to anxiety or depression is similarly correlated with heightenened nocebo effects. In contrast, optimists are more likely to experience placebo effects, and it is conceivable (though needs empirical validation) that they are reciprocally less likely to experience nocebo effects. Empirical data of this sort can be valuable for caregivers in

46 Benedetti et al., op. cit. note 2.

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assessing the amount of suffering they are likely to cause to different patients, and thus guide their moral judgment regarding the dilemma of the NEIC.

It might be argued that suffering more pain is not a dangerous side effect, and so cannot offset the duty to disclose; but (aside from the fact that ongoing pain can lead to sedentariness or depression, and these can form positive feedback cycles with pain, and indeed set off lethal cascades of pathologies) we surely ought not to be dismissive toward the gravity of causing real suffering to patients. Respect for autonomy ought not to fall into the moral trap of relying on the fact that ‘every person has enough resilience to endure the agony of others,’ as the Duke de La Rochefoucauld put it, with typical wit. It might be argued further that the gravity of the problem of the NEIC is mitigated by the fact that, on the one hand, the nocebo effect usually does not involve serious medical complications, and on the other hand, when the adverse symptoms are not medically very consequential, the duty to obtain informed consent is less rigorous to begin with. While there is some truth in this observation, we must think of the duty to obtain informed consent as spanning a wide range of practices, from the most formal to much less formal patterns of information sharing. Seen in this light, the potential for the dilemma of the NEIC to arise in various medical settings is substantial and merits our close attention, both conceptually and practically. And there are no doubt cases where serious repercussions of the NEIC may be seen in settings where the most explicit informed consent is needed. An example discussed above that may illustrate this is that the medical benefit from implantation of electrodes in the brain (of parkinsonian patients) is susceptible to nocebo effects.51

Beyond questions of nondisclosure, the responsibility to prevent the NEIC refers also to the question of how to disclose information, invoking the issue of framing. The way any message is framed affects the way it is accepted and hence its effects, and this well-known truth obviously holds with respect to medical information as well. For example, when information on side effects of drugs (in information leaflets) used less ominous frequency adverbs – ‘seldom’ instead of ‘sometimes’ – patients experienced fewer side effects.52 In such cases of framing, it is often not clear whether the reformulations that are meant to manipulate amount to deception at all. In the example just mentioned, it seems that the change of adverbs is not deceptive, as the study also showed that the precise meaning of those frequency words is ill-defined in the population (with near-total overlap in the ranges of frequencies people stated as defining those two adverbs); hence substituting the one for the other does not create a change of meaning that constitutes an untruth. If or when the framing amounts to deception, then the dilemma of the NEIC may arise; when it does not, then there is no dilemma: the potential for the NEIC creates a straightforward moral duty to use the formulation that causes fewer side effects. Similar cases of framing that do not amount to deception are the stating of treatment outcomes as the probability of survival versus the complementary probability of dying53 the more rather than less frequent use of professional terms as opposed to vernacular terms, or vice versa, and so on.

The danger of hurting the trust between doctor and patient is often rightly invoked when discussing placebo treatment. But in cases such as these, it is hard to see how the framing manipulation which does not amount to deception injures trust. An important element of the trust of the patient in the doctor is surely that the latter will not harm him; and this should be the dominant consideration in these cases. The extent to which patients perceive marginally deceptive framing effects as injuring trust and how this should be optimally calculated against the loss of trust in harming the patient through nocebo effects are important questions which need empirical examination. (Most of the literature on nocebos as well as on informed consent deals with the research setting. In the therapeutic setting, however, the patient is not recruited for the potential benefit of humanity, but rather stands to benefit individually; the weight of the reasons that can legitimately counterbalance the required respect for autonomy is therefore greater.)

The duty to disclose information to patients is a basic duty in medical ethics. Its precise interpretation in practice is less than straightforward, however, and encompasses questions such as: the scope of that which ought to be disclosed (physicians’ levels of competence, various institutional policies, genetic information, minor medical mistakes, etc.), the obligation to disclose uncertain diagnoses and other uncertain medical assessments, the conditions under which nondisclosure amounts to deception, and more. This paper is an attempt to shed light on another, important question: the optimal balance between disclosure and nonmaleficence, which assumes an especially critical form in the dilemma of the NEIC. Further research into the nocebo effect coupled with philosophical attention to the problem of the NEIC can help determine how best to minimize harm to patients, while treating them with due respect.

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51 Benediti et al., op. cit. note 5.