

# Placebo effects and racial and ethnic health disparities: an unjust and underexplored connection

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## ABSTRACT

While a significant body of bioethical literature considers how the placebo effect might introduce a conflict between autonomy and beneficence, the link between justice and the placebo effect has been neglected. Here, we bring together disparate evidence from the field of placebo studies and research on health inequalities related to race and ethnicity, and argue that, collectively, this evidence may provide the basis for an unacknowledged route by which health disparities are exacerbated. This route is constituted by an uneven distribution of placebo effects, resulting from differences in expressions of physician warmth and empathy, as well as support and patient engagement, across racial and ethnic lines. In a discussion of the ethical implications of this connection, we argue that this contribution to health disparities is a source of injustice, consider ways in which these disparities might be ameliorated and suggest that this conclusion is likely to extend to other realms of inequality as well.

## INTRODUCTION

To date, bioethical scholarship concerning the placebo effect in clinical settings has overwhelmingly focused on the conflict that arises between patient autonomy and clinical beneficence when placebo treatments are deceptively prescribed to patients. For decades, a wealth of bioethics literature has pivoted on the questions of whether it is ethical to deceive patients for the sake of their well-being, whether placebos undermine patient autonomy and whether deception is morally justified on the grounds that placebo effects are therapeutically significant.<sup>1–5</sup> This paper draws attention to another key principle of biomedical ethics that we believe has been eclipsed within the placebo discourse: the principle of justice.

In order to illuminate a connection between placebo effects and justice, we present data from two subfields of research: (1) findings related to several key factors thought to mediate placebo effects within the clinical encounter, and (2) healthcare inequalities related to the quality of patient–physician interactions across lines of race and ethnicity. In light of this evidence, we argue that placebo effects that are mediated by aspects of the clinical encounter are likely to be unevenly distributed across different populations and furthermore, and that this uneven distribution is likely to be exacerbating health disparities along racial and ethnic lines. While the evidence we present focuses on how membership of certain racial or ethnic groups may diminish the prospects of patients' experiencing placebo effects in clinical interactions, as will be discussed further below, it is quite plausible

that these concerns also apply to other groups who experience differential treatment within healthcare (eg, along lines of gender identity, socioeconomic status, sexuality, weight and so on).

In what follows, we offer a brief introduction to the value of patient–physician interactions, followed by an overview of the placebo effect. We describe the mechanisms by which placebo effects are produced and offer evidence that depicts their role in the clinical encounter. After a brief discussion of health disparities, we connect this evidence to research investigating the presence of inequalities in healthcare, drawing on a wealth of research that demonstrates how race and ethnicity can influence the quality of patient–physician interactions. Linking these two distinct bodies of literature leads us to the conclusion that when it comes to the distribution of placebo effects, some individuals may be unwittingly disadvantaged in terms of experiencing their benefits. We argue that this constitutes a hitherto unacknowledged source of inequality within healthcare encounters and that it is likely to be contributing to the significant health disparities that exist. We conclude with a discussion of the ethical implications of this connection.

## THE VALUE OF PATIENT–PHYSICIAN INTERACTIONS

In 1993, the WHO extolled effective patient–doctor interaction and communication as 'central to doctor and patient satisfaction, to the clinical competence of doctors, and to the health outcomes of their patients'.<sup>6</sup> Since the publication of this WHO report, empirical research on the value of patient–physicians interactions has burgeoned. The conclusion of this research has further corroborated the WHO finding that the quality of patient–physician interactions is at the heart of healthcare. Mounting evidence shows that physicians have a fundamental role to play in steering the quality of the consultation by engaging in clear, understandable dialogue and providing empathic care. Physicians' verbal skills (the content of conversation, their affective tone, the number of interruptions) as well as non-verbal cues (maintaining eye contact, warm facial expressions, upright posture, attentive listening) are cited as key components of effective, empathic communication with patients.<sup>7–8</sup> The effects of such communication include improvements in patient adherence to medication and treatment recommendations, increases in patient satisfaction, and benefits to patient well-being and health outcomes.<sup>9–10</sup>

In this paper we focus on the last of these considerations: the direct benefits of patient–physician



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interactions on health outcomes. This link has been well documented. A systematic review of experiments investigating the role of communication on clinical outcomes found that higher quality communication appeared to impact ‘emotional health, symptom resolution, function, physiologic measures (ie, blood pressure and blood sugar level) and pain control’.<sup>7</sup> Showing emotional support and empowering patients have also been shown to lead to significant reductions in time spent in the hospital.<sup>11 12</sup> While a variety of pathways are likely to be involved in this link between the patient–physician relationship and improved clinical outcomes,<sup>13</sup> we are specifically interested in how placebo effects produced within the clinical encounter may improve patient outcomes.

## THE PLACEBO EFFECT

Rather than consider placebos as *treatments* (in a clinical setting) or as *controls* (in a research setting), we are interested in placebo *effects* (which occur in both clinical and research settings). Placebos as treatments in clinical contexts refer to pills or medications that are prescribed to patients (rightly or wrongly) with the intention of ameliorating patients’ symptoms and/or placating patients’ health concerns. Although the distinction has been criticised, the so-called ‘pure placebos’ (eg, ‘sugar pills’) or ‘impure placebos’ (eg, antibiotics prescribed for viral infections) may be prescribed to patients, even though there is no active pharmacological ingredient in the medication that is effective for their condition or symptoms. Such prescriptions are quite common; in the UK, 77% of primary care doctors report that they use placebos at least once per week,<sup>14</sup> while in the USA 55% of internists and rheumatologists report using placebos at least once during the previous year.<sup>15</sup> Placebos in research contexts, on the other hand, are used as controls rather than treatments. In a typical randomised placebo controlled trial, a third are allocated to no-treatment waiting list, a third of the participants are randomised to receive placebos, while the remaining third receive the active treatment. In this way, the two ‘treatment’ groups are subject to all factors within the trial (eg, the natural progression of disease, regression to the mean, placebo effects) apart from the active treatment, and the difference in outcomes between these two groups can be used to determine the efficacy of the active treatment.

So what are placebo effects? While there is no consensus among placebo researchers regarding how the term placebo effect is best defined, there is stable agreement among researchers that placebo effects are positive health changes that occur as a result of distinctive psychobiological mechanisms. While placebo effects are the beneficial effects of these mechanisms, the negative effects elicited through these mechanisms are known as nocebo effects. While many mechanisms have been cited as underpinning placebo effects, two chief mechanisms that play a clear role in placebo and nocebo effects are expectations and conditioning.<sup>16</sup>

Placebo effects that operate through the mechanism of expectations occur when positive clinical effects are brought about by the experience of anticipating them. The role of expectancy in inducing placebo effects can be seen most clearly in experiments that demonstrate the significant difference in pain relief when patients are aware that a painkiller is being administered, compared with when it is administered covertly from another room. In one experiment, patients in the covert condition required a dose of 50% more painkillers in order to reduce pain to the same degree as those in the

overt condition.<sup>17</sup> Conditioning, on the other hand, refers to repeated associations between a neutral stimulus and an active medication (or unconditioned stimulus), which lead to the neutral stimulus eliciting the effects of the unconditioned stimulus on its own. In medical contexts, conditioning can result in objectively measurable placebo effects, such as when anise-flavoured syrup is combined with infusions of cyclophosphamide, which reduces white blood cells, and after several pairings, exposure to just anise-flavoured syrup leads to a reduction in white blood cells.<sup>18</sup> The relationship between expectations and conditioning is not entirely clear; each mechanism may contribute to placebo and nocebo effects individually, additively or through an interactive effect.<sup>19</sup>

Some symptoms and conditions appear to be very responsive to placebo and nocebo effects (eg, pain, motor impairments in patients with Parkinson’s, depression, irritable bowel syndrome), while there is little to no evidence of placebo effects impacting other conditions (eg, tumours, viral infections).<sup>16</sup> It is noteworthy that no placebo pill or treatment is required to elicit placebo effects; they can be brought on by factors such as the prior beliefs of patients or the language used during treatment. Experiments have demonstrated that individuals who believe that acupuncture is an effective treatment for pain and who expect to personally benefit from it tend to report more pain relief, even 6 months after treatment.<sup>20 21</sup> Additionally, words used by physicians prior to the administration of treatments have been found to significantly impact patients’ experiences of pain. In one experiment, half of the participants were told before receiving an analgesic, “You are going to feel a big bee sting; this is the worst part of the procedure”, while the other half were told “We are going to give you a local anesthetic that will numb the area and you will be comfortable during the procedure”. Those patients who received the first description rated the painfulness of the injection as 5/10 on average, while the other group reported it as 3/10 on average.<sup>22</sup> Similarly, in a powerful demonstration of the nocebo effect in practice, half of a group of men were told that they might experience sexual side effects as a result of a medication they were being prescribed, while the other half were not told. Of those who were told about the potential side effects, 44% reported experiencing them, while only 15% of those who were not told reported any sexual side effects.<sup>23</sup> Finally, it is important to underscore that placebo effects also play a role in augmenting the effectiveness of treatments as usual, including commonly used medications such as painkillers—a point that is likely to be underappreciated among physicians.<sup>24</sup>

## EVIDENCE FOR PLACEBO EFFECTS IN THE CLINICAL ENCOUNTER

Research on the relationship between patient–physician interactions and patient outcomes suggests that several distinct components of the clinical encounter may impact placebo and nocebo effects, primarily through shaping patient expectations, although conditioning and social learning are likely to play a role as well. Here, we focus on evidence related to two aspects of the clinical encounter that impact health outcomes by way of the placebo effect: clinician warmth and empathy, and support and patient engagement.

### Clinician warmth and empathy

Recent research suggests that placebo effects may be mediated by the perceived warmth and competence of the clinician.

Howe *et al*<sup>25</sup> found that after inducing an allergic reaction in participants, those who had both positive expectations of allergy relief and who interacted with a provider who demonstrated high warmth and high competence displayed the largest reduction in their allergic reaction (as measured by the size of the weal) compared with other groups who had negative expectations and/or providers with low warmth and competence. Similarly, in an experiment involving patients with a common cold, it was found that 48 hours after the clinical encounter, those who rated their clinician as high in empathy had higher measures of interleukin 8 (an immune biomarker) and reported that their cold lasted on average 1 day less than those who rated their clinician as low on empathy.<sup>26</sup> Finally, in an experiment in which individuals were given either real or sham physical therapy for chronic low back pain and placed in either limited or enhanced therapeutic alliance conditions, the results demonstrated that the degree of therapeutic alliance was just as important for pain relief as whether they were receiving real or sham therapy.<sup>27</sup>

### Support and patient engagement

Relatedly, the ways in which healthcare professionals support and engage with patients have been shown to contribute to placebo effects that influence clinical outcomes. A working group examining the treatment of headaches found that patients who felt that clinicians fully discussed their headache with them were 3.4 times more likely to report that their headache was resolved than patients who did not, and that this factor was the strongest predictor of resolution.<sup>28</sup> Similarly, an experiment within a family practice indicated that the level of agreement between a patient and physician on the nature of the problem significantly predicted a decline in patient symptoms.<sup>29</sup>

In a clear investigation of how placebo effects can be generated by increased support and patient engagement in the clinical encounter, Ted Kaptchuk and colleagues conducted an experiment involving 262 patients with irritable bowel syndrome, randomised into three conditions.<sup>31</sup> The first group received no treatment but participants were required to respond to a series of questionnaires at three points during the experiment, the second received these questionnaires as well as sham acupuncture, which was administered in a 'business like' interaction with the practitioner, while the third received both the questionnaires and sham acupuncture, but the latter was delivered in a 'highly organized ritual which included an augmented patient – healer interaction that included taking medical and psychosocial histories and demonstrations of compassion, support, attentive-listening, 20 [seconds] of thoughtful silence and expressions of confidence'.<sup>30</sup> Outcomes found that adequate relief was experienced by 28% of the first group, 44% of the second group and 62% of the third group.<sup>31</sup> These findings offer a powerful demonstration of how incremental additions of support and engagement within the clinical encounter can lead to incremental improvements in symptom relief for patient.

This evidence demonstrates that, for certain conditions and symptoms, placebo effects mediated by the clinical encounter play a significant role in contributing to patient outcomes. In light of this, the next section offers a brief overview of the prevalence of health disparities along racial and ethnic lines, and in the following section, we examine data related to inequalities in care that correspond with the two aspects of the clinical encounter discussed above.

### HEALTH DISPARITIES

A substantial body of evidence suggests that one's race and ethnicity can significantly impact the healthcare one receives.<sup>i</sup> In 2003, the Institute of Medicine (IOM) (now the National Academy of Medicine) published a landmark report entitled *Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care*, and concluded that 'Evidence of racial and ethnic disparities in healthcare is, with few exceptions, remarkably consistent across a range of illnesses and health care services'.<sup>32</sup> Evidence suggests that while Asian Americans are the most likely population to die from cancer, they are the least likely to be recommended for cancer screening.<sup>33</sup> In Canada, Aboriginal people are half as likely to advance from referral for transplantation to the transplant waiting list as non-Aboriginal people.<sup>34</sup> Black and Hispanic patients in the USA are significantly more likely to undergo primary caesarean delivery than whites (54% and 12%, respectively).<sup>35</sup> Recent findings show that disparities have not narrowed since the publication of the IOM report,<sup>36</sup> although the American Medical Association recently amended its Code of Medical Ethics to include a section stipulating that both individual physicians and the medical profession have an ethical obligation to increase awareness of health disparities and to put in place measures to eliminate them.<sup>37</sup>

Many explanations have been given for disparities in health outcomes. These explanations can be roughly divided into four categories: environmental factors, factors found in the healthcare system, patient factors and clinician factors. Environmental explanations focus on socioeconomic status, stress that results from discrimination, as well as differences in exposures to hazards or pollutants. Explanations related to the healthcare system point to the ways in which inequality grows as a result of differential access to care, patterns of referrals, language barriers, bureaucratic difficulties and the fragmentation of healthcare services. Patient factors examine differences in attitudes and behaviours related to health, adherence to treatment, potential genetic differences, and how stereotype threat might impact minority health. Finally, clinician factors involve examinations of how discrimination within the patient–physician relationship, resulting from both implicit and explicit biases, might lead to differences in terms of both screening and treatment.<sup>38</sup> While each of these factors contributes to the existence of health disparities, here we identify an unacknowledged avenue by which differences in health outcomes between populations may be exacerbated: by way of placebo effects mediated in the clinical encounter.

### EVIDENCE OF INEQUALITY IN THE CLINICAL ENCOUNTER

Aspects of the clinical encounter such as physician communication and setting patient expectations may be considered by health providers integral to the 'art of medicine' but dispensable when it comes to objective outcomes. As the research cited above demonstrates, this is not the case. Therefore, it is worth taking a closer look when a systematic review of patient–physician communication concludes that minority patients 'are less likely to engender empathic response from physicians, establish rapport with physicians, receive sufficient

<sup>i</sup>The scope of this discussion may be limited because the vast majority of these data come from the USA, Canada and the UK, where data on health in terms of race and ethnicity are collected. Several other countries in the Global North, including France, the Netherlands, Norway and Italy, do not collect information related to race or ethnicity within health data.

information, and be encouraged to participate in medical decision making'.<sup>39</sup> In line with this, we present data below from research related to inequalities in healthcare, mirroring the two categories discussed above: clinician warmth and empathy, and support and patient engagement.

### Clinician warmth and empathy

Warmth and empathy expressed by clinicians appear to differ across populations of patients. For example, one experiment involving independent observers who watched interactions between patients and physicians through a one-way mirror found that physicians spent more time with white patients, and scored higher on the dimensions of interviewing and empathy when they were meeting with white patients, as compared with Latino patients.<sup>40</sup> Another study found that physicians used significantly fewer positive expressions when engaging with Latino patients as compared with non-Latino patients, but that levels of empathy were similar in both groups.<sup>41</sup> Further investigations into inequality in the clinical encounter show that high scores on implicit racial bias, as determined by a test derived from the Implicit Association Test (IAT),<sup>ii</sup> correlate with lower ratings of positive affect in patients and higher ratings of clinician-dominated dialogue during the encounter.<sup>42</sup> Another analysis of patient-physician interactions by independent coders who listened to audio recordings of patient visits found that physicians were more contentious with black patients than white patients, and guessed that black patients were less satisfied with the care they received.<sup>43</sup> Finally, and while not a direct measure of empathy or warmth, a study by van Ryn and Burke<sup>44</sup> found that after meeting with a number of patients and then completing short surveys about each of them, physicians were more likely to see black patients as less intelligent, more likely to engage in risky behaviour and less likely to adhere to medical advice, when compared with white patients. Physicians were also less likely to agree that black patients were 'the kind of person they could be friends with' in comparison with white patients.<sup>44</sup>

### Support and patient engagement

Differences in support and patient engagement appear to be influenced by race and ethnicity as well. In an experiment involving patients with breast cancer, it was found that physicians spent significantly less time engaging in relationship-building behaviours with black patients as compared with white patients.<sup>45</sup> Independent raters of audio tapes of patient visits reported that when clinicians were interacting with black patients, they engaged in 33% less patient-centred communication than when they were speaking to white patients, showed less positive affect and were 23% more verbally dominant.<sup>46</sup> Studies have also found that when white physicians interact with black patients, they tend to engage in less shared decision making and provide less information than when they engage with white patients.<sup>47</sup> Corroborating this evidence, Cooper-Patrick *et al.*<sup>48</sup> found in a telephone survey that black patients tend to rate their medical visits as significantly less participatory than their white counterparts, while another experiment found that black

patients give worse ratings for patient-centred care to clinicians with greater implicit racial biases, as measured by the IAT.<sup>iii49</sup>

### EVALUATING THE EVIDENCE: DISPARITIES IN PLACEBO EFFECTS

The evidence presented above urges us to dig deeper into how differences in the delivery of care impact the distribution of placebo effects within the context of care. While no direct evidence speaks to how placebo effects are influenced by inequality in the clinical encounter, these two bodies of literature offer strong indirect evidence to suggest that differences in placebo effects are occurring along lines of race and ethnicity. While the primary mechanisms of expectations and conditioning that contribute to placebo effects are likely to be mediated by expressions of warmth and empathy by physicians, as well as degrees of support and patient engagement, it can be directly inferred from the evidence presented above that these aspects of the clinical encounter arise significantly less frequently within clinical interactions with minority patients. This suggests that individuals who are members of racial and ethnic minority groups may receive less therapeutic benefit via placebo effects and experience more harm via nocebo effects. Furthermore, this unequal distribution of placebo and nocebo effects, we argue, is likely to exacerbate existing inequalities related to health outcomes along lines of race and ethnicity, constituting another route by which health disparities are exacerbated.

Further indirect evidence for the role of placebo effects in health disparities can be found in the high prevalence of health conditions that show robust responses to placebo and nocebo effects in racial and ethnic minorities. As mentioned above, these conditions include pain, psychiatric disorders, Parkinson's disease, and several types of functional somatic syndromes, such as irritable bowel syndrome. In line with this, several types of pain (eg, chronic non-malignant, acute, cancer) and Parkinson's disease have been shown to have disproportionately high prevalence rates in racial and ethnic minorities.<sup>50 51</sup> Interestingly, evidence suggests that while racial and ethnic minorities do not have an increased lifetime risk of psychiatric disorders, the persistence of such disorders is more common among minorities, perhaps partly as a result of differences in care.<sup>52</sup> Unlike these other conditions, irritable bowel syndrome appears to be more prevalent among whites than racial and ethnic minorities, although this gap may be narrowing.<sup>53 54</sup> Of course, evidence for racial and ethnic disparities in placebo-responsive conditions does not imply either that placebo effects cause these conditions or that there aren't other important explanations for these disparities (eg, socioeconomic status, exposure to stress). The data, however, do provide additional indirect evidence for the role of placebo and nocebo effects in contributing to racial and ethnic health disparities.<sup>iv</sup>

<sup>ii</sup>The IAT is a favoured tool within the literature on inequalities in healthcare and was designed to measure levels of implicit associations that individuals may have, despite their explicit beliefs (eg, one may explicitly believe that gender makes no difference to one's scientific capacity, but still hold an implicit association between men and science). It should be noted that many concerns have been raised in relation to this tool, so evidence relying on it ought to be taken with a grain of salt.<sup>89-91</sup>

<sup>iii</sup>Levels of trust also appear to vary across racial and ethnic populations, at least in the USA, which has been linked to both the history of racism within medical research as well as current experiences of discrimination in healthcare.<sup>92</sup> Some evidence suggests that blacks and Latinos trust healthcare professionals less than whites,<sup>93 94</sup> while one experiment found that physician trust was similar in black and white patients diagnosed with lung cancer before a clinical visit, but after their visits black patients had lower ratings of physician trust.<sup>47</sup> While it is not clear that levels of trust contribute to placebo effects or impact patient outcomes, it is a hypothesis worth investigating further.

<sup>iv</sup>Many thanks to an anonymous reviewer for encouraging us to make this additional link.

## ETHICAL IMPLICATIONS

What can we take away from this? While there are many directions a discussion of the ethical implications of the link between placebo effects and racial and ethnic inequalities in healthcare could be taken, here we focus on four ethical questions in particular. These questions include whether or not an uneven distribution of placebo effects constitutes an injustice, how the standard of care might be expanded to harness the placebo effect and counteract these inequalities, how providers' implicit biases might be reduced, and how other lines of inequality might intersect with placebo effects and health disparities.

### Unequal distribution of placebos as an injustice

If, as we have hypothesised, health disparities along racial and ethnic lines are increasing as a result of an uneven distribution of placebo effects, as mediated within the clinical encounter, this raises the question of whether such disparities constitute an injustice. It might be granted that other contributors to health disparities, such as differences in treatment or diagnosis, can be reasonably thought of as instances of injustice, but that patients who are fortunate enough to engage with a supportive and empathic physician are merely the recipients of a lucky, therapeutic boost to their care. One might argue that the former scenario has serious repercussions for individual health outcomes and implicates the clinical competence of physicians, and so constitutes an injustice, while the latter scenario only involves different degrees of friendliness, which cannot significantly impact health outcomes and does not violate reasonable expectations of physician behaviour, and so does not constitute an injustice.

With regard to the impact of such a scenario on clinical outcomes, as outlined in detail above, aspects of the clinical encounter that contribute to the distribution of placebo and nocebo effects can significantly influence clinical outcomes across conditions and symptoms. Research has demonstrated that saline injections delivered with positive verbal suggestions can have the equivalent impact of 6–8 mg of morphine administered surreptitiously, suggesting that placebo effects are quite powerful indeed.<sup>55</sup> Taking this into account, an uneven distribution in placebo effects might appropriately be thought of as a freely administered treatment for certain privileged demographic groups.

The more serious objection holds that while differences in diagnosis and treatment are central to a physician's clinical role, placeboogenic aspects of the clinical encounter, such as warmth and support, are above and beyond what we require from our doctors, so any failure to express these qualities cannot constitute an injustice. However, the fact that the role of these qualities in impacting health outcomes is not widely acknowledged cannot constitute a defence; medical practice must follow the evidence. Professional medicine is concerned with the appropriate prescription and use of medications and surgical interventions: call these the 'tools of medicine'. However, the fact that other tools, such as empathy, may not be conventionally considered part of this toolkit does not thereby constitute a justification for their not being classified as such. Rather, it merely reflects the habits and practices of orthodox medicine. Force of habit, however, is no defence against the charge of ignorance.

In these ways, we argue, the unequal distribution of placebo effects which, we argue, is likely to be contributing to systematic disparities within the delivery of patient care constitutes an injustice.

### Expanding the standard of care

When medical students are taught what the standard of care is for a particular condition, they learn about which interventions are known to produce the best results, given the population they are working with and given the other risks present. What they are not typically taught is the way in which the manner they administer an intervention can impact clinical outcomes. The evidence above raises the question of whether the standard of care ought to be expanded to include not just *what* treatment ought to be administered, but *how* a treatment ought to be administered. This question brings with it a host of practical and ethical issues, including what conditions would be appropriately included in the enhanced standard of care, how to communicate with patients regarding these aspects of treatment, whether one might bill for the manner in which a treatment is delivered and whether the placebo-maximising aspects of the clinical encounter can truly be taught. While more research is surely needed before such a shift could be implemented, it is worth briefly exploring these questions.

Importantly, if the standard of care was expanded to include not just what, but how medical interventions are delivered, it would first be essential to follow the evidence in terms of what kinds of expansions would be warranted. As mentioned above, research into placebo and nocebo effects shows that some symptoms and conditions are likely to be impacted by the aspects of the clinical encounter discussed above, while others may be unresponsive. Experiences of pain are highly susceptible to placebo effects, as are some psychiatric disorders (including depression and anxiety), Parkinson's disease and several functional somatic syndromes, so these might be better candidates for expanded treatment models than others.<sup>56</sup> Then again, it is likely that anyone in poor health can stand to benefit from positive direct effects of therapeutic communication. While tumour growth may be unaffected by the clinical relationship, cancer-related fatigue has been shown to be responsive to placebo treatments.<sup>57</sup>

In addition if the standard of care was expanded to account for the powerful role placebo effects can play within the clinical encounter, this would raise difficult questions regarding how much the patient should be told, given that physicians cannot avoid communicating in one way or another and framing information that they provide.<sup>58</sup> It has been observed that a tension arises between commitments to transparency that are commonly embraced within medical codes of ethics and the way in which placebo effects remain unacknowledged in the clinical setting.<sup>59</sup> If true transparency is the goal, should patients be told that the number of minutes, smiles and tests they receive during their visit may all impact their health? Should they be informed about possible disparities in the delivery of care? Indeed, the latter question becomes even more troubling if we try to picture what transparency might look like, since telling patients that their quality of care may be undermined due to non-clinical factors like race could lead to an increase in the likelihood of nocebo effects occurring.

Translating these findings into improved outcomes in practice will not be an easy task. In fee-for-service models of healthcare, where clinicians are reimbursed for components of treatment piece by piece, it may even be considered necessary to bill for placebo-maximising aspects of the clinical encounter in order to see them implemented in practice. This could bring about a bizarre reality in which clinicians are reimbursed \$20 for shaking hands with a patient, \$30 for 20s of thoughtful silence and \$50 for a short conversation about the weather. These may seem laughable, but some evidence suggests that paying for such

improvements within the clinical encounter may come out on top within a cost–benefit analysis. As mentioned above, it has been found that better communication skills and an increase in emotional support can lead to significant reductions in postsurgical days spent in the hospital.<sup>11 12</sup>

Another question arises in terms of whether the aspects of the clinical encounter that make a real difference are aspects that can readily be taught to clinicians. While some factors, such as the length of time spent with a patient, may be easy to increase, others, it might be argued, such as the degree of empathy expressed and the participatory style of communication, are harder to teach. However, there is encouraging evidence that short training interventions can significantly improve physicians' communication skills and perceived levels of empathy among patients.<sup>60</sup> Indeed, it was the introduction of short courses which focused on teaching surgeons to increase patient empowerment and communicate better that led to the reductions in days spent at the hospital mentioned above. These findings suggest that, at least to a certain degree, placebo-maximising behaviours may both be teachable and, in the long term, increasingly feasible in clinical encounters. Perhaps more important, however, is eliminating the behaviours that lead to differential treatment of minority patients in the first place.

### Reducing implicit bias

As noted, an abundance of research shows that patients from racial and ethnic minority groups are vulnerable to inferior care. A wealth of indirect evidence suggests that these differences in care are likely to be, at least in part, the result of implicitly held biases related to race and ethnicity.<sup>38</sup> While most physicians are unlikely to explicitly report biases towards minority groups, like the rest of the population, most display substantial implicit biases grounded in racial and ethnic stereotypes, and at least sometimes, these biases appear to correlate with clinical decision making.<sup>61</sup> Evidence also suggests that reliance on stereotypes tends to increase with cognitive load, suggesting that healthcare professionals, who are typically engaging in many tasks while under time pressures, are more likely than others to fall back on such stereotypes while making decisions or interacting with patients.<sup>62</sup> Some have also hypothesised that the culture of medicine may exacerbate tendencies to frame one's experience through stereotypes, either through derogatory humour<sup>63</sup> or through the 'ethical erosion' that happens to medical students during their training.<sup>64</sup> Unfortunately, the nature of these implicitly held biases, as unconscious and automatic beliefs, poses a significant challenge in terms of both their identification and reduction.<sup>38 65</sup>

Fortunately, a growing literature from social psychology has been exploring techniques for reducing implicit racial biases, although methodological weaknesses and a lack of randomised control trials suggest that conclusions from this realm of research should be approached tentatively. Despite these shortcomings, a review of this literature suggests that counteracting racial bias among healthcare providers should involve strategies that illuminate what underlies biases, motivate practitioners to reduce them, emphasise partnership within the clinical context, encourage confidence related to interacting with patients from different ethnic or racial groups, and help providers to experience empathy in both its cognitive and emotional dimensions.<sup>65</sup> Research has also found that requiring students to take the IAT and reflect on their own biases and incorporating curricula related to health disparities and minority health into medical school can be effective in reducing implicit biases.<sup>66</sup> Techniques that have shown promise outside of the clinical context include

repeated exposures to counter-stereotypes<sup>67</sup> and increased contact with those who are the target of one's biases.<sup>68</sup> Unfortunately, the long-term effects of these training interventions are not known.

Another important area of related research explores the impact of racial concordance on patient experiences. Some evidence from this realm suggests that when patients and clinicians are of the same race, patient visits are longer, satisfaction is higher, more positive affect is expressed, and patient and clinician assessments of pain are more closely aligned.<sup>69 70</sup> These outcomes align well with the aspects of the clinical encounter that contribute to placebo effects discussed above, suggesting that perhaps a way to increase placebo effects in minority populations is to increase the number of racially concordant patient–physician relationships. However, the experiments measuring the impact of racial concordance mentioned above did not examine health outcomes, and a recent meta-analysis suggests that there is inconclusive evidence for the claim that racial concordance has a positive effect on clinical outcomes.<sup>71</sup> It is likely that more research is needed before any efforts are made to match skin tones or ancestry within clinical settings, especially given the unintended effect of perpetual racial segregation this could lead to.<sup>v</sup>

### Other forms of inequality

While the discussion above has focused on inequality in relation to race and ethnicity, there are countless other individuals who face stigma, discrimination and bias within healthcare settings.

Differences in patient weight, mental health, substance use, socioeconomic status, age, gender identity, sexuality, attractiveness, criminal records, HIV status, street involvement and marriage status, among other factors, all contribute to experiences of discrimination and differences in treatment within clinical settings.<sup>63 72–84</sup> This suggests that individuals from any of these groups may be less likely to experience placebo effects during healthcare interactions, further increasing inequality in health outcomes along countless other dimensions. In addition, for those patients among whom two or more of these identities intersect, negative experiences within healthcare may be even more likely.

The ubiquity of discrimination within healthcare settings is alarming and raises pressing questions related to justice. In thinking through the possibility of implementing strategies to increase placebo effects within the clinical encounter, arguably the greatest priority should be given to those who are most vulnerable to stigmatisation within healthcare settings. Concerns arise, however, regarding whether flagging patients at risk for discrimination and intentionally treating them differently is the right solution to reduce the effects of stigma. The many forms in which bias appears within clinical settings is an important issue however, and the way in which it may be directly contributing to an increase in health disparities by way of placebo effects has, to date, been overlooked. Further investigation into the ways in which this occurs, the extent to which it occurs and the ways in which we can ameliorate its effects, we argue, should be a research priority.

### CONCLUSION

On a slightly more positive note, it is important to refrain from giving clinicians more credit (and more blame) than they deserve. If we consider again the mechanisms by which placebo and nocebo effects appear to operate, via expectations and

<sup>v</sup>Thank you to Mira Schneiders for encouraging us to emphasize this point.

conditioning, it is clear that there are many other avenues by which placebo effects are likely to be initiated. The elicitation of placebo effects through social learning has been well documented, and the role of culture and community is likely to be significant as well.<sup>85</sup> This suggests that both harnessing placebo effects and counteracting nocebo effects are possible outside of the clinical encounter, and we would do well to avoid seeing the clinician as all-powerful when it comes to shaping clinical outcomes. There is hope that a better understanding of placebo effects can help us to see ways in which these effects can be employed to increase the agency of patients in their own care. Preliminary research into the efficacy of open-label placebo treatments has shown promising results,<sup>86 87</sup> and there is also hope that placebo conditioning may allow for reductions in medication dosages, which will thereby minimise harmful side effects.<sup>88</sup>

While bioethical discussions of the placebo effect have long focused on conflicts raised between patient autonomy and beneficence, the intersection of placebo effects and justice deserves sustained philosophical treatment as well. We have argued here that an important and unacknowledged route by which disparities in health status may arise is through differences in the distribution of placebo effects. Aspects of the clinical encounter, including the tone and emotional presence of the clinician, and the support and engagement involved in a consultation, have been found to directly shape clinical outcomes, and yet are experienced differently by different racial and ethnic groups. This constitutes a significant injustice related to clinical care. We suggest that a closer look at the relationship between inequality and placebo effects is long overdue.

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