Demystifying the Placebo Effect

Phoebe Friesen

The Graduate Center, City University of New York

How does access to this work benefit you? Let us know!
Follow this and additional works at: https://academicworks.cuny.edu/gc_etds

Part of the Alternative and Complementary Medicine Commons, Applied Ethics Commons, Bioethics and Medical Ethics Commons, Medical Sciences Commons, and the Philosophy of Science Commons

Recommended Citation
Friesen, Phoebe, "Demystifying the Placebo Effect" (2018). CUNY Academic Works.
https://academicworks.cuny.edu/gc_etds/2775

This Dissertation is brought to you by CUNY Academic Works. It has been accepted for inclusion in All Dissertations, Theses, and Capstone Projects by an authorized administrator of CUNY Academic Works. For more information, please contact deposit@gc.cuny.edu.
DEMYSTIFYING THE PLACEBO EFFECT

by

PHOEBE FRIESEN

A dissertation submitted to the Graduate Faculty in Philosophy in partial fulfillment of the requirements for the degree of Doctor of Philosophy, The City University of New York

2018
Demystifying the Placebo Effect

by

Phoebe Friesen

This manuscript has been read and accepted for the Graduate Faculty in Philosophy in satisfaction of the dissertation requirement for the degree of Doctor of Philosophy.

_________________________ ______________________

Date [Peter Godfrey-Smith]

Chair of Examining Committee

_________________________ ______________________

Date [Nickolas Pappas]

Executive Office

Supervisory Committee:

Peter Godfrey-Smith

Jesse Prinz

John Greenwood

THE CITY UNIVERSITY OF NEW YORK
ABSTRACT

Demystifying the Placebo Effect

by

Phoebe Friesen

Advisor: Peter Godfrey-Smith

This dissertation offers a philosophical analysis of the placebo effect. After offering an overview of recent evidence concerning the phenomenon, I consider several prominent accounts of the placebo effect that have been put forward and argue that none of them are able to adequately account for the diverse instantiations of the phenomenon. I then offer a novel account, which suggests that we ought to think of the placebo effect as encompassing three distinct responses: conditioned placebo responses, cognitive placebo responses, and network placebo responses. Next, I consider implications of the placebo effect’s role in complementary and alternative medicine for discussions of how to demarcate between science and pseudoscience within philosophy of science. Finally, I offer a bioethical argument that maintains that the neglect of the placebo effect within medicine may be contributing to an increase in health disparities along lines of race and ethnicity.
# Table of Contents

**Introduction** .................................................................................................................................................. 1

**Chapter 1. The Ubiquitous Placebo Effect: Evaluating Accounts Alongside Evidence** ......................................................................................................................... 5

I. **Introduction** ............................................................................................................................................... 5

II. **Traditional Roles of the Placebo in Research and Practice** .................................................................... 5

III. **What We Have Learned About the Placebo Effect** ................................................................................. 8
   IIIa. Examples of the Placebo Effect .............................................................................................................. 8
   IIIb. Placebo Mechanisms ............................................................................................................................. 10
   IIIc. Individuality and Placebo Responses .................................................................................................... 13
   IIIId. Revisiting the Two Roles of the Placebo Effect .................................................................................... 14

IV. **Accounts of the Placebo Effect** ........................................................................................................... 15
   IVa. The Outcome of the Placebo Arm ........................................................................................................... 15
   IVb. The Placebo as Inert ............................................................................................................................... 16
   IVc. The Placebo as Non-Specific
        IVc1. Non-specific Mechanisms ............................................................................................................. 17
        IVc2. Non-specific Effects ......................................................................................................................... 18
        IVc3. Non-specific Treatments .................................................................................................................. 19
   IVd. The Placebo as Psychological .............................................................................................................. 21
   IVe. The Placebo as Incidental ....................................................................................................................... 24

V. **The Placebo as Mediated by Meaning and Context** .............................................................................. 27

VI. **Conclusion** .............................................................................................................................................. 29

**Chapter 2. An Account of the Placebo Effect: Conditioned, Cognitive, and Network Placebo Responses** .................................................................................................................................................. 30

I. **Introduction** ............................................................................................................................................ 30

II. **The Goals of an Account of the Placebo Effect** ...................................................................................... 30

III. **Conditioned, Cognitive, and Network Placebo Responses** .................................................................. 34
   IIIa. Conditioned Placebo Responses ............................................................................................................ 35
   IIIb. Cognitive Placebo Responses .............................................................................................................. 38
   IIIc. Network Placebo Responses ............................................................................................................... 41
Chapter 3. Expanding The Demarcation Project: Protoscience, the Placebo Effect, and Complementary and Alternative Medicine

I. Introduction

II. Placebo Responses within Complementary and Alternative Medicine

III. CAM as Pseudoscience?

IV. Theories of Demarcation

V. CAM as Protoscience

VI. Conclusion

Chapter 4. Placebo Responses and Racial and Ethnic Health Disparities: An Unjust and Underexplored Connection
# Table of Contents

I. Introduction .................................................................................................................. 83

II. Health Disparities and Placebo Effects ....................................................................... 84
   IIA. Health Disparities .................................................................................................. 84
   IIB. Placebo Effects ................................................................................................... 86

III. Confronting the Evidence ......................................................................................... 89
   IIIA. Evidence of Placebo Effects ............................................................................... 89
   IIIB. Beliefs and Expectations Related to Treatment .................................................. 90
   IIIC. Clinician Empathy and Communication Style ................................................... 91
   IIID. Patient Engagement and Participation ............................................................... 93

IV. Evidence of Inequality in the Clinical Encounter ..................................................... 95
   IVIA. Beliefs and Expectations Related to Treatment .................................................. 95
   IVIB. Clinician Empathy and Communication Style ................................................... 97
   IVIC. Patient Engagement and Participation ............................................................... 99

V. Ethical Implications .................................................................................................... 99
   VA. Expanding the Standard of Care ............................................................................ 100
   VB. Reducing Implicit Bias ......................................................................................... 103
   VC. Other Forms of Inequality ..................................................................................... 106

VI. Conclusion ................................................................................................................ 108

Final Remarks .................................................................................................................. 108

I. Demarcation within Evidence Based Medicine: The RCT ........................................ 111
II. The Unique Features of Pseudoscience in CAM ....................................................... 114

Appendices ...................................................................................................................... 120

   Appendix A. Open versus hidden administration of morphine .................................. 120
   Appendix B. Immune parameters affected by behavioral conditioning paradigms ... 121
   Appendix C. Categorization of complementary and alternative medicine therapies ... 121
   Appendix D. Effective elements in homeopathic communications .............................. 122

Bibliography .................................................................................................................... 123
Introduction

The placebo effect is popularly understood to be a kind of magic, both in the sense of a sleight of hand, where nothing really occurred but the illusion was there (“it was just a placebo effect!”), and also in the sense of something impressive occurring without a clear causal route (e.g. it was a placebo effect!). This popular understanding of the phenomenon reflects the two distinct meanings of the term ‘placebo’ that are used in a medical context. In a research setting, participants receiving ‘treatments’ are randomized to either the placebo arm or the active intervention arm, and the outcomes between the two conditions are compared throughout the trial to determine how efficacious the active treatment is. In this way, the placebo arm offers a control condition, since both arms will be exposed to other factors in the trial (e.g. participant bias, natural disease progression), and placebos are prescribed to participants precisely because of their lack of effect. In a clinical setting, placebo treatments (sometimes sugar pills, but more often ‘dirty placebos’, treatments meant for something other than the condition the patient has) are prescribed frequently in order to ameliorate symptoms or pacify the patient. In this setting, placebo effects are prescribed to patients precisely for their effect.

For a brief moment during the second half of the twentieth century, academics and scientists took great interest in the placebo effect, and several rich theoretical and empirical accounts of the phenomenon were produced. However, the topic quickly fell out of favour and has been largely neglected until a recent resurgence of research into the
placebo effect in the last twenty or so years. This research is taking place in the new and
growing field of placebo studies, and suggests that the placebo effect is quite powerful
indeed. It can be produced not only through placebo treatments, but also through beliefs
that individuals hold about treatments, through words spoken by a health care
professional, through social learning, or through classical conditioning. While not all
conditions are susceptible to placebo effects, there are many that consistently show robust
placebo responses (e.g. pain, mood disorders, functional somatic syndromes).

With the exception of several bioethicists, philosophers have paid little attention to this
fascinating phenomenon, despite its diverse implications for discussions within
philosophy of science, philosophy of mind, and philosophy of medicine. My dissertation
seeks to make a start at a philosophical investigation of the placebo effect. In the first
chapter, I offer an overview of what we have learned about the placebo effect in the past
several decades, and consider how this new body of evidence connects to several
theoretical accounts of the phenomenon that have been put forward. I consider several of
these accounts, including categorizing the placebo effect as the outcome measure of the
placebo arm in a trial, as an inert treatment, as non-specific (non-specificity in terms of
mechanisms, effects, and treatments are each considered), as psychological, and as
incidental. In response, I argue that each account is either theoretically inconsistent or
incapable of accounting for the diverse instantiations of the phenomenon, and highlight
features that must be present in any account of the placebo effect for it to cohere with
current evidence.
The second chapter develops such an account. In response to three primary goals that I argue an account of the placebo effect ought to strive towards - demarcating placebo phenomena, highlighting explanatorily relevant features of the placebo effect, and providing promising avenues of direction for future research - I suggest that rather than seeking to develop one cohesive account of placebo phenomenon, we should be responsive to causal processes underlying placebo effects. These causal processes point towards an account of the placebo effect which encompasses three types of responses: *conditioned placebo responses*, *cognitive placebo responses*, and *network placebo responses*. I offer a description of each of these types of placebo responses by way of their primary mechanisms, central features, and through the use of prototypical examples.

The third chapter investigates the link between the placebo effect and complementary and alternative medicine (CAM), and how this link might impact discussions of demarcation between science and pseudoscience within philosophy of science. In response to frequent characterizations of CAM as pseudoscience, I offer an overview of evidence indicating that practices within CAM are especially capable of producing robust placebo responses, and argue that this distinguishes these practices from other domains that are typically thought of as pseudoscientific. I suggest that CAM may be better thought of as a protoscience than a pseudoscience, and offer an account of protoscience that is able to capture the distinction between CAM and other prototypical examples of pseudoscience, such as astrology and creationism.

Finally, in the last chapter, I bring together two distinct bodies of literature, that of
evidence related to the placebo effect and that which tracks inequalities according to race and ethnicity within the clinical encounter. I connect these literatures through highlighting shared features that appear to play a role in the placebo effect and that appear to be deficient in experiences of racial and ethnic minorities: beliefs and expectations related to treatment, clinician empathy and communication style, and patient engagement and participation. In response, I suggest that medicine’s current neglect of the role of the placebo effect in practice may be unwittingly contributing to an increase in health disparities, and discuss the ethical implications of this claim.
Chapter 1. The Ubiquitous Placebo Effect: Evaluating Accounts Alongside Evidence

I. Introduction

This chapter seeks to make room for a new understanding of the placebo effect by exploring popular accounts of the phenomenon alongside current evidence. The first section briefly describes the two most prominent roles the placebo has played in the past, as a control in research and as a deceptive tool in practice. The following section describes what we have learned about the placebo effect in the past few decades, suggesting there may be space for a much larger role for the phenomenon to play. The third section offers critical evaluations of several accounts of the placebo effect that have been put forward, arguing that they are unable to account for this new evidence that points to the variability and potency of the placebo effect. Taking inspiration from two available conceptions of the placebo effect in the literature, the final section gestures towards an account that seeks to capture the phenomenon more fully.

II. Traditional Roles of the Placebo in Research and Practice
Throughout history, the placebo has been primarily known for two conflicting roles it has played within research and practice. I will briefly outline each of these roles here, before moving on to describe what we know of the phenomenon that does not fit within these roles.

In the realm of research, the placebo is known for the role it plays as a control. Most famously, the placebo is a crucial component of the randomized double-blind placebo-controlled trial, the gold standard of evidence-based medicine. This role understands the placebo as a treatment rather than an effect, but importantly it is meant to be a treatment that has no (or at least a minimal) effect. Specifically, participants in a randomized control trial (RCT) will often be divided into two groups, called the active arm and the placebo arm. The placebo arm is meant to be identical to the active arm in all aspects of the trial except those that are being evaluated for clinical efficacy. In this way, the trial can distinguish between effective and ineffective treatments, because significant differences in clinical outcomes can only be attributable to the active treatment, the only difference between the two arms. Ethical issues arise in relation to placebo-controlled trials investigating treatments for ailments for which an established intervention already exists, since to randomize participants with such ailments to a placebo arm is to refrain from treating those in the placebo condition, and therefore to refrain from acting in their best medical interests. For this reason, the Declaration of Helsinki permits placebo-controlled trials only in cases where no established intervention exists.
The role of placebos in clinical practice is quite unlike their role in RCTs, as placebos are used in practice precisely for their powerful effects, as opposed for their lack of effect. Interestingly, placebos are prescribed frequently in clinical practice, and yet are tinged with an air of immorality for their association with deception. Placebo use has been widely reported as commonplace by physicians surveyed in Canada (Raz et al. 2011), the US (Tilburt et al. 2008), the UK (Howick et al. 2013), Denmark (Hrobjartsson and Norup 2003), and Israel (Nitzan and Lichtenberg 2004). Those who were asked reported that they were much more likely to prescribe impure placebos (e.g. antibiotics or vitamins) than pure placebos (e.g. saline solution or a sugar pill) (Tilburt et al. 2008, Raz et al. 2011, Howick et al. 2013), which is probably because the deception seems less substantial when an active (although ineffective for the particular condition) treatment is being prescribed. Placebos were not always aligned with deception, but became so after World War II when the field of bioethics developed in response to the horrific medical research conducted by the Nazi party and emphasized the importance of autonomy and beneficence in medical research, and became even more so after the Declaration of Helsinki (Shorter 2011). Since then, much has been written on the question of whether the deceptive use of placebos in practice is justified (Foddy 2009, Brody 1982, Cabot 1907, Bok 1974). In 2008, the American Medical Association (AMA) banned the deceptive use of placebos in clinical practice, writing that “the use of a placebo without the patient’s knowledge may undermine trust, compromise the patient-physician relationship, and result in medical harm to the patient” (Bostick et al. 2008).
While the placebo has been known predominantly for these two roles, I hope to make space for a third role within this chapter, which sees the placebo effect as a valuable phenomenon in its own right. In the following section, I outline what we have learned about the placebo effect in the last several decades, in order to lay the groundwork for a broader understanding of the phenomenon. Next, I will consider several proposed accounts of the placebo effect in relation to this new evidence.

III. What We Have Learned About the Placebo Effect

IIIa. Examples of the Placebo Effect

To begin, here are six examples of placebo responses\(^1\) that help to demonstrate how variable and powerful the phenomenon is:

Example 1: Three levels of therapeutic ultrasound, mock ultrasound (placebo), and control (no treatment) were evaluated for reducing inflammation and pain in a double-blind trial of 150 patients having impacted third molars removed. Significant reductions in facial swelling, trismus (jaw spasm), pain, and serum C-reactive protein (which correlates with inflammation) occurred in all groups except the control group. Since low-level ultrasound and mock ultrasound were consistently more effective for reducing inflammation than high-level ultrasound, the authors concluded that the majority of the

\(^1\) I will use placebo effect and placebo response interchangeably in this manuscript.
reductions in inflammation were attributable to the placebo effect (Hashish, Harvey, and Harris 1986b).

Example 2: Patients with nonspecific chest pain were randomly allocated either to have a routine electrocardiogram and serum creatine phosphokinase tests (test group) or to have all diagnostic tests withheld (no-test group). Results of the tests did not alter the treatment of any patients. While 46% of the no-test group reported short-term disability, only 20% of the test group did (Sox, Margulies, and Sox 1981).

Example 3: Patients with the common cold who rated their clinicians as high in empathy reported the cold to last on average a day less than those who found their clinicians to be lower on empathy, and had measures of the immune biomarker IL-8 that were more than double the low-empathy group (Rakel et al. 2009).

Example 4: Significant dopamine release in Parkinson’s patients in response to a placebo depended on two factors: 1) response to prior medication and 2) beliefs about the likelihood of receiving active medication. Patients who believed there was a 25% or 50% chance they were going to receive active medications were significantly less likely than patients who believed there was a 75% chance they would receive active medications to show a substantial placebo response (Lidstone et al. 2010).

Example 5: Multiple sclerosis patients were given four monthly cyclophosphamide infusions, which decrease blood leukocyte (white blood cell) numbers, paired with the
taste of anise-flavored syrup. After conditioning, eight of ten patients showed a decreased in leukocyte counts after exposure to anise-flavored syrup alone (Giang et al. 1996).

Example 6: Half of a group of 107 men prescribed finasteride for benign prostatic hyperplasia (prostate gland enlargement) were warned of potential sexual side effects. Of those warned, 44% reported experiencing sexual side effects, whereas only 15% of those who were not warned group reported any sexual dysfunction (Mondaini et al. 2007).

These examples offer a small but diverse selection of where and how the placebo effect can occur. They are varied both in terms of the placebo treatments that are given and the placebo responses that occur. Placebo treatments in the examples include fake ultrasounds, routine diagnostic tests, clinician empathy, manipulations of patient expectations, and classic conditioning, while placebo responses take the form of reductions in inflammation, pain, cold symptoms, and white blood cells, and increases in dopamine release and sexual dysfunction. The last example involving sexual side effects demonstrates how placebo mechanisms can also induce negative clinical outcomes, which are often called nocebo effects. How these diverse examples relate should become clear in the next subsection, where I describe the mechanisms that mediate the placebo effect.

IIIb. Placebo Mechanisms
There is widespread agreement within the field of placebo research that the phenomenon operates primarily through two mechanisms: expectancy and conditioning (Stewart-Williams and Podd 2004, Kirsch et al. 2004, Benedetti et al. 2003, Pacheco-Lopez et al. 2006). I will briefly present evidence regarding each of them, and how they relate, below.

Conditioning has long been thought to be central to the placebo effect (Ader 1989, Voudouris, Peck, and Coleman 1989, 1990). Classical conditioning involves pairing a new, neutral stimulus (a ringing bell, for example) reliably with another stimulus, called the unconditioned stimulus or US. Before conditioning, the US reliably leads to an unconditioned response (UR), and after conditioning, the neutral stimulus becomes a conditioned stimulus (CS) that can induce the UR (which is now a conditioned response or CR) without the presence of the US. A classic example involves a dog hearing a bell sound while also salivating at the sight of food. After repeated pairing, the dog salivates when exposed only to the sound of the bell (with no food in sight). Placebo responses have been induced in both animals and humans through classical conditioning. In a well-known early experiment by Ader and Cohen, the researchers conditioned an immune response in lupus-prone mice by repeatedly pairing a sweetener with a small dose of an immunosuppressive drug that would be unable to delay the disease alone. The onset of lupus was significantly delayed in these mice, as compared to mice who received the sweetener and immunosuppressive drug separately (Ader and Cohen 1982). Classic conditioning has proved fruitful in humans as well, especially with regards to immune responses (Pacheco-Lopez et al. 2006). An example can be found in an experiment that managed to condition reductions in cortisol levels by pairing a distinctive beverage with
dexamethasone (an anti-inflammatory that reduces cortisol levels) (Sabbioni et al. 1997). Ted Kaptchuk has emphasized the connection between placebo conditioning and the importance of ritual in both Western and alternative forms of healing, stressing the importance of the healer’s prestige and costume, as well as the gestures and recitations that form a part of all medical rituals (Kaptchuk 2011, 1850). Aligned with the theory of conditioning as a mediator of placebo responses, the phenomenon appears to be enhanced by one’s adherence to treatment (Horwitz et al. 1990) as well as the frequency of an intervention (de Craen et al. 1999).

The second major explanation for the placebo effect is found in the role expectancy plays. Many experiments have documented the important role of expectations in producing placebo effects through verbal manipulations, especially with regards to pain and other subjective responses. As an example, when asthmatic subjects were given a placebo inhaler containing saline and told that they were inhaling irritants which could cause bronchoconstriction, 12 out of 40 subjects experienced asthmatic attacks, which were subsequently reversed by another placebo inhaler that they were told would provide relief (Luparello et al. 1968). In addition, simply framing interventions as more or less painful appears to lead to analgesic placebo or nocebo effects. In one experiment, women who were told before receiving an analgesia while giving birth “You are going to feel a big bee sting; this is the worst part of the procedure” rated the pain of the injection as 5/10 while women who were told “We are going to give you a local anesthetic that will numb the area and you will be comfortable during the procedure” rated the pain of the injection as 3/10 (Varelmann et al. 2010). It’s also been demonstrated that the
effectiveness of pharmacological and non-pharmacological therapies is significantly reduced when the administration of such therapies is hidden (e.g. morphine administered through a PICC line that is activated by a computer in the next room) (Benedetti et al. 2003). Of note, deception is not required to induce placebo responses mediated by expectations, as many experiments have demonstrated (Sandler and Bodfish 2008, Kam-Hansen et al. 2014, Kaptchuk et al. 2010, Park and Covi 1965).

Other factors that tend to enhance placebo effects and may be mediated by conditioning, expectations, or a combination of the two, are the invasiveness of the treatment (Ernst and Resch 1995, Kaptchuk et al. 2000, de Craen et al. 2000), physician empathy (Rakel et al. 2009), social observation (seeing a demonstrator respond positively to a placebo analgesic) (Colloca and Benedetti 2009), and brand names (Kam-Hansen et al. 2014). While both conditioning and expectancy have been shown to induce placebo effects on their own (Sabbioni et al. 1997, Jensen et al. 2012, Benedetti et al. 1999), they appear to also mediate each other and produce compounded effects when used in combination (Kirsch et al. 2004).

**IIIc. Individuality and Placebo Responses**

Considering that conditioning and expectancy primarily mediate placebo effects, it should be unsurprising that individual values and histories are important in giving shape to placebo and nocebo responses. In particular, evidence suggests that beliefs in the efficacy of a therapy can positively or negatively affect clinical outcomes, as can beliefs about one’s illness (Kalauokalani et al. 2001, Juergens et al. 2010). Treatment which
aligns with personal goal satisfaction and being given a choice as to what treatment one receives have both been found to lead to enhanced placebo responses (Hyland 2011, Rose et al. 2012). It has also been demonstrated that people identify therapies that are more congruent with their values as more efficacious, an effect that can lead to higher expectations and an increase in placebo responses (Whalley and Hyland 2009).

**III. Revisiting the Two Roles of the Placebo Effect**

As described above, the placebo effect appears to encompass much more than what is contained within its roles as a control in clinical research or as a deceptive tool in practice. When we think of placebo treatments as merely controls, the effective, powerful nature of the phenomenon is lost, and when we think of the placebo effect as one produced by deception, we miss out on the many ways in which conditioning and expectations can shape clinical outcomes without the involvement of any deception. This implies that thinking of the placebo in these two roles leads to an incomplete picture of the phenomenon. Part of the reason for the prominence of these narrow conceptions may be that many popular accounts of the placebo effect are misleading. In the section that follows, I consider several accounts of the placebo effect that have been put forward, and consider whether any of them are able to capture the phenomenon in this larger sense. After ruling out five potential accounts as inadequate, in the final section I will combine two available conceptions from the literature that I see as better able to represent the ubiquity and potency of the placebo phenomenon.
IV. Accounts of the Placebo Effect

IVa. The Outcome of the Placebo Arm

Benedetti has suggested that the most common and widespread interpretation of the placebo effect is simply the outcome measure of the placebo arm in an RCT (Benedetti 2009). The problem with this account is that it is far too inclusive. In fact, many factors beyond the placebo effect can contribute to the outcome of the placebo group in an RCT, including spontaneous remission, patient bias, rater bias, co-interventions, and statistical regression (a phenomenon that predicts that individuals selected for abnormal measures, like patients enrolled in an RCT, will tend to score closer to the mean when measured a second time) (McDonald, Mazzuca, and McCabe 1983)\(^2\). Ernst and Resch called the collection of all these factors that contribute to placebo outcome the perceived placebo effect, and pointed out that all of these must be accounted for and subtracted from a placebo group’s outcome in order to measure true placebo effect (Ernst and Resch 1995). This account of the placebo effect, while far too large to capture the placebo phenomenon in itself, underscores the importance of including an additional control group (usually a waitlist group or another placebo group) in clinical trials if conclusions are to be drawn about the true placebo effect.

\(^2\) Statistical regression can be accounted for by taking two baseline measures at the start of a trial.
The placebo has been widely thought of as ‘inert’ in contrast to the active treatment in an RCT (Shapiro 1968). As noted by Miller and Kaptchuk, the placebo effect has a long history of being defined negatively by what it is not (Miller and Kaptchuk 2008), which is derived directly from thinking of the placebo as a control. While this refers to placebos as treatments rather than to the placebo effect, the implication for the placebo effect if placebos are inert is immediately clear: it is a misnomer. Several additional issues arise when we think of the placebo as inert. One concerns the fact that most physicians use impure placebos in practice, which are not inert but active. Another more substantial concern arises when we consider that the placebo effect can be induced through much more than ‘inert’ sugar pills, but can be elicited through verbal manipulations, social observation, and classical conditioning, all of which prove to be far from inert. Most importantly, as the wide range of examples in the previous section demonstrated, the placebo effect is a powerful phenomenon that can have substantive effects; it is best described as anything but inert.

A more serious contender is Shapiro’s 1968 account, which proposes that “the placebo effect is defined as the non-specific psychologic or psychophysiologic effect produced by a placebo.” (Shapiro 1968) While the term non-specific has been criticized as vague (Grunbaum 1986), its likely that the confusion is at least in part due to the way the term
‘non-specific’ has proliferated into many versions within the literature concerning placebo effects (Critelli and Neumann 1984). In order to cover these distinct conceptions, I will consider three interpretations of non-specific here: 1) there are no specific mechanisms that cause the placebo effect 2) there are no specific effects on the condition being treated when placebo treatments are given 3) there is nothing specific in placebo treatments that causes the effect. The first of these bears on the cause of placebos, the second involves the placebo effect, and the third pertains to placebo treatments.

IVc1. Non-specific Mechanisms

This interpretation in itself makes room for two interpretations. The first suggests that there are no specific mechanisms that cause the placebo response because the effect is simply other known phenomena, such as regression to the mean and/or rater bias, that have been mislabeled as the placebo effect. However, many well-designed experiments that measure true placebo effects and account for potentially conflating effects refute this interpretation. Secondly, and relatedly, this interpretation could suggest that there are no specific mechanisms that cause the placebo effect, but a variety of unknown and unrelated mechanisms that have been grouped together due to a lack of research and analysis. While there may be some truth in this interpretation, as there is a great deal more to learn about various placebo mechanisms, it is clear from the discussion above that placebo responses are mediated primarily by the specific mechanisms of conditioning and expectancy.
**IVc2. Non-specific Effects**

The second interpretation of Shapiro’s account of placebo effects suggests that non-specificity lies in the effect of placebo treatments on the condition being treated. This seems to be what Shapiro is suggesting in his original account and is closely aligned with the definition given by the AMA (Bostick et al. 2008). Under this conception of non-specific, the placebo effect is understood as a generic experience of anxiety relief or high hopes that can mislead researchers into perceiving an improvement in the clinical condition under investigation. However, a quick glance at research into placebo responses indicates that the effects on particular conditions can be very specific indeed. As we have seen, pain and asthmatic attacks can be induced or reduced merely from suggestion. Additionally, migraines can be cured (Kam-Hansen et al. 2014), itches can be brought on (van Laarhoven et al. 2011), sexual dysfunction can be triggered (Mondaini et al. 2007), common colds can be exacerbated (Rakel et al. 2009) and memory performance can be improved (Stern et al. 2011). These effects are, without a doubt, specific. Along with subjective measures, there is also evidence showing changes in more objective measures as a result of placebo effects – white blood cell counts (Giang et al. 1996), respiratory depression (Benedetti et al. 1999), inflammation (Hashish, Harvey, and Harris 1986b), as well as dopamine release (Lidstone et al. 2010) and decreases in arm rigidity (Benedetti et al. 2004) in Parkinson’s patients.

Another interpretation of placebo effects as non-specific might be that there is nothing in common in terms of the effects brought about as a result of placebo treatments, in that a
variety of positive responses can be produced through placebos (e.g. pain relief, increases in agility). This kind of non-specificity captures the heterogeneity of placebo responses, but fails to offer any grounding with regards to how we might draw boundaries around placebo effects as a phenomenon. If placebo effects are merely a variety of positive effects, then how are we to go about determining what is and isn’t a placebo effect? Unfortunately, such an account says nothing about what a placebo effect is and how we might identify the existence of one.

Finally, a third interpretation of placebo effects as non-specific might be that there is nothing in common in terms of the effects brought about as a result of placebo treatments, in that they indiscriminately impact a variety of conditions by bringing about a variety of responses (e.g. pain relief, increases in agility). However, while it is the case that a variety of responses can be brought about through placebo treatments, these responses do not appear indiscriminately. There is a pattern to their responsiveness, in that placebo effects, as far as we know, are the types of effects that can be brought about via the mechanisms underlying placebo responses, expectancies and conditioning. Furthermore, we can draw clear boundaries around several conditions that placebo effects do not impact (e.g., tumors, viruses), suggesting that placebo effects are specific to some conditions and not others.

IVc3. Non-specific Treatments
In a later article on the placebo effect, Shapiro and his co-writer Morris suggest a third interpretation of non-specific when they write “specific activity is the therapeutic influence attributable solely to the contents or processes of the therapies rendered” (Shapiro 1978). A similar account offered by Stewart-Williams and Podd, who suggest that the placebo effect is “not due to the inherent powers of that substance or procedure” (Stewart-Williams and Podd 2004). This kind of non-specificity or lack of inherent power in a placebo treatment suggests that the primary cause of the placebo effect cannot be found in the actual treatment itself, be it a pill, a sham surgery, or a fake ultrasound, but in the individual who is receiving the placebo treatment. This account taps into the important aspect of placebo effects discussed above, in that they change shape as a result of individual histories, values, and expectations. However, it is not clear that because particular features of individuals alter placebo responses, the causal power is not inherent in placebo treatments.

It could be argued that placebo treatments have inherent powers in that blue and green pills consistently produce sedative experiences (while red and orange pills are felt as stimulants) (de Craen et al. 1996). In response, one might ask if the sedative power of blueness is inherent in the way that benzodiazepines are inherently sedative, suggesting that the relationship between blue pills and sedative effects is different than the relationship between benzodiazepines and sedative effects, in that the former is contingent and could be conditioned away over time, while the latter is necessary and could not be altered. However, it’s not clear that all placebo treatments share this contingent quality. Could placebo responses generated by empathy and positive framing
be conditioned away? It seems doubtful. The tendency of more invasive procedures to produce more robust placebo effects seems linked to an entrenched risk-reward calculation that might not be so easy to undo. Is the relationship between expectation and pain really contingent if it reliably releases endogenous opiates for placebo manipulations and cholecystokinin for nocebo manipulations (Benedetti, Amanzio, et al. 2006, Amanzio et al. 2001)? Additionally, as Stewart-Williams and Podd point out, a phenomenon called biological preparedness leads us as a species to be especially inclined to associate some kinds of stimuli and responses, making us predisposed to certain kinds of conditioning. It’s not clear that our responses to placebo treatments are not as deeply instilled in us, and therefore less inherent or specific, as the way we respond to benzodiazepines (Stewart-Williams and Podd 2004).

It seems possible that what is driving intuitions that placebos have no inherent causal power is the fact that with placebos, our minds, as opposed to our bodies, appear to be mediating the response. As Lichtenberg has pointed out “a more fundamental difficulty with a definition referring to non-specific effects is that behind it lurks a faulty dualistic conception of body and mind, as if to say that while ‘real medicine’ works by some defined, or at least in theory definable, physiological mechanism, the placebo has a psychological, that is to say non-specific, effect” (Lichtenberg, Heresco-Levy, and Nitzan 2004). This is precisely the route taken by Kirsch in defining the placebo effect.

IVd. The Placebo as Psychological
Kirsch’s account of the placebo proposes that “the placebo effect is that portion of the treatment effect that was produced psychologically, rather than through physical means” (Kirsch 2005). This account aligns with the role of the placebo as a deceptive tool in practice, in that it is not uncommon to hear of associations between those who are psychologically weak and those who are likely to be tricked by placebos into feeling better (see (Wolff, Dubois, and et al. 1946) for an early example). An implication that falls immediately out of the account is that any psychological treatment must result in a placebo effect, and so all psychotherapy constitutes a placebo treatment. Kirsch is fine with this; he says the very idea of a placebo psychotherapy is both a synonym (in that a placebo treatment is just any psychologically facilitated treatment) and an oxymoron (in that it is impossible to design a placebo treatment for psychotherapy research because it would have to be identical to the therapy) (Kirsch 2005). In addition to all psychotherapies, any treatments that are psychologically mediated would fall into the category of placebo treatments – cognitive exercises for dyslexia, theory of mind training for individuals with autism, exposure therapy for phobias, behavioral therapy for obsessive-compulsive disorder. While I am not opposed to expanding the placebo conception as widely as Kirsch does, and these treatments share quite a bit of territory with placebo treatments (exposure therapy is basically a form of conditioning, while empathy and explanation play a significant role in any therapeutic encounter), there is something more problematic about Kirsch’s account of the placebo effect that is worth considering.

The real worry about demarcating placebo effects as psychological effects is that it commits us to a metaphysically messy and unnecessary dualism between mind and body.
It is unclear how we are to understand the routes different kinds of treatments take as either physical or psychological. We might say that a treatment is physical if the body is manipulated in some way and psychological otherwise. However, when we consider that a manipulation that seems purely psychological (the words “this will make you feel much better”) lead to relief through physical means (the release of endogenous opiates), the distinction loses clarity. It seems that the same phenomenon can be called either psychological or physical depending on how much information we have and what explanatory level we choose to use. In response, one might say instead that a treatment is physical if the body is directly manipulated, and psychological otherwise; this way comforting words would surely constitute placebos. Where, then, would we place the placebo effects mediated by unconscious conditioning? If a learned association between a distinct flavour and buprenorphine begins to produce respiratory depression after exposure only to the flavour (Benedetti et al. 1999), is this a physical or a psychological effect? The pairing seems like a direct manipulation of the body, but the taste, which is producing the effect, seems psychological. It appears that taking on dualism in an account of the placebo effect simply costs too much in clarity.

What’s great about Kirsch’s account is that it helps us to see how impactful our dualistic intuitions are with regards to what we see as real. Controversy regarding the placebo effect has often lingered on the fact that subjective measures correlate with higher placebo responses and the related fact that psychological ailments seem to be most transformed by placebo treatments (see (Hrobjartsson and Gotzsche 2001)). As Parloff observed decades ago,

If the disorder to be treated is viewed primarily as physiological, then any psychological
effects (subjectively reported) not supported by independent evidence of objective physiological amelioration may be viewed as artifactual and classified as spurious, transitory, and tangential to the ultimate goals of treatment. (Parloff 1986)

This mood dominates medicine still, and is much of why the placebo effect has been relegated to the roles of control and deceptive tool for so long. However, now with newfound abilities to show itself in the physical, the placebo effect is starting to be taken seriously as a real phenomenon.

IVe. The Placebo as Incidental

We’ve now seen the difficulty of characterizing the placebo effect according to its necessary features. Grünbaum offered a unique solution to tracing the boundaries of the placebo effect by placing the key to what counts not in the phenomenon itself, but in the current theories of the medical community. He proposed that “whether a given positive effect on [target disorder] D is or is not a placebo effect depends on whether it is produced by the incidental treatment factors or the characteristic ones” (Grunbaum 1986).

For Grünbaum, what counts as a characteristic treatment factor or an incidental treatment factor depends on the theory behind the treatment. For example, if a pill includes ingredient A, a stimulant which is considered necessary for the required treatment, and ingredient B, a red dye which is considered unnecessary for the required treatment, then ingredient A will be a characteristic factor and ingredient B will be an incidental factor. Effects on the condition that are produced by ingredient B are placebo effects.

Grünbaum’s account should be praised for its clarity, because at least in principle, we can determine the placebo components of any particular treatment just by consulting the theory of the treatment and comparing it to investigations of what is doing the real causal
work in terms of clinical outcomes. If the characteristic factors are responsible, the treatment is a success, and if the incidental factors are responsible, the treatment is mediated by placebo responses.

Several worries arise upon examination of Grünbaum’s account of the placebo effect though. The first is that incidental and characteristic factors don’t always divide along clean lines. There are cases in which the characteristic factors seem to depend on the incidental factors to be effective. As we have seen, analgesics and inhalers only provide relief if the individuals relying on them believe that they can (Luparello et al. 1968, Kam-Hansen et al. 2014). Grünbaum seems aware of such cases when he suggests that “the incidental treatment factors may serve initially as catalysts or icebreakers for the operation of the characteristic ones” (Grunbaum 1986). However, if the incidental factors (beliefs) are necessary for the characteristic factors (analgesics) to operate, are these incidental factors appropriately called incidental? They seem to be characteristic factors that are missing from the theory of the treatment.

A similar confusion arises when one considers evidence regarding the success of sham surgeries. Since surgeries are amongst the most invasive interventions, they often generate significant placebo effects, which in some cases, leads the medical community to continue performing surgeries that are effective not as a result of their characteristic factors, but because of their incidental ones (Bretlau et al. 1989, Moseley et al. 2002). An example raised by Miller and Colloca outlines how vertebroplasty, a widely used treatment for painful vertebral fractures that involves injecting cement into the spine, was...
recently found to reduce pain no more than sham surgeries (which are identical but without the cement injection) (Buchbinder et al. 2009, Kallmes et al. 2009) (cited in (Miller and Colloca 2011)). This suggests that what really reduces pain in patients who undergo vertebroplasty are the incidental factors; it was a placebo all along. Because the sham surgery is so effective, one can imagine the medical community changing the theory of treatment to include everything involved in the sham surgery and transforming the incidental placebo features into characteristic factors. This raises a more significant worry regarding Grünbaum’s account, which is that placebo boundaries that are drawn by medical theories become moving targets. In one treatment, empathy can constitute a characteristic treatment factor that contributes to the treatment’s success, while in another treatment, empathy can be considered an incidental treatment factor that contributes to placebo effects. This implies that what is or isn’t a placebo can change frequently, depending on the particular treatment under investigation and the theories of the medical community. There is also an assumption in Grünbaum’s account that the medical community agrees as to what the characteristic and incidental factors are for each treatment. If not, what falls under the heading of placebo may change from hospital to hospital, or from doctor to doctor.

The biggest concern that falls out Grünbaum’s account is that if the line between characteristic and incidental isn’t clear, and if it frequently changes position depending on the treatment, the physician, the time, and the place, the account is simply not informative. By calling placebo effects the clinical results of incidental factors, Grünbaum tells us nothing about what the placebo effect is, how it works, and how we
might investigate it further. The following section aims to provide some grounding for such an analysis.

V. The Placebo as Mediated by Meaning and Context

It should be clear from the above discussion that many proposed accounts of the placebo effect are inadequate. Many of them suffer from conceptual flaws, and many of them point away from the effective nature to the phenomenon towards the narrow conceptions of the placebo as a control or as a deceptive tool in clinical practice. In this section, I hope to gesture towards the development of positive account of the placebo effect by pointing towards two richer conceptions of the phenomenon that have been offered in the literature. While neither of these accounts is sufficient to encompass the placebo effect on their own, each of them captures integral aspects of the phenomenon that have been largely neglected in the literature.

The first comes from Kaptchuk and Miller, who suggest that the placebo effect would be better reconceptualised as contextual healing. They define it as “that aspect of healing that is produced, activated or enhanced by the context of the clinical encounter, as distinct from the specific efficacy of treatment interventions” and elaborate further that “factors that may play a role in contextual healing include the environment of the clinical setting, cognitive and affective communication of clinicians, and the ritual of administering treatment.” (Miller and Kaptchuk 2008) Di Blasi and Benedetti have similarly referred to placebo effects as ‘context effects’ (Di Blasi et al. 2001, Benedetti 2009). While this
account is certainly a step forward in acknowledging the strength and multiplicity of placebo effects, it is still too narrow. One worry regarding reconceptualising the placebo effect as contextual healing is that it gives too much weight to conditioning, ritual, and factors external to the individual, and leaves out the importance of individual expectations that may not stem from the particular context. Another concern that arises in relation to this account is that the placebo is defined in contrast to treatment interventions, leaving no room for placebo treatments to be used as interventions in their own right, and falling prey to the same worries as Grünbaum’s account in that placebos are defined in contrast to what is contained in theories of medical treatments. Finally, by focusing on healing exclusively, the term contextual healing excludes the important phenomenon of nocebo effects.

The second conception comes from Moerman and Jonas, who argue that “practitioners can benefit clinically by conceptualizing this issue in terms of the meaning response rather than the placebo effect” (Moerman and Jonas 2002), my emphasis). The term meaning response is meant to capture the wide variety of placebo effects that can occur, as well as the importance of what a particular treatment means to an individual in generating those effects. This term nicely directs one towards the importance of individual histories and values in shaping and eliciting placebo and nocebo effects. However, in contrast to contextual healing, meaning response seems to focus too heavily on the conscious expectations of an individual, and leaves little space for placebo responses mediated by unconscious conditioning.
Looking at these two accounts in relation, it appears that each of them focus primarily on one of the two mechanisms known to underlie placebo effect. While Kaptchuk and Miller focus on the role of conditioning in producing placebo effects, Moerman and Jonas highlight the importance of expectations in mediating the phenomenon. Rather than painting the phenomenon as powerless, as a control in research, or as differentiated by the inconsistent minds of providers, these accounts focus on the positive nature of the placebo effect and the causal processes by which it is produced. An effective theoretical account of the placebo effect ought to follow suit, looking to the mechanisms that underlie the placebo effect rather. I hope to offer such an account in the following chapter.

VI. Conclusion

This chapter offered a summary of recent evidence related to how the placebo effect operates as well as an evaluation of several theoretical accounts of the phenomenon that have been proposed. I have argued that none of the proposed accounts is sufficient to capture the positive and powerful nature of the phenomenon, but have highlighted features of two accounts that make a start at capturing that which constitutes placebo effects.
Chapter 2. An Account of the Placebo Effect: Conditioned, Cognitive, and Network Placebo Responses

I. Introduction

This chapter lays out my account of the placebo effect. I begin by introducing three primary goals that I argue an account of the placebo effect ought to strive towards: demarcation, explanation, and direction, along with a brief discussion of how these goals relate to accounts that have previously been proposed. Next, the bulk of the chapter is spent introducing the account, which divides the phenomenon into three types of placebo responses: conditioned placebo responses, cognitive placebo responses, and network placebo responses. Following this exposition, I briefly describe the ways in which this account is able to meet the three primary goals.

II. The Goals of an Account of the Placebo Effect

A first step in developing an account of the placebo effect is to ask what the purpose of such an account might be. A minimal requirement that immediately comes to mind is one of demarcation. The term ‘placebo’ is notoriously slippery, and as we saw in the last chapter, it is best known for the conflicting roles it has played as a non-effective control in a research setting and as an effective deceptive tool in a clinical setting. So, at the very
least, an account of the placebo effect ought to say what falls inside and outside the boundaries of placebo. Similarly, an ideal account of the placebo effect will not only provide tools for distinguishing between placebo effects and non-placebo effects, but will provide tools that are explanatorily relevant. By explanatorily relevant, I mean that the account should cohere with existing empirical data related to the phenomenon and should highlight aspects of that data that help to explain why, how, where, and when the placebo effect occurs. Finally, a successful account of the placebo effect ought to provide direction for future research. This goal is closely related to the second goal of explanation, but is unique in that it is forward-looking towards the unknown, or not yet known, as opposed to backward-looking or present-looking towards what we already have learned. Keeping this goal in mind as distinct is likely to give shape to a slightly different account of the placebo effect than simply focusing on demarcation and explanation, as the goal of direction points towards potentially salient areas of investigation that are yet to be fully explored. This goal seems especially important for an account of the placebo effect because in-depth research into the nature of the phenomenon is in the early stages and much remains to be uncovered.

Taken together, the goals that this account of the placebo effect aspires towards are to demarcate the phenomenon, to highlight explanatorily relevant features of the placebo effect, and to provide promising avenues of direction for future research. It should be noted that each of these goals is intimately related to the other two, such that an account that is too wide or narrow and fails to adequately demarcate the phenomenon will struggle to pinpoint that which is explanatorily relevant, while that which fails to
highlight the features of the placebo effect that are explanatorily relevant will be unlikely to guide future research in fruitful directions. Crucially, an account of the placebo effect ought to aim towards achieving each of these goals in balance, for focusing too much on only one can lead away from the others and detract from understanding of the phenomenon. If we briefly revisit the accounts of the placebo effect considered in the last chapter, we can see how an over-estimation of the importance of the goal of demarcation detracted from the goals of explanation and direction.

In taking inspiration from the role of the placebo as a control to be compared to ‘active’ interventions in research settings, several accounts have proposed to demarcate placebo effects from other effects based on the form of treatment administered. For example, Grünbaum’s account of placebo effects as produced by incidental treatment factors (those considered not necessary to the treatment) as opposed to characteristic treatment factors (those considered necessary to the treatment) draws the boundaries of the placebo effect within the form of treatment, and the way clinicians or communities understand treatments (Grunbaum 1986). While this account is successful in drawing a sharp line between what constitutes a placebo effect and what doesn’t, it contains very little information about what is explanatorily relevant to the phenomenon, or where researchers ought to look next. Shapiro’s account of the placebo effect as a ‘non-specific effect’, which generates a kind of generic relief or anxiety through the experience of receiving medical care, highlights not the form of treatment, but the type of effect produced (Shapiro 1968). This account also aims towards the goal of demarcation, by contrasting ‘non-specific’ placebo effects with the ‘specific effects’ that were thought to result from
‘active’ medical interventions. As we’ve seen, placebo effects can be very specific\(^3\), so in retrospect this account also failed to capture what’s explanatorily relevant about placebo effects.

Upon reflection, it becomes clear why these accounts and others, which focus on the form of placebo treatments and the effects of placebo treatments, missed out on explanatorily relevant information. The empirical research available today suggests that there is virtually a limitless number of things that might constitute the ‘treatment’ that initiates a placebo effect – a statement, a smell, a smile, a particular setting, etc – and there also a wide variety of forms that the placebo effect might take – pain relief, a reduction in Parkinson’s tremors, a boost in one’s immune functioning, asthmatic relief, etc. This suggests that drawing boundaries around that which contributes to a placebo response or the way in which a placebo response takes shape might prove to be a very difficult, if not impossible, task. Granted, a lot less was known about what constituted placebo effects at the time when Grünbaum and Shapiro were developing their accounts, and so focusing on the form of treatment or the kind of effects produced was an entirely reasonable thing to do; when one doesn’t have knowledge of the causal structure of a phenomenon, the best one can do is offer a description of when it seems to turn up\(^4\).

---

\(^3\) See Chapter 1, Section IVc2.

\(^4\) For example, the DSM (Diagnostic and Statistical Manual of Mental Disorders), now in its fifth edition, still takes an atheoretical position with regards to the cause of any of the mental disorders it includes within its taxonomy, a stance that reflects the lack of consensus concerning how we ought to understand the causal processes contributing to mental disorders (4).
Fortunately, looking retrospectively at these accounts, among others, we can start to see where we might find better building blocks for an account of the placebo effect that can contribute to the goals of demarcation, explanation, and direction. Rather than focusing on the form a placebo treatment might take, or the kinds of effects it might produce, we could try looking towards the causal processes that constitute placebo phenomena – an approach that is very likely to be both explanatorily relevant and effective with regards to demarcation\textsuperscript{5}. This is what I hope to offer in the following section.

III. Conditioned, Cognitive, and Network Placebo Responses

As described in the previous chapter, the last two decades have produced a wealth of data in terms of the kinds of mechanisms that underlie placebo effects. Evidence points towards two primary causal processes that constitute placebo responses: conditioning and expectancy (Stewart-Williams and Podd 2004, Pacheco-Lopez et al. 2006, Enck, Benedetti, and Schedlowksi 2008). In constructing an account of the placebo effect that sees these causal processes as central, the first question to ask is whether there are in fact two distinct placebo effects, or if these processes might share enough features to be united under one account. While most accounts to date have sought to capture all placebo

\textsuperscript{5} Irving Kirsch’s account of the placebo effect does aim towards the goals of explanation and demarcation by focusing on causal processes. He argues that “the placebo effect is that portion of the treatment effect that was produced psychologically, rather than through physical means” (4). As discussed in the previous chapter, however, his account of the placebo effect fails to capture placebo responses that are initiated through unconscious conditioning processes, and so is too limited in scope – see Chapter 1, Section IVd.
phenomena under one heading (with the exception of Fabrizio Benedetti, who has proposed a particularism with regards to placebo effects (Benedetti 2009)), it appears to me that there are more differences than similarities between the causal processes of conditioning and expectancies. In light of this, and keeping in mind the three goals of demarcation, explanation, and direction, I propose that an account of the placebo effect should encompass three kinds of placebo responses that impact clinical outcomes (both positively and negatively), including both a *conditioned placebo response* and a *cognitive placebo response*, as well as a third kind of response called a *network placebo response*.

While the first two of these responses, conditioned and cognitive placebo responses, fall fairly directly out of the mechanisms that underlie them, a description of network placebo responses has yet to be articulated in the literature. I will argue, however, that making space for this third form of placebo response in a taxonomy of placebo phenomena is worthwhile, in that it is likely to contribute to the three goals of demarcation, explanation, and in particular, direction. In what follows, I will describe each type of response in detail, by way of their primary mechanisms, central features, and through the use of examples. I will discuss the responses primarily through discussion of placebo responses, as opposed to nocebo responses (the negative version of a placebo effect), but it should be kept in mind that what follows applies equally as well to conditioned, cognitive, and network *nocebo* responses.

*Illa. Conditioned Placebo Responses*
Classic conditioning occurs in two phases. The first phase is called acquisition and includes pairing a neutral stimulus with an unconditioned stimulus that reliably produces a response, sometimes repeatedly. The second phase, evocation, occurs after the association has been acquired, and occurs once the neutral stimulus, which has now become a conditioned stimulus, is able to reliably produce the response on its own (Pavlov 1927). This is the basic mechanism that underlies conditioned placebo responses, which can be thought of as unconscious processes of classical conditioning that impact clinical outcomes. Conditioned placebo responses primarily impact immune and endocrine (hormone) functioning (Benedetti 2009). See Appendix B for a depiction of the immune parameters that have been found to be impacted by conditioned placebo responses.

Conditioned placebo responses appear to be deeply-engrained responses that evolved long ago. In 1982, Ader and Cohen demonstrated that the onset of autoimmune disease in lupus-prone mice could be delayed by using a conditioning procedure and an amount of immunosuppressive drug too insignificant to delay the onset on its own (Ader and Cohen 1982). Since then, conditioned placebo responses have been observed across many species (Kawai et al. 2004, Paradis and Cabanac 2004, Schedlowski 2006, Ader 2003, Klosterhalfen and Enck 2006). In a discussion of what they call ‘learned placebo effects’, Schedlowski & Pacheco-López describe their understanding of how this response evolved:

It can be hypothesized that this capacity was acquired during evolution as an adaptive strategy in order to protect the organism and prepare it for danger. For example, the exposure to a specific antigen and its categorization as an allergen might be centrally
associated (i.e., a learning process) with a specific environment or food. An adaptive response is then elicited (i.e., a memory process), consisting first of behavioral modifications to avoid the place or food associated with the antigen. If avoidance is not possible, the organism will try to reduce the contact with the allergen, for instance by coughing or sneezing. At the same time, the immune system may prepare the body for interaction with the antigen, e.g. by mast cell degranulation or antibody production. (Schedlowski and Pacheco-López 2010)

An example of this phenomenon in humans can be seen in an experiment that exposed asthmatic children to either a vanilla odor only, an inhaler only, or a vanilla odor *paired* with an inhaler twice a day for 15 days. Afterwards, the children who had been exposed to the paired odor and inhaler had increased pulmonary function after being exposed only to the vanilla odor, while children in the other conditions did not (Castes et al. 1998).

Another experiment exposed subjects in the experimental condition to an immunosuppressive drug paired with a distinctively-flavoured drink (green-coloured strawberry milk plus 1 drop lavender oil) over four sessions. After acquisition, these subjects were given the same drink but paired with placebo pills instead of the immunosuppressive pills, and afterwards, several measures indicated a significant dip in their immune functions (Goebel et al. 2002).

While some have argued that conditioned placebo responses are always mediated by expectations (Kirsch et al. 2004), evidence suggests that the conditioning process often occurs without, or despite, individual awareness. In one experiment, conditioned placebo responses were shown in subjects who had acquired an association between lemon lime Kool-Aid and a drug that reduced their cortisol levels, even though poor guesses as to whether they were receiving the drug or placebo capsule on any given day suggests that participants were unaware of what condition they were in (Sabbioni et al. 1997). Another experiment elicited conditioned placebo responses in participants through pairing an injection with a drug that increases growth hormones (participants in the control
condition were injected with saline solution), and found that even when subjects were
told to expect that they were being injected with a drug that decreases growth hormones,
their levels showed an increase (Benedetti et al. 2003). This suggests that at least in terms
of conditioned placebo responses related to endocrine functions, the effect can occur
unconsciously.

III. Cognitive Placebo Responses

Cognitive placebo responses are likely to have evolved much later than conditioned
responses, as they are mediated by expectations and belief. Most research on cognitive
placebo responses involves placebo analgesia (pain relief), since it is easy to control in an
experimental paradigm and shows a strong placebo response. An important component of
research into cognitive placebo analgesia responses is the hidden treatment paradigm,
because administering treatment covertly (usually through an IV from an infusion
machine in another room) eliminates individual expectations, providing a good model for
representing the placebo effect. Results from research involving this paradigm suggest
that the relief from painkillers and anti-anxiety drugs regularly involves a significant
placebo component as well as the effect of the active ingredient (Levine and Gordon
1984, Levine et al. 1981, Colloca et al. 2004). These experiments also demonstrate that
cognitive placebo analgesic responses can be very powerful, indicating that “telling a
patient that a painkiller is being injected (actually a saline solution) is as potent as 6–8 mg
of morphine” (Colloca and Benedetti 2005, 548). See Appendix A for a comparison of
the effect of open and hidden injections and interruptions of morphine treatment on pain intensity.

Apart from many types of pain, cognitive placebo responses can also impact inflammation, asthmatic reactions, as well as tremors, rigidity, and bradykinesia (slowness of movements) in Parkinson’s patients (Hashish, Harvey, and Harris 1986a, Benedetti et al. 2007, Luparello et al. 1968). In a double-blind experiment that examined the effects of expectation on Parkinson’s patients implanted for deep brain stimulation, motor performance consistently declined when the stimulator was turned off, and continued to decline when the stimulator was left on but patients were told that it was being turned off. Additionally, when the patients were subsequently told to expect an improvement in their motor performance, the decline in performance was entirely reversed (Benedetti et al. 2003). In a demonstration of long term cognitive placebo responses, a large double-blind surgery trial investigating the effectiveness of transplanting human embryonic dopamine neurons in the brains of Parkinson’s patients assessed individual’s quality of life a year later. What predicted a significant improvement in quality of life was not the actual treatment group that individuals had been assigned to (real surgery or sham surgery), but the treatment group they believed they had been assigned to (McRae et al. 2004).

Neuroscientific evidence has shown that cognitive placebo analgesia responses often involve the release of endogenous opioids or the endocannabinoid system (Carlino, Pollo, and Benedetti 2011), while nocebo hyperanalgesia responses (which lead to an increase
in pain rather than pain relief) activate either CCK-ergic systems or pathway linked to anxiety in the brain (Benedetti 1997, Benedetti, Amanzio, et al. 2006). Additional evidence for these pathways can be found in research demonstrating that placebo analgesic responses are blocked by the opioid antagonist naloxone or by the CB1 cannabinoid receptor antagonist rimonabant, while nocebo hyperanalgesia can be blocked by either the CCK antagonist proglumide or the anti-anxiety drug diazepam (Enck, Benedetti, and Schedlowski 2008, Benedetti, Amanzio, et al. 2006).

Evidence also suggests that the prefrontal cortex plays an important role in cognitive placebo analgesic effects, as temporary or permanent inhibition to the area disrupts the response (Krummenacher et al. 2010, Zubieta and Stohler 2009, Watson et al. 2009). In line with this, it has been shown that individuals who have prefrontal impairment due to Alzheimer’s disease require additional painkillers to feel pain relief since they no longer experience the cognitive placebo component of analgesia (Benedetti, Arduino, et al. 2006). In Parkinson’s disease, cognitive placebo responses appear to be mediated by the release of dopamine in the dorsal striatum (de la Fuente-Fernandez, Schulzer, and Stoessl 2004), although significant dopamine release only occurs if individuals believe there is a high likelihood (over 75% in one experiment) that they will be receiving an active intervention (Lidstone et al. 2010). This is consistent with data demonstrating that in general, placebo responses are greater in clinical trials where the likelihood of being in an active treatment group is higher, suggesting that the higher individual expectations are that they will be receiving an active treatment, the better their outcomes are (Enck et al. 2013).
Some research has indicated that the line between conditioned and cognitive placebo responses may not be so clear cut. There’s no doubt that conditioning procedures can impact the strength and duration of placebo analgesic responses (Colloca et al. 2010), and can even determine whether the analgesic response is mediated by opioids or non-opioids (Amanzio and Benedetti 1999). Additionally, similar brain areas appear to mediate conditioned and cognitive analgesic responses (Watson et al. 2009). However, this data is consistent with evidence that suggests that conditioned analgesic responses are mediated by expectations (Montgomery and Kirsch 1997, Price, Chung, and Robinson 2005). This hypothesis is corroborated by the fact that conditioned analgesic responses can be overridden by a suggestion of hyperalgesia (Benedetti et al. 2003). Research that demonstrates an impact on pain by unconscious classical conditioning has been recently reported, however, suggesting that either unconscious cognitive mechanisms mediate this effect, or that cognition isn’t always involved in analgesic placebo responses (Jensen et al. 2012).

IIIc. Network Placebo Responses

While the existence of conditioned and cognitive placebo responses is widely agreed upon, the third type of placebo response I describe here has received no mention in the placebo literature to date. While this third type of placebo response does not fall directly out of known causal placebo processes as the conditioned and cognitive placebo responses do, it involves unique features that cannot be explained by conditioned and cognitive placebo responses, and so is better off placed in a new category.
Before introducing the network placebo response, it is necessary to describe what a symptom network is and how it contrasts with an alternative picture of illness, the latent variable model. The work of a group of psychometricians from the University of Amsterdam led by Denny Borsboom highlights the way in which the tools used to measure psychiatric phenomena rely implicitly on a model of psychiatric conditions as latent variables (Borsboom 2002, Borsboom and Cramer 2013, Borsboom et al. 2011). A latent variable can be thought of as a single underlying cause that leads to the expression of many symptoms. In contrast, a symptom network lacks a single common cause, but involves an illness which is constituted by symptoms that causally influence each other within a network. An example can be seen in the interrelatedness of symptoms of Major Depressive Disorder (MDD), in which trouble sleeping leads to fatigue which leads to difficulties in concentration which leads to thoughts of inferiority and worry which leads back to trouble sleeping (Cramer et al. 2010, 140-141).

As psychometricians, Borsboom and colleagues are primarily concerned with how we might better measure the presence of mental disorders, but this model has interesting implications for intervention as well. While the latent variable model suggests that intervention should occur at the level of the common cause (e.g. antibiotics treating a bacterial infection), symptom network models suggest that intervention can occur at many sites within the network, since the symptoms are embedded in causal networks with each other. The widespread assumption that latent variables underlie mental disorders has contributed to many attempts to find a common pathway that explains efficacious
treatment of MDD through both antidepressants and psychotherapy, which taken together have been largely unsuccessful (Leuchter et al. 2002, Linden 2006, Mayberg et al. 2002, Pampallona et al. 2004). The symptom network model suggests that this search may be in vain, since there may be several distinct routes of intervention that can positively or negatively impact a disorder like MDD, which is in fact what the evidence shows (Pampallona et al. 2004). This suggests that, at least in terms of MDD, the symptom network model better explains the data than the latent variable model.

Returning to the placebo effect with this discussion of symptom networks in mind, there appears to be a handful of psychosomatic conditions that consistently show robust placebo responses, and that also share the feature with MDD of being responsive to various psychological and physical treatments (Ford et al. 2009, Hofmann et al. 2010, Cuijpers et al. 2013, Afari and Buchwald 2003). These conditions include irritable bowel syndrome, chronic fatigue syndrome, and panic disorder, among others (Patel et al. 2005, Pitz, Cheang, and Bernstein 2005, Vase et al. 2003, Hayden 1991, Coryell and Noyes 1988). MDD has been found to be very responsive to placebo treatments as well (Kirsch 2010). This indicates that these conditions might also be better thought of as symptom networks rather than as constituted by latent variables, since there appear to be multiple potential sites of intervention. Interestingly, each of these conditions has strong links to immune deficiencies, suggesting a relationship to conditioned placebo responses (Barbara et al. 2011, Dantzer et al. 2008, Leonard and Song 1996, Bansal et al. 2012, Rosenkranz

---

6 It should be noted that a recent meta-analysis suggests that placebo responses in chronic fatigue syndrome are not as big as once thought (59).
Anxiety and mood disorders are also consistently implicated in these psychosomatic conditions, suggesting that cognitive placebo responses may play a role too (Janssens et al. 2015, Moffitt et al. 2007, Lee et al. 2009). Placing this in a larger literature that has been describing the connections between the immune system and mood disorders for decades, it appears that disorders that occur at the margins of the mind and body may be important sites of interaction between conditioned and cognitive placebo responses (Segerstrom and Miller 2004, Chapman, Perry, and Strine 2005). Despite this link, network placebo responses cannot simply be reduced to conditioned and cognitive placebo responses.

A good example of why reduction doesn’t work can be seen in an experiment led by Ted Kaptchuk involving a group of individuals suffering from irritable bowel syndrome (IBS). Participants were enrolled in a clinical trial and randomized to either the control condition (no treatment) or the open-label placebo treatment condition, where participants knowingly took two “placebo pills” (the bottle was marked with these words) twice a day while thinking about how powerful the placebo effect can be. At the end of three weeks, the open-label placebo group had significant improvements compared to the control group on both measures of symptom reduction and quality of life (Kaptchuk et al. 2010). While conditioned and cognitive placebo responses both appear to be related to the placebo phenomena that occurred in this experiment, it is also clear that neither response adequately explains this data. Conditioned placebo responses are unable to account for the outcomes since there is no unconditioned stimulus in the experiment that reliably produces a response and underlies the acquisition phase (e.g. Pavlov’s dog food...
that the bell is paired with). Similarly, the expectations and beliefs that typically underlie cognitive placebo responses are inconsistent with the participants’ knowledge that they are taking sugar pills, and so cognitive placebo responses cannot explain the outcomes either.

Conceiving of this as a network placebo response, however, better explains why such a robust placebo response might occur in response to an open label placebo treatment. If IBS consists a network of interactive symptoms, both psychological and somatic, then the condition involves multiple sites of intervention that can be impacted through both psychological and physical treatments. In this experiment, several minor effects on symptoms, induced by the repeated act of focusing on the efficacy of the placebo pills, the ritual of taking them twice a day, and knowledge that one has the support of the clinical team, might lead to significant relief overall through the interaction of different symptom effects, each of which are initiated by a combination of conditioning or expectations. This explanation is consistent with another placebo experiment involving patients with IBS that demonstrated that the more ritual, sympathy, and support built in to the patient-healer interaction, the better the clinical outcomes were. In the most intensive condition, which also included treatment with fake acupuncture, the effect was better than any pharmaceutical ever tested for IBS (Kaptchuk et al. 2008).

While much is still unknown about network placebo responses, the evidence suggests that a new category is warranted. Placebo effects in these conditions appear to be important sites of overlap and perhaps interaction between conditioned and cognitive placebo
responses, but are not adequately explained by them. Thinking of these conditions as symptom networks and conceiving of the placebo responses they involve as network placebo responses better explains why these conditions are so sensitive to placebo treatments. If a condition is constituted by causal relationships between symptoms, as opposed to a single common cause, we would expect to see larger placebo responses, since there are multiple avenues of intervention that might provide relief, and this is precisely what we do see.

IV. Returning to the Three Goals

IVa. Demarcation

The account of the placebo effect laid out in the previous section has little trouble demarcating the placebo effect from other types of effects, at least in theory. Any clinical outcome that can be attributed to either classical conditioning or expectancies counts as a placebo response on this account. If the response only involves classical conditioning, then it is a conditioned placebo response, while if it only involves expectancies or beliefs, it is a cognitive placebo response. If it involves both, it may be either an additive effect of both conditioned and cognitive responses (in pain relief, for example) or if it occurs within a complex network of symptoms, it is a network placebo response.

Within practice, there is likely to be many occasions in which it is unclear what the causal processes that led to a placebo response are. This is often the case in clinical trials,
when the placebo group shows a significant improvement, but there are many factors, related to conditioning, expectations, or other factors (e.g. regression to the mean, patient bias, etc), that could be responsible. There is also a limited amount of research related to the causal mechanisms that contribute to network placebo responses, and since both conditioned and cognitive responses are likely to be involved, the causal processes that underlie these responses will often be underdetermined.

It is possible, and perhaps likely, that with time and additional research, the boundaries around these three types of responses will shift. It may turn out that network placebo responses can be explained by reference to conditioned and cognitive placebo responses, or that all three responses can be collapsed into a single mechanism\(^7\). Such changes should be welcomed, as it is often the case that once we have more information about the explanatory relevant features of a phenomenon, we start to redraw the boundaries, a process that William Bechtel has deemed ‘reconstituting the phenomenon’ (Bechtel 2008). While this account may be less stable than one which relies on the form or effect of a placebo treatment, it is certainly worth sacrificing for the degree of explanatory relevance gained.

\textit{IVb. Explanation}

\(^7\) Some have suggested that conditioned and cognitive placebo responses may operate through the same immune pathways (5) or that they make up the unconscious and conscious components of one placebo response (74), but there is currently insufficient evidence to support either position.
Since the importance of developing an account based on causal processes was already discussed in detail at the start of this chapter, I will provide minimal justification here for how this account contributes to the goal of explanation. In comparison to previous accounts, the account of the placebo effect as constituted by conditioned, cognitive, and network placebo responses relies explicitly on the causal processes that underlie placebo effects to give it shape, except in the case of network placebo responses where the mechanisms are still unknown. This leads to an account that is able to explain several important features of the phenomenon.

Importantly, the account is able to explain why placebo responses can happen as a result of either unconscious or conscious triggers, and how those triggers can range from Kool-Aid to fake acupuncture to open label sugar pills. Similarly, the account explains how measures as diverse as pain, white blood cell count, and fatigue can all be impacted by placebo treatments. The account also explains nocebo effects as well as it does placebo effects, since conditioning can lead to either positive or negative clinical outcomes, and expectations can be led in both directions as well. Additionally, the account is able to explain why it is that we see such large placebo effects in conditions that involve both psychological and somatic symptoms, especially when those symptoms are linked to both immune and anxiety pathways. In the next section (not included within this writing sample), I will say more about how the account is able to explain related placebo phenomena such as clinician empathy, placebo by proxy, alternative medicine, and positive psychology.
IVc. Direction

Perhaps the most important goal that the account is able to contribute to is that of pointing towards future directions for research. It’s clear that both conditioned and cognitive placebo responses require a lot more investigation with regards to the details of the causal mechanisms underlying them, as well as in terms of how they might be harnessed to produce the most beneficial effects. The promise of harnessing conditioning placebo responses so that pharmacological doses can be lowered and harmful side effects can be avoided has already been noted (Ader 1989, Pacheco-Lopez et al. 2006) and additional explorations of the impact of prescribing open label placebo pills are being explored (Kaptchuk et al. 2010, Kelley et al. 2012). Quite a bit of excitement has also been generated over the possibility of conditioned placebo responses occurring while individuals are receiving chemotherapy, especially since conditioned stimuli related to the chemotherapy context often trigger symptomatic responses such as nausea long after treatment, but it is too early to say if conditioned placebo responses induced during chemotherapy can impact cancer progression (Exton et al. 2000, Bovbjerg 2003, Lekander et al. 1995, Fredrikson et al. 1993).

In terms of placebo research, however, is likely that the most untapped potential lies within network placebo responses. The analysis of this third type of response given in the previous section suggests that placebo researchers ought to spend more time exploring conditions that arise at the boundaries of the psychological and the somatic, since we can anticipate increased placebo responsiveness there. Some conditions that have not been
investigated, but according to this account can be expected to be sensitive to placebo treatments, are those that are often grouped under functional somatic syndromes or bodily distress syndromes, including multiple chemical sensitivity, the sick building syndrome, repetition stress injury, the Gulf War syndrome, and chronic whiplash (Budtz-Lilly et al. 2015, Barsky and Borus 1999). Other psychological disorders related to anxiety should also be explored in terms of their relations to placebo responses, including obsessive compulsive disorder, post-traumatic stress disorder, social anxiety, trichotillomania, and sexual dysfunction.

In addition, network placebo responses carry implications for what kinds of treatments should be given priority when conditions are made up of psychosomatic symptom networks. While both psychological and pharmacological treatments are available for psychosomatic conditions that fall under the domain of the DSM, like depression and panic disorder, those that are primarily thought of as medical conditions are primarily treated by pharmacological means. Perhaps for this reason, individuals suffering from conditions like irritable bowel syndrome, chronic fatigue syndrome, and other functional somatic syndromes, who rarely respond well to treatment, are often met with disdain by health care professionals who see their suffering as ‘all in their heads’. One clinician complains that “the suffering of these patients is exacerbated by a self-perpetuating, self-validating cycle in which common, endemic, somatic symptoms are incorrectly attributed to serious abnormality, reinforcing the patient’s belief that he or she has a serious disease” (Barsky and Borus 1999).
If psychosomatic conditions do not fit within a latent variable model where one treatment would be expected to fix the problem, then it should come as no surprise that the pharmacological one-size-fits-all treatments available to individuals with these conditions are minimally effective. This (and the nocebo-minefield attitude expressed above) might help explain why individuals suffering from psychosomatic ailments are very likely to seek alternative forms of treatment outside the medical model (Fava and Sonino 2000).

If, on the other hand, these psychosomatic conditions are better thought of as complex symptom networks, then we would expect to see limited positive results from a single treatment, and better results when multiple treatments are used in conjunction. This aligns with evidence that both psychological and pharmacological treatment of depression consistently leads to greater improvements than treatment with one or the other alone (Pampallona et al. 2004). This suggests that psychosomatic conditions might require both psychological and somatic treatments to ensure the best clinical outcomes. As two placebo researchers recently observed, “the bias against merely symptomatic treatments has contributed to neglect of the contextual variables that can powerfully affect the outcomes of such treatments” (Miller and Colloca 2011).

V. Conclusion

In this chapter, I have presented an account of the placebo effect that describes the phenomenon as made up of three types of responses: conditioned placebo responses, cognitive placebo responses, and network placebo responses. Conditioned placebo responses are mediated by classical conditioning, cognitive placebo responses are mediated by expectations and beliefs, while network placebo responses occur in
conditions that are constituted by complex symptom networks, and involve the interplay of both conditioned and cognitive placebo responses. I argue that this account is better able to meet the goals of demarcation, explanation, and direction than other available accounts of the placebo effect.
Chapter 3. Expanding The Demarcation Project: Protoscience, the Placebo Effect, and Complementary and Alternative Medicine

I. Introduction

The question of demarcation, or how to distinguish between science and pseudoscience, has been taken up in fits and starts throughout the history of philosophy of science, although some have argued that it should be put to rest indefinitely (Laudan 1983). Despite this, it is currently undergoing something of a revival, as evidenced by a recent anthology entitled Philosophy of Pseudoscience: Reconsidering the Demarcation Problem (Pigliucci and Boudry 2013b). Within this anthology, nearly half of the 23 chapters contained in the book offer complementary and alternative medicine (CAM)\(^8\), or homeopathy, a practice that falls under the CAM heading, as a prototypical example of pseudoscience. In the introduction, the editors of the volume, Massimo Pigliucci and Maarten Boudry, argue that pseudoscience ought not to be considered a “harmless pastime”, given that it “has swindled people of billions of dollars in the form of “alternative” medicine like homeopathy”, among other crimes (Pigliucci and Boudry

\[^8\] The term ‘alternative medicine’ is frequently used by those who disapprove of the practices encompassed within it, while ‘complementary medicine’ is often favoured by proponents. I will use the more neutral, and more compact, term, complementary and alternative medicine (CAM), here.
In agreement with the editors, Martin Mahner aims to impress upon readers the importance of determining what constitutes pseudoscience, as the project can help us respond to pressing questions like “should public health insurances cover magical cures like homeopathy or Therapeutic Touch?” (Mahner 2013, 35).

In this chapter, I raise questions about the categorization of CAM as a pseudoscience, by examining what we know about the role of the placebo effect in these practices, and argue that CAM would be better conceived of as a protoscience. In the first section, I give an overview of evidence that suggests that some CAM practices may be exceptionally efficient at harnessing the placebo effect, despite their pseudoscientific appearance. In the second section, I suggest that this implies that there is a meaningful difference between CAM practices and other prototypical examples of pseudoscience, and that theories of demarcation ought to be able to capture this meaningful difference. In the third section, I consider whether any theories of demarcation that have been put forward have the tools to account for this meaningful difference. After determining that they do not, in the fourth section, I sketch out a theory that may be able to account for this difference, by distinguishing between pseudosciences, sciences, and protosciences.

It is worth noting at the outset that examples of pseudosciences have not remained constant throughout history, as the term’s “precise meanings have been able to vary with the identity of the enemy” (Thurs and Numbers 2013, 123). Currently, along with CAM, the most beloved targets of demarcationists include some old favourites, such as astrology and parapsychology, as well as some slightly more modern endeavors such as
Intelligent Design and ufology (Pigliucci and Boudry 2013b). Interestingly, before creationism was considered to be a paradigmatic example of pseudoscience, the most common referent of the term pseudoscience was evolution (Thurs and Numbers 2013). It seems that the more politically entwined an epistemological endeavor is, the more likely it is to be called a pseudoscience; Daniel Thurs and Ronald Numbers report on how global warming, stem cell research, and the demotion of Pluto from planetary status have all been called pseudosciences (Thurs and Numbers 2013, 137). As Thomas Nickles puts it, “Historically, then, demarcation has typically been a conservative exercise in exclusion, an attempt to preserve the purity of modern science as the primary engine of social progress” (Nickles 2013, 105).

Despite, or perhaps because of, its charged nature, the question of demarcation has both importance and impact. Even while arguing that philosophers ought to abandon the problem of demarcation, Laudan argued that, “Precisely because a demarcation criterion will serve as a rationale for taking a number of practical actions which may well have far-reaching moral, social and economic consequences, it would be wise to insist that the arguments in favor of any demarcation criterion we intend to take seriously should be especially compelling” (Laudan 1983, 120, emphasis in original). Similarly, Lakatos called the problem of demarcation of “vital social and political relevance” (Lakatos 2009, 514). This is particularly true within the realm of medicine, where both the harms of getting it wrong, and the benefits of getting it right, are hard to overestimate. Keeping this in mind, I now turn to the role of the placebo effect within CAM practices.
II. Placebo Responses within Complementary and Alternative Medicine

Complementary and alternative medicine includes a wide and diverse range of practices, including but not limited to acupuncture, meditation, homeopathy, reiki, herbalism, massage therapy and chiropractic manipulations. See Table 1 from (Frass et al. 2012) in Appendix C for a categorization of CAM therapies. Usage of CAM practices and visits to CAM practitioners are reported to be significant and increasing, although prevalence rates vary between 5% and 75% in wealthy nations (Frass et al. 2012). While it differs by country, treatments that fall under the domain of CAM are often not covered by insurance, so clients usually pay out of pocket. According to survey data from 2007, adults in the United States spent $34 billion on CAM that year (Nahin et al. 2009). In Germany, where coverage of CAM is more extensive, 1/10 of costs for general medical care went towards CAM practices (Frass et al. 2012 citing Marstedt and Moebus 2002).

While scientific evidence for the majority of CAM practices is fairly minimal, it is hard to believe that nothing positive is happening as a result of them, given their persistence and growth. While I do not wish to speculate as to the efficacy of the many distinct mechanisms said to underlie practices within the domain of CAM, evidence that suggests that part of why CAM practices are embraced so widely is because of their exceptional ability to harness the placebo effect. Reasons suggesting that practices within the domain of CAM produce strong placebo effects include the features of the clinical encounter that are seen as central to CAM, the views of CAM practitioners on the placebo effect, and the types of conditions that CAM practitioners treat most often. I will discuss each of
these briefly in turn, as well as how they apply to the specific case of homeopathy. Given the diversity of practices that are included in this domain, it is difficult to make generalizations with regards to all of the practices encompassed within this category; I do so here with caution, and introduce important distinctions CAM practices in the following section.

IiA. Features of CAM Practices

In most CAM practices, the therapeutic alliance is seen is central to the clinical encounter, as are displaying empathy and helping the client to understand his or her unique experience (Anthony 1987, Carter 2003). In CAM, Kaptchuk and Eisenberg suggest, “A patient never has to fear that an illness will be branded as existing "only in their head." A "real" cause will be found for any sensation” (Kaptchuk and Eisenberg 1998). Distilling hope is also seen as an important aspect of treatment within CAM. As put by Stub and colleagues, “Patients’ positive beliefs and expectations about the treatment play a significant role in the healing process. The more hope the therapist can bring about, the more easily the patient can start believing that it is possible to get well” (Stub, Foss, and Liodden 2017, 1). Importantly, consultations in CAM are often much longer than in mainstream medicine, giving more time for positive expectations and conditioning to occur (Stub, Foss, and Liodden 2017). In line with this, in his chapter in the anthology Understanding the Placebo Effect in Complementary Medicine, Edzard Ernst suggests that there are five components of CAM that are likely to enhance the placebo effect: the unusualness or exoticism of the interventions, the warmth and confidence of the therapist, the length of time spent with patients, the positive
expectations of the patient, as well as the therapeutic setting. Indeed, as placebo research by Kaptchuk and colleagues demonstrates, incremental additions of practitioner warmth, consultation time, and expressions of confidence can lead to significant gains in clinical outcomes for individuals with irritable bowel syndrome (Kaptchuk 2011).

The features of the clinical encounter that are embraced by CAM practitioners are not lost on patients either. When asked what their experiences of CAM treatments have been like and why they continue to seek out such practices, patients report that they feel that they play an active role in their health, that they are treated like a whole person rather than mere symptoms, and that they experience the therapeutic relationship as authentic and meaningful (Luff and Thomas 2000, Sirois, Salamonsen, and Kristoffersen 2016, Vincent and Furnham 1996). Patients also regularly report the belief that CAM will be more effective for their particular health issue than conventional medicine, and that it is more congruous with their beliefs and values than allopathic medicine (Vincent and Furnham 1996, Astin 1998).

**IIb. Practitioner Views on the Placebo Effect**

Self-healing is widely recognized within the domain of CAM, and at times the placebo effect is explicitly called out as an important causal factor within CAM practices. Reporting on qualitative research involving CAM practitioners, Segar reports that “CAM practitioners often point out that their therapeutic interventions simply help to speed up the body’s innate ability to heal itself. They argue that the placebo effect is simply a demonstration of the wonderful way that the body can heal itself and an illustration of the
power of the human mind” (Segar 2011, 376). In line with this, one CAM practitioner, interviewed by Stub et al., said:

Placebo effect is probably what we refer to as the patient’s self-healing power. That [the self-healing power] I think you stimulate in many ways during a consultation. Actually, I think from the moment you step inside the office. That you’re welcomed, that you’re seen, that we talk together, that you’re understood, that you can tell your story to a person who listens and tries to interpret and understand. And all the things we talk about to the remedy that you give. To the advice you give. And to the needles you insert. And the better all of this is, the more the patient feels that he is taken care of. (Stub, Foss, and Liodden 2017)

This quote captures the importance that many CAM practitioners place on aspects of the treatment that go beyond the particulars of the intervention, be it acupuncture or reiki. In line with this, many CAM practitioners see the idea of the treatment working alone, apart from the therapeutic alliance between the patient and practitioner, and apart from the patient’s own self-healing, as a strange aspect of conventional medicine (Anthony 1987).

IIc. Conditions Commonly Treated within CAM

The types of concerns that individuals tend to visit CAM practitioners with include functional somatic syndromes such as fibromyalgia and irritable bowel syndrome, mood disorders such as depression and anxiety, and chronic pain, as a result of musculoskeletal issues, cancer, or HIV (Bausell, Lee, and Berman 2001). These are conditions that are characterized by “indecisive and subjective symptoms” and that conventional medicine lacks effective tools for (Stub, Foss, and Liodden 2017, 5). Additionally, many of these conditions are precisely those that were highlighted in Chapter 2, as the types of conditions that exemplify network placebo responses and that consistently display robust placebo effects. Correspondingly, individuals seeking CAM treatment often report feeling dissatisfied with the treatment they have received within conventional medicine (Vincent and Furnham 1996).
**IIIh. Homeopathy**

Given the difficulty of generalizing across CAM practices and the attention homeopathy has garnered within the philosophy of pseudoscience literature, I briefly consider the homeopathic consultation here as an example of the features that frequently turn up within CAM. While the typical visit to a physician’s office lasts 15 minutes, a consultation with a homeopath usually lasts between one and several hours (Tai-Seale, McGuire, and Zhang 2007, Hartog 2009). Within this time, the patient’s concerns are explored in detail, and the homeopath focuses on forming connection, establishing a genuine and trusting therapeutic relationship and expressing empathy (Eyles et al. 2011). An important part of the homeopathic consultation is that the patient is seen as an agent and as an expert with regards to their own experience. Through this lens, the practitioner helps the patient to construct a narrative surrounding their concerns that make sense for them (Hartog 2009). In her analysis of the homeopathic consultation, Christiane Hartog explicitly acknowledges the importance of instilling hope in the patient, suggesting that the “inherent “therapeutic optimism” ” of homeopathy “may have an effect on outcome, since hopelessness is a nocebic state of mind” (Hartog 2009, 176). See Appendix D for a table developed by Hartog listing the effective elements in homeopathic communication.

Homeopathy is a favourite target of those interested in drawing a line between science and pseudoscience because of the biological implausibility of the theories that underlie the practice. Homeopathy is based on a principle of similarity, that like cures like, and so
infinitesimal doses of a substance meant to resemble the symptoms or condition the patient is dealing are diluted within alcohol or water, and prescribed to patients (Ernst 2002b)⁹. As Gorski and Novella argue, “homeopathy violates multiple laws of physics with its claims that dilution can make a homeopathic remedy stronger and that water can retain the ‘memory’ of substances with which it has been in contact before” (Gorski and Novella 2014, 475)¹⁰. However, as can be seen by the description of the consultation given above, homeopathy is much more than these claims. Regardless of the plausibility of the mechanisms of action that are espoused by homeopaths, it seems more than likely that robust placebo responses are produced within the consultation. In line with this, a recent RCT suggests that positive clinical effects of homeopathy in rheumatoid arthritis patients were the result of the consultation as opposed to the particular homeopathic remedies (Brien et al. 2011).

III. CAM as Pseudoscience?

IIIa. A Meaningful Difference

In reflecting on the role of the placebo effect in complementary and alternative medicine, it appears that many within the field of CAM are in touch with and intentionally

⁹ Some have even argued that the presence of this kind of “resemblance thinking” should be thought of as sufficient to mark something as pseudoscientific (Thagard 1979).
¹⁰ It should be noted that the principle of similarity has recently been defended on the basis of research into cell sensitivity to ultra-low doses (Bellavite et al. 2015)
manipulating a real, scientifically interesting, phenomenon in order to produce benefits\textsuperscript{11}. This suggests that there is something importantly different underlying the practices within CAM, as compared to other prototypical pseudoscientific practices of “flat Earthers, biblical creationists, proponents of laetrile or orgone boxes, Uri Geller devotees, Bermuda Triangulators, circle squarers, Lysenkoists, charioteers of the gods, \textit{perpetuum mobile} builders, Big Foot searchers, Loch Nessians, faith healers, polywater dabblers, Rosicrucians, the-world-is-about-to-enders, primal screamers, water diviners, magicians, and astrologers” (Laudan 1983, 121). With the exception of faith healers and possibly primal screamers, as they too may be harnessing the placebo effect, CAM appears to be somewhat of an outlier in this list of pseudoscientific exemplars, because of its success in recognizing the benefits of inducing placebo responses and learning to manipulate them. These other examples of pseudoscience, while they may see themselves or present themselves as scientific, lack a scientific phenomenon that is being put to the test. On the other hand, CAM practitioners, while their explanations for what they are doing may vary widely, appear to consistently be producing a real effect within their practices. This suggests that there is a significant distinction between what is taking place within CAM and the epistemic projects of flat Earthers and that theories of demarcation ought to be able to capture this distinction.

\textit{IIIc. Diversity of CAM Practices}

\textsuperscript{11} This is not to say anything with regards to the efficacy of the mechanisms reported to underlie any CAM practices. It is certainly possible that there is more than the placebo effect occurring in many of these practices, but here I am only concerned here with the observation that these practices tend to be very good at producing placebo responses.
However, the challenge is not quite so simple. While it appears that many CAM practices have found a way to regularly produce effective placebo effects in their clients, these practices are incredibly diverse, and so are the ways they present themselves. Importantly, many CAM practitioners, researchers, and communities engage in behaviours that are characteristically pseudoscientific, including cherry picking studies and success stories to demonstrate efficacy, using scientific sounding terminology in order to sound more legitimate, and ignoring scientific evidence from other fields that might challenge their practice.

Countless websites of CAM practitioners include pages of personal anecdotes that attest to the efficacy of the treatment, without making any reference to more systematic evidence (Homeopath). When research is cited, it is often only successful studies that are included, while those that failed to demonstrate efficacy are left out (Ernst 2010). Furthermore, methodological issues have often been brought up in response to research related to CAM (Linde et al. 2001), although proponents of CAM often argue that traditional methods for investigating biomedical treatments are insufficient for measuring the effects of CAM (Carter 2003). A somewhat extreme example of dressing up one’s claims as scientific can be found in Body Vibes stickers, wearable stickers developed and sold by celebrity Gwyneth Paltrow as part of her wellness brand “Goop”. These stickers are said to have been “pre-programmed to an ideal frequency, allowing them to target imbalances” and are sold for $60 for a pack of 10 (goop.com). When first released, they were said to have been made with the “same conductive carbon material NASA uses to line space suits so they can monitor an astronaut’s vitals during wear”, although this
statement was later removed after NASA released a statement denying that carbon materials line their suits (John 2017).

Additionally, while some practitioners are happy to use terms like self-healing and placebo effect to describe what occurs during CAM practices, most maintain that there are other contributors to positive clinical outcomes, some of which are embedded within metaphysical pictures that are largely incompatible with contemporary scientific theories and difficult to test (e.g. homeopathy, energy healing). The ways in which these metaphysical pictures contrast with theories that are widely accepted in other scientific realms is often left unconsidered in explorations of the practice. However, other CAM practices are surprisingly congruent with contemporary biomedicine, such as Craniosacral Therapy (CST). CST is a practice related to osteopathy in which practitioners provide “gentle manual force to address somatic dysfunctions of the head and the remainder of the body” through the manipulation of the craniosacral system, which consists of “the membranes and cerebrospinal fluid surrounding the spinal cord and brain, the bones to which these membranes attach and connective tissue related to these membranes” (Jakel and von Hauenschild 2012, 457). While the practice is based on the work on an osteopath from the 1930s, it has recently been growing in popularity, but there have only been a few studies evaluating its effectiveness. A recent systematic review suggests that there are indications that CST contributes to both pain reduction and an increase in general wellbeing in clients, but that the evidence is scant and methodologically questionable, so one should refrain from drawing any conclusions at this point (Jakel and von Hauenschild 2012). It is likely that the placebo effect is
contributing to positive outcomes, in that treatment sessions usually last between 40 minutes to an hour, but these effects may be smaller than in homeopathy, in that CST involves more bodywork and less conversation between the practitioner and client (Jakel and von Hauenschild 2012).

IIIc. Capturing Distinctions

These examples demonstrate the diversity of practices that fall under the domain of CAM, as well as several ways these practices may resemble pseudosciences. This diversity suggests that making distinctions within the field of CAM may also be important in examining their status as pseudoscientific, as we may want to characterize some, such as Body Vibes stickers, as more pseudoscientific than others, such as CranioSacral Therapy. This presents two challenges for theories of demarcation. The first is to distinguish between CAM practices such as homeopathy, which are pseudoscientific in character, and yet appear to have hold of a scientifically interesting phenomenon which underlies the practice, from practices such as ufology or the search for the Loch Ness monster, which appear to be clear cases of pseudoscience. Similarly, an effective theory of demarcation ought to be able to distinguish between CranioSacral Therapy and Body Vibes stickers, which differ substantially in terms of their pseudoscientific claims, but both of which are likely to be inducing some placebo responses. In the following section, I consider whether theories of demarcation that have been put forward contain the tools to make these distinctions.

IV. Theories of Demarcation
Theories of demarcation can be broadly categorized into those that locate the criterion for science or pseudoscience within the theory, the practice, the practitioners, or some combination of these. I consider each of these in turn below.

IVa. Theory as the Criterion of Demarcation

Karl Popper, who put forth was is likely the best known, and perhaps the most thoroughly defeated, criterion of demarcation, argued that falsification is what allows one to distinguish between scientific and pseudoscientific statements. After examining three theories that he had no respect for, namely astrology, Marxism, and individual psychology (that of both Freud and Adler), Popper noticed that what they each had in common was that confirming instances of the theories could be found everywhere (Popper 1953). In response to this observation, he argued that a scientific theory ought to make predictions that forbid possible events and that only a hypothesis that can be falsified can fall under the proper domain of science. In sum, he argued that “statements or systems of statements, in order to be ranked as scientific, must be capable of conflicting with possible, or conceivable observations” (Popper 1953, 12).

Popper’s falsification criterion of demarcation has long been criticized for letting in too much and too little. It is easy to find statements that are potentially falsifiable within pseudoscientific projects, since all that is required is a claim that is empirical in principle. ‘There was a UFO at this place on this day’ or ‘The world will end in 3000 years’ can certainly suffice, making Popper’s criterion of demarcation overly inclusive. On top of that, the Duhem-Quine thesis reveals the relationship between a theory and auxiliary
hypotheses, suggesting that falsification of a theory need not mean falsification of a theory, but merely that particular version of the theory. A scientific theory can always be adapted in order to accommodate incompatible evidence, so the criterion of falsification also fails to capture such theories that act like moving targets. As Lakatos puts it, “Popper’s criterion ignores the remarkable tenacity of scientific theories. Scientists have thick skins. They do not abandon a theory [merely] because facts contradict it. They normally either invent some rescue hypothesis to explain what they then call a mere anomaly and if they cannot explain the anomaly, they ignore it, and direct their attention to other problems” (Lakatos 2009, 516). This is the case for both characteristically scientific endeavors (e.g. physicists saying “the measurement must be wrong”) and characteristically pseudoscientific ones (e.g. creationists saying “God made it look that way”) (Pigliucci 2013).

For these reasons, Popper himself, and many interested in demarcation since, shifted the focus of demarcation from the theory or statements contained within the theory to the behaviors or attitudes of the those engaging in science or pseudoscience (Godfrey-Smith 2009)\textsuperscript{12}. Beyond his focus on the falsifiability of statements within a theory, Popper was interested in the importance of taking risks within science. He emphasized the way in which scientists tend to make “risky predictions” and expose their hypotheses to tests that could refute their theories if the predictions were not borne out (Popper 1953, 11). In contrast, pseudoscientists avoid such tests by making their “interpretations and prophecies sufficiently vague”, allowing all evidence to appear as corroboratory for their

---

\textsuperscript{12} Some argue that Popper never focused on theories alone, but always found the criterion for demarcation in the relationship between the theory and practitioners (Ladyman 2013).
theories (Popper 1953, 11-12). Popper also highlighted the way in which pseudoscientists respond to evidence that conflicts with their theories, arguing that in light of such unwelcome evidence, Marxists reinterpreted both the theory and the evidence in order to avoid refutation. There are two threads here, one focusing on the practice of scientists and one focusing on their critical attitudes towards hypotheses and evidence. Demarcationists after Popper picked up on each of these threads as the basis for developing novel theories of science and pseudoscience.

IVb. Practice as the Criterion of Demarcation

In response to Popper’s work, several demarcationists have focused on the practice of science in order to distinguish scientific pursuits from pseudoscientific pursuits. Thomas Kuhn argues that communities that are engaged in problem solving tasks that characterize what he calls ‘normal science’ are participating in science, while those who have no such problems or are not engaged in solving them, are unable to participate in science (Kuhn 1970). In a comparison of astronomy and astrology, he points to the ways in which astronomers engage in science by making predictions, and when these predictions fail, they will examine their instruments, calculations, and theory to understand what has occurred. Astrologers, on the other hand, do not recognize any failures to predict within their theory, as everything that occurs appears to be explained equally well by the theory. They have “no puzzles to solve and therefore no science to practice”, Kuhn explains, and therefore cannot constitute science (Kuhn 1970, 9). Similarly, Imre Lakatos focuses on the progressiveness of scientific practice, in terms of its ability to make novel predictions. He argues that one must demarcate between science and pseudoscience at the level of research programmes, which are composed of a “stubbornly defended” core, a flexible
protective belt, and problem-solving machinery (Lakatos 2009, 517). While both scientific and pseudoscientific research programmes will share this composition, the way to determine which is a science is to examine its progress, in terms of the novel facts it predicts, “facts which had been either undreamt of, or have indeed been contradicted by previous or rival programmes” (Lakatos 2009, 517).

While Kuhn and Lakatos both developed accounts in recognition of the limitations of the demarcation theory of falsification, their own proposals faced problems of their own. Critics have pointed out that it is hard to characterize both the problem-solving that occurs within Kuhn’s normal science, or the progressiveness that characterizes scientific research programmes according to Lakatos. Paul Thagard has argued that astrology may be the perfect example of normal science, as it concerns itself with solving every day problems and stays away from foundational, philosophical questions that only appear, according to Kuhn, in periods of extraordinary science (Thagard 1978). Relatedly, Lakatos’ criterion has received criticism for running into an issue of relativity. Nickles points out that “phlogiston, caloric, and ether programs may have been the best available in their day, but anyone defending them today is surely unscientific” (Nickles 2013, 109). Despite these criticisms, these theories of demarcation that look to the practice and products of scientific theories are capturing something important about the way in which science is done.

IVc. Critical Attitudes as the Criterion of Demarcation
Picking up on Popper’s second thread, other demarcationists have argued that scientific status can be located in the critical attitudes of scientists towards their work. Noretta Koertge suggests that “one characteristic differentiating typical science from typical pseudoscience is the presence of critical communities, institutions that foster communication and criticism through conferences, journals, and peer review” (Koertge 2013, 177). She outlines the ways in which epistemic communities thought of as pseudosciences fail to engage critically among themselves and with others, while paradigmatic scientific disciplines constantly face criticism both from within their own discipline and from the sciences surrounding them. James Ladyman suggests that the pseudoscientist is like the bullshitter, “less in touch with the truth and less concerned with is than either the fraudster or the liar”, all the while presenting an enterprise that is “falsely pretended to be scientific” (Ladyman 2013, 45, 48). Similarly, Sven Ove Hansson emphasizes that a practice cannot be pseudoscientific unless it is falsely defended as scientific by practitioners or the community. He suggests that while two homeopaths might both claim their remedy is superior to conventional medicine, only the one who claims there is a scientific basis for the treatment is engaging in pseudoscience (Hansson 2013, 69).

Of course, to suggest that pseudoscientists are only those falsely claiming to engage in science is to beg to question of what is a scientific endeavor and what is not, so Ladyman and Hansson do not take us very far in resolving the question of demarcation. Nevertheless, something quintessentially pseudoscientific is being gestured towards here, the tendency to dress up one’s claims as scientific, as seen within the claims of
association with NASA spacesuits in the marketing campaign of Body Vibes stickers. Koertge’s criterion also comes up short, as there are many scientists who do not take part in critical communities through conference and journals, but we still want to say they are engaging in science (e.g. a biohacker in their garage) (Landrain et al. 2013). Similarly, there are bad scientists, who engage in sloppy reasoning and hold onto hypotheses for far too long, but a bad scientist is different from a pseudoscientist. Furthermore, Lugg has pointed out that there is something dissatisfying about locating the source of pseudoscience in someone’s head (or many heads), given that what’s really philosophically of interest in the demarcation project is to determine which scientific projects are worthwhile and which ones are bunk, not which individuals are behaving badly (Lugg 1987).

IVd. Pluralist Theories of Demarcation

Partly as a result of these criticisms, many more recent attempts to pin down that which underlies pseudoscience rely on a combination of factors. These theories of demarcation resist the idea that there is likely to be one criterion that can distinguish between every scientific practice and every pseudoscientific practice, arguing instead that we ought to recognize the diversity of scientific and pseudoscientific approaches to epistemic projects. Exemplary of these is Massimo Pigliucci’s proposal that while pseudoscientific practices are unlikely to share necessary and sufficient conditions, they may share a Wittgensteinian family resemblance with each other. He suggests that measures of two intersecting criteria, empirical knowledge and theoretical understanding, will position practices according to the extent that they resemble science, on the one hand, or pseudoscience, on the other hand (Pigliucci 2013). Similarly, Martin Mahner offers a list
of questions concerned with both the community and the logic of a practice that can help us to determine if it is a science or a pseudoscience. These questions include “Does it accept the canons of valid and rational reasoning?” and “Is there an extensive mutual exchange of information, or is there just an authority figure passing on his doctrines to his followers?”, which point towards property clusters that characterize both science and pseudoscience (Mahner 2013, 38). Similarly, Maarten Boudry points towards a variety of features exhibited by pseudoscientific practices in order to create an “impression of epistemic warrant” (Boudry 2013, 88). These include pretending to risk refutation, make empirically bold claims, and succeed in confirmation, pretensions which are aided by the presence of multiple endpoints, moving targets, shadowy retreats, conspiracy thinking, invisible escape clauses (Boudry 2013).

These pluralist accounts offer a refreshing take on the demarcation question, shifting away from the search for a single necessary and sufficient feature of science, and capturing a wide array of features that scientific practices tend to display. One concern that arises in relation to theories such as these, however, is that demarcation criteria that allow for more discretion in the process of diagnosing pseudoscientific practices may also allow for more unfounded use of the term to enter the discussion. One might argue that the reason we want to distinguish science from pseudoscience is to prevent the term from being applied on a purely political basis, as has been the case for much of history. Therefore, when the criteria for distinguishing between science and pseudoscience become less stringent, we may need to take extra caution that knowledge projects are not being labelled pseudoscientific purely on the basis of an ideological clash.
Taking inspiration from several of the theories of demarcation presented here, in the next section, I return to the challenge for demarcationists laid out in the previous section. How might the demarcationist offer an account that captures both the meaningful difference between CAM practices that have learned to manipulate and reliably produce the placebo effect, and domains such as astrology and creationism, which have no such phenomenon, as well as between the range of pseudoscientific behaviors exhibited by CAM practitioners, from Body Vibes stickers to CranioSacral Therapy?

V. CAM as Protoscience

In order to capture these important distinctions, I propose that rather than focusing only on the difference between pseudosciences and sciences, demarcationists ought to take up a third category, that of protoscience. As opposed to either a pseudoscience or a science, CAM can be better thought of as a protoscience, a budding science which has yet to establish the terms, tools, and theories that will make it a truly scientific endeavor, but that has the potential to become one. Different CAM practices, however, can be seen as engaging in varying degrees of pseudoscience, despite their shared status as protoscience. In this section, I examine two theories of protoscience that have been put forward by demarcationists, but conclude that neither of them have the tools to capture the meaningful difference between CAM practices and other prototypical pseudoscientific projects. I then offer a novel theory of protoscience, drawing on theories of demarcation
that focus on scientific practice, and argue that protosciences may differ in terms of their pseudoscientific qualities, making for a range of possible protoscientific projects.

**Va. Protoscience in Discussions of Demarcation**

There is surprisingly little discussion of the task of distinguishing between a protoscience and a pseudoscience within the literature on demarcation. There does seem to be some acknowledgement of the importance of the issue though. Mahner asks, “When exactly is an alternative theory a piece of pseudoscience and when just a heterodox view? This distinction is important because heterodoxy should be welcomed as stimulating critical debate, whereas pseudoscience is just a waste of time” (Mahner 2013, 31). Relatedly, many who have written on the question of demarcation have remarked on the potential that often lies within practices labeled as pseudoscientific. Oliver Wendell-Holmes points out that “A Pseudo-science does not consist wholly of lies. It may contain many truths, and even valuable ones” ((Holmes 1892) cited in (Thurs and Numbers 2013)), while Popper acknowledges that in origin, sciences are often indistinguishable from myth (Popper 1953). Several others agree, offering examples of practices that were called pseudosciences in the past, but turned out to be protosciences (e.g. evolution, Wegener’s theory of continental drift, alchemy as a precursor to chemistry) (Pigliucci 2013, Tuomela 1987). In contrast, Mario Bunge warns of the danger of hoping that pseudosciences are in fact protosciences, pointing out that there is a tendency to “fear that some gold nuggets may lie hidden in a pile of pseudoscientific rubbish” (Bunge 1984, 44). With even more conviction, he expands on his point: “Superstition, pseudoscience, and antiscience are not rubbish that can be recycled into something useful; they are intellectual viruses that can
attacked anybody, layman or scientist, to the point of sickening an entire culture and turning it against scientific research” (Bunge 1984, 46).

**Vb. Tuomela’s Theory of Protoscience**

In what may be the most extensive discussion of the distinction between protoscience and pseudoscience in the literature, Raimo Tuomela offers a proposal for how to distinguish between a protoscience and a pseudoscience, stemming from his theory of what constitutes science (Tuomela 1987). Drawing on the work of Bunge, Tuomela argues that science consists of a cognitive field that is characterized by twelve features, including being connected to and responsive to research in other scientific domains, engaging in autonomous inquiry about real objects and cognitive problems related to them, and using up-to-date logic, mathematics, and information that is both testable and testworthy, among other features (Tuomela 1987). Pseudosciences, he argues, are characterized by twelve opposite features to these, including the tendency to shun logic, to think anachronistically, and an unresponsiveness to research in other scientific domains, while protosciences are characterized by all of the features that a science is, except the presence of up-to-date math and logic and information that is both testable and testworthy. The social sciences, he suggests, are exemplary protosciences.

Unfortunately, Tuomela’s criteria meant for distinguishing between protoscience and pseudoscience appear to be the product of another time, as social sciences both contain up-to-date math and logic and are testable and testworthy. Furthermore, they are of little help in identifying a difference between CAM, on the one hand, and astrology and creationism, on the other, as none of these practices are particularly inclined to engage
with up-to-date mathematics or logic, while they are all, at least in principle, both testable and testworthy. It seems that, despite the use of the term protoscience, Toumela’s project is something other than distinguishing between projects that resemble sciences in some ways and pseudosciences in others, especially on the basis of a comment he makes after presenting his theory: “a greater difficulty for science is to distinguish from one another a budding, promising, and possibly unorthodox protoscience, and enticing unorthodox research which eventually turns out to be an unproductive hybrid and possibly a pseudoscience” (Tuomela 1987, 100).

*Vc. Shermer on Borderlands Science*

Touching directly on the question of whether CAM ought to be considered a pseudoscience or a protoscience, Shermer suggests that we ought to think of chiropractic, acupuncture and “other alternative medical practices as yet untested by medical researchers” as borderlands science rather than pseudoscience or science, along with SETI (the Search for Extraterrestrial Intelligence), string theory, and theories of consciousness (Shermer 2013, 206). What distinguishes a borderlands science from a pseudoscience, Shermer holds, is “that the practitioners in the field are professional scientists who publish in peer-reviewed journals and are trying to devise ways to test their theories and falsify their hypotheses” (Shermer 2013, 207). In explanation of the limitations of borderlands sciences, Shermer suggests that the reason something like SETI doesn’t constitute science is that “its central theme has yet to surface as a reality” (Shermer 2013, 206). Hypnosis, Shermer proposes, also falls into the category of borderlands sciences because it is “tapping into something else in the brain, and sound scientific evidence may very well support some of its claims” (Shermer 2013, 207).
While one could certainly say that the central theme of CAM has yet to surface as a reality and that sound scientific evidence may well support some of its claims, one could also say this about pretty much any developing epistemic field. This suggests that what is doing the work in distinguishing between a pseudoscience and a borderlands science, for Shermer, is whether a practice has peer-reviewed journals and is attempting to test theories and falsify hypotheses. The presence of peer-reviewed journals, which is often a sign of attempts to test theories and falsify hypotheses, does appear to capture significant differences between CAM practices. While there are several peer-reviewed journals devoted to research within CAM, including the Journal of Complementary and Alternative Medicine and Complementary Medicine Research, some practices also have their own journals (e.g. Acupuncture in Medicine, Homeopathy), while others have no peer-reviewed journals but have a small research base (e.g. CST), and still others have no journals and no research basis whatsoever (e.g. Body Vibes stickers). The presence of peer-reviewed journals, however, does little to distinguish between sciences and protosciences though, since such peer-reviewed journals are present across these domains, representing the existence of testing of hypotheses related to hypnosis, homeopathy, and consciousness, as well as physics, astronomy, and chemistry.

_Vd. An Account of Protoscience_

How might we distinguish between sciences, protosciences, and pseudosciences? Between chemistry, CAM, and astrology? Here, I sketch the beginning of a theory of demarcation that captures these distinctions, based on several accounts of demarcation discussed above. Drawing on Lakatos’ criteria for demarcation, I argue that we can locate the meaningful difference between CAM and other prototypical pseudosciences in the
nature of these practices, and specifically in their ability to make successful predictions. Drawing on pluralist theories of demarcation, I argue that we can distinguish between different CAM practices by their degree of pseudoscientific engagement, which can be found in a variety of factors. In this way, a spectrum of epistemic projects appears, increasing in legitimacy and potential, ranging from pseudosciences, to protosciences, to sciences.

Protosciences can be thought of as characterized by a mix of pseudoscientific features and scientific potential. Displacing Lakotos’ demarcation criterion from the boundary between science and pseudoscience and shifting it towards the boundary between protoscience and pseudoscience, I propose that engagement with scientific practice through making successful predictions is the mark of a protoscience (Lakatos 1978). While many pseudosciences may have scientific-sounding target (e.g. creationism, flat earth theories), they have failed to successfully make any predictions about the phenomenon they are interested in. These predictions must be specific and novel, which rules out the successful predictions of horoscopes, which are too vague to impress. A protoscientific endeavor such as homeopathy, however, is able to predict that if several individuals experiencing anxiety are treated through homeopathic sessions, some of them are likely to improve. Furthermore, the more homeopathic sessions that take place and the more features of homeopathy that are present (e.g. hope is being instilled, clients and practitioners are engaging in a mutual process of sense making), the more likely these individuals are to show improvement.

What prevents protosciences from crossing the line into sciences, however, is that they tend to engage in characteristically pseudoscientific behaviors. This could occur in a
variety of forms, as is seen by the diversity of pseudoscientific aspects of CAM practices. A protoscience may ignore important conflicts between the theory it espouses and other widely accepted scientific theories (e.g. energy healing), or it may dress its claim up as scientific while offering little by way of explanation (e.g. adding ‘neuro’ as a prefix, despite having no engagement in neuroscience). Alternatively, a protoscience may offer an explanation for the evidence that takes on much more metaphysical baggage than is borne out by the evidence (e.g. homeopathy), or it may select only confirmatory data in support of its claims, while ignoring other findings. Both Mahner’s list of scientific indicators and Boudry’s list of pseudoscientific techniques can provide the basis of such a pluralist account of pseudoscience (Boudry 2013, Mahner 2013). This account of protoscience aligns well with other examples of protosciences that have been offered, such as alchemy as a precursor to chemistry (Pigliucci 2013). In this case, successful predictions were taking place, but for a time, the explanation of what was happening took on more metaphysical baggage than was necessary and tensions with other scientific projects were neglected. A pluralist approach to assessing the presence of pseudoscientific tendencies allows us to distinguish between protosciences that are more or less promising, depending on their degree of engagement with pseudoscientific behaviors. Homeopathy, which makes novel predictions that are frequently borne out, but that offers an explanation of the predictions that is quite distant from the evidence, can be

13 While such a multipronged account will be better able to capture the diversity found within CAM practices and other epistemic projects, as mentioned above, there is also a danger in such an account in that it leaves more space for interpretation in determining which cases constitute a pseudoscience and which constitute a protoscience. For this reason, demarcationists should proceed with caution, as diagnosing pseudoscience is already a project deeply intertwined with values.
thought of as more pseudoscientific than CST, which appears to sometimes make novel predictions, and does not offer an explanation that requires one to reassess other scientific theories that are widely accepted. Body Vibes stickers, on the other hand, appears to be entirely pseudoscientific, because no predictions are being made and the way the stickers are described is prototypically pseudoscientific.

Unlike Lakatos, I argue that the level at which distinctions between pseudosciences, protosciences, and sciences ought to take place is a much narrower one than research programmes; each research project should be evaluated in isolation. Evaluating epistemic practices at the level of research programmes risks sweeping up too much in one pronouncement. Rather than designating an entire field as pseudoscientific or scientific, it is worth acknowledging the differences that can occur within a particular domain. This allows for research examining the impact of homeopathic substances on one’s health to be classified as a protoscience, while research that is attempting to distinguish which features of the homeopathic encounter are creating placebogenic responses in clients can be classified as science. Similarly, pseudoscientific projects taking place within domains that are widely accepted as sciences (e.g. presenting cherry-picked data to represent a lack of global warming) can be designated as such.

This reduction to the level of each research project also solves a problem that arises within demarcationist projects with regards to when the determination of an epistemic

---

14 It is not clear what role the placebo effect might be playing in Body Vibes stickers, although it is noteworthy that more expensive treatments have been found to produce larger placebo effects, so perhaps the $60 per pack will prove beneficial for clients who can afford them (Espay et al. 2015). If this is the case, the brand “goop” still would not constitute a protoscience, since no predictions are being made or tested.
practice as scientific or pseudoscientific can take place. Several theorists have raised the
question of whether it is possible to determine whether an epistemic practice is a
pseudoscience prospectively, when it is at an early stage, or only retrospectively, after it
has had a chance develop into a scientific practice. Laudan observes that for a long time,
philosophers took it for granted that demarcation would take place only retrospectively
once a scientific practice had a chance to bloom (although it wasn’t called demarcation
then), but that Popper’s proposal of the prospective criterion of falsification led to a phase
of demarcation that let far too much in (Laudan 1983). Similarly, Lakatos praised his own
theory of demarcation in contrast to Popper’s, for only making judgements
retrospectively: “As opposed to Popper, the methodology of scientific research
programmes does not offer instant rationality. One must treat budding programmes
leniently: programmes may take decades before they get off the ground and become
empirically progressive” (Lakatos 2009, 518). If Laudan and Lakatos are right, and only
theories of demarcation that take place after a scientific endeavor has had a chance to
develop, then the task of distinguishing between protosciences and pseudosciences may be
an impossible one. At what point has an epistemic project has enough time to develop
and can a judgement be made? Fortunately, by evaluating research projects rather than
research programmes, this issue does not arise. Rather than waiting for an entire
epistemic field to develop, one can examine each research project on its own, asking
whether predictions are being made and borne out, and whether pseudoscientific features
are present within the practice.

VI. Conclusion
In this chapter, I have made the case that the project of demarcating between science and pseudoscience ought to be expanded to one of demarcating between science, protoscience, and pseudoscience. Expanding the project in this way allows for demarcation to account for a meaningful difference that can be found between CAM practices and other favored examples of pseudosciences, such as astrology and creationism. This meaningful difference lies in the role of the placebo effect in CAM, which practitioners have learned to manipulate in order to create and predict positive effects in their clients, suggesting that they have more scientific potential than other pseudoscientific projects. I have argued that protosciences should be thought of as epistemic practices that are able to engage in successful science through making novel and specific predictions, but that also have pseudoscientific tendencies, which can turn up in a variety of behaviors and features across protosciences and pseudosciences. This allows us to distinguish between different degrees of pseudosciences, protosciences, and sciences, and can help to sort out which epistemic practices should be nurtured and which should be welcomed into the realm of science fiction.
Chapter 4. Placebo Responses and Racial and Ethnic Health Disparities: An Unjust and Underexplored Connection

I. Introduction

A significant amount of bioethical scholarship has focused on the relationship between placebo effects and the clinical goals of beneficence and respecting patient autonomy. This literature explores questions such as whether a physician is ever justified in deceiving a patient if it is likely to benefit her, what fully informed and non-maleficent consent should look like, and the cases in which open label placebos ought to be prescribed (Bok 1974, Foddy 2009, Blease, Colloca, and Kaptchuk 2016, Kolber 2009, Fortunato, Wasserman, and Menkes 2017). While each of these questions has led to fruitful ethical discussions, they have taken place largely at the level of the individual. A topic that has not been taken up in bioethical literature related to the placebo effect is what impact the phenomenon may be having when approached from a societal perspective, particularly with an eye to the question of justice. In hopes of initiating a conversation on just this topic, I argue here that an uneven distribution of placebo effects within clinical encounters may be exacerbating health disparities along racial and ethnic lines.

---

15 This chapter has been jointly developed with philosopher Charlotte Blease into a manuscript which was published in the Journal of Medical Ethics (Friesen and Blease 2018). This version is entirely my own words.
In what follows, I offer a brief introduction to both health disparities and placebo effects. I then offer overview of how placebo effects operate within the clinical encounter by way of a discussion of empirical evidence, as well as a complementary examination of evidence related to inequalities in the clinical encounter that track differences in race and ethnicity. Based on the significant overlap between these two bodies of literature, I argue that there is a high likelihood that differences in placebo effects constitute an additional, unacknowledged route by which disparities in health outcomes are exacerbated. Finally, I conclude with a brief discussion of what the ethical and practical implications of this conclusion might look like.

II. Health Disparities and Placebo Effects

IIa. Health Disparities

A substantial and growing body of evidence suggests that one’s race and ethnicity can significantly impact the health care one receives\(^{16}\) (Institute of Medicine 2003, Dovidio et al. 2008, Klonoff 2009, Frohlich, Ross, and Richmond 2006). Asian Americans are the least likely of any population to be recommended for cancer screening and yet the most likely to die from cancer (Ibaraki, Hall, and Sabin 2014). In Canada, Aboriginal people

\(^{16}\) It should be noted at the outset that the scope of this discussion may be limited because the vast majority of this data comes from the United States, Canada, and the United Kingdom, where data on health in terms of race and ethnicity is regularly collected. This is in part because 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.
are half as likely to advance from referral for transplantation to the transplant waiting list as non-Aboriginal people (Tonelli et al. 2005), while Aboriginal women are significantly more likely than non-Aboriginal women (15.7% vs. 3.6%) to receive inadequate prenatal care (Heaman, Gupton, and Moffatt 2005). Black and Hispanic patients in the United States are significantly more likely to undergo primary cesarean delivery than whites (54% and 12% more respectively) (Chung et al. 2006), while both explicit process criteria and implicit review have shown that Black patients with congestive heart failure or pneumonia receive a lower quality of care than other patients (Ayanian et al. 1999). When two groups of dentists were given vignettes involving a patient in need of dental care, which were identical except with regards to the patient’s race, 26% of those in the group with a patient described as Black said the decayed tooth should be extracted, while only 16% of those in the group with a patient described as white thought the tooth should be extracted (Cabral, Caldas, and Cabral 2005). While these discrepancies are striking, minorities are not always given lower quality health care, and it has been shown that long term treatment plans, strong patient-physician relationships, checks and balances among the care team, and clear treatment guidelines protect against these gaps in care (Blair et al. 2014).

While the evidence for racial and ethnic disparities in health care mentioned above elucidates differences in treatment and screening that can occur between different groups, many explanations have been given for disparities in health outcomes, all of which are likely to account for part of the phenomenon. These explanations can be roughly divided into four categories: environmental factors, factors found in the health care 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 (Stuber et al. 2003, Pascoe and Smart Richman 2009). Explanations related to the health care system point to the way in which inequality grows as a result of differential access to care, patterns of referrals, language barriers, bureaucratic difficulties, and the fragmentation of health care services (Klonoff 2009). 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 (Dovidio et al. 2008, Burgess et al. 2010). 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 (Dovidio et al. 2008, Klonoff 2009, van Ryn and Fu 2003). While each of the these factors are likely to contribute in some part to the existence of health disparities, here, I am interested in an additional and unacknowledged avenue by which differences in health outcomes between populations may be exacerbated. It falls both within the realm of patient factors and clinician factors, but does not involve differences in patient behaviour or differences in treatment. Rather, this causal pathway operates by way of placebo effects that are mediated by the clinical encounter.

IIIb. Placebo Effects

It is important to note at the outset that while the term ‘placebo’ is often best known as a sugar pill and/or an inert substance offered to research participants, neither of these uses
of the term are what I am concerned with here. Rather than consider placebos as treatments (in a clinical setting) or as controls (in a research setting), I am interested here in placebo effects. While there is no consensus among placebo researchers regarding how the term placebo effect is best defined, it is helpful to look to the primary mechanisms that appear to underlie the phenomenon in order to better grasp what falls within its borders (Grunbaum 1986, Benedetti 2009, Moerman 2002, Miller and Kaptchuk 2008). Two mechanisms that play a clear role in placebo and nocebo effects are expectations and conditioning (Stewart-Williams and Podd 2004, Kirsch et al. 2004, Benedetti et al. 2003, Pacheco-Lopez et al. 2006). The role of expectations can be seen most clearly in experiments that demonstrate the enormous difference in pain relief when patients are aware that an analgesic is being administered, in comparison to when it is administered covertly from another room. In one experiment, patients in the covert condition required a dose of 50% more analgesics in order to reduce pain to the same degree as those in the overt condition (Amanzio et al. 2001). Conditioning, on the other hand, occurs through simple pairing, such as when anise-flavored syrup is combined with infusions of cyclophosphamide, which reduces white blood cells, and after several pairings, exposure to just anise-flavored syrup leads to a reduction in white blood cells (Giang et al. 1996). While the relationship between expectations and conditioning is not entirely clear, there is good reason to think that they both contribute to placebo and nocebo responses, either individually, additively, or through an interactive effect (Kirsch 2000). It should also be noted that some symptoms and conditions appear to be very responsive to placebo and nocebo responses (e.g. pain, motor impairments in Parkinson’s patients, depression, irritable bowel syndrome), while there is little to no evidence of placebo responses in
relation to other conditions (e.g. tumors, viral infections) (Benedetti et al. 2004, Kirsch et al. 2008, Kaptchuk et al. 2008).

Placebo researchers largely agree that the clinical encounter is rich with placebo and nocebo responses, although there is some disagreement with regards to classification (Benedetti 2002, Kaptchuk 2002, Benedetti et al. 2007, Blease 2012, Annoni and Miller 2016, Kaptchuk et al. 2008) 17. Given the role of expectations and conditioning, however, it seems clear that the clinician has the power to influence a patient’s beliefs and expectations regarding her condition and the treatment she may receive, and as well as the associations she forms in relation to healing practices, both of which may either improve or worsen her health. In a clever experiment, Kaptchuk et al. demonstrated just how powerful placebo effects within the clinical encounter can be. The experiment involved 262 patients with irritable bowel syndrome who were randomized into three conditions. 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-

17 Some have argued that the impact of the therapeutic alliance should be distinguished from the placebo effect (Verhulst et al. 2013) while others have argued that all treatment effects that are produced psychologically are placebo effects (Kirsch 2005). Of course, depending on how one defines the placebo effect, any of the experiments discussed within this section may fall inside or outside the boundaries of the term.
listening, 20 [seconds] of thoughtful silence and expressions of confidence” (Kaptchuk 2011, 1856). Outcomes found that adequate relief was experienced by 28% of the first group, 44% percent of the second group, and 62% of the third group (Kaptchuk et al. 2008). These findings demonstrate that incremental additions of support and engagement within the clinical encounter can lead to incremental improvements in symptom relief for patients.

III. Confronting the Evidence

IIIa. Evidence of Placebo Effects

In order to further elucidate the ways in which interactions between the patient and physician can give rise to placebo responses, below I offer a summary of a substantial body of evidence relating to how clinical outcomes are impacted by three aspects of the clinical encounter: (a) beliefs and expectations related to treatment, (b) clinician empathy and communication style, and (c) patient engagement and participation, all of which have been demonstrated to contribute to placebo effects. While these aspects of a visit to the doctor are often discussed, they are generally considered inessential to the real work of

---

I acknowledge that aspects of the clinical encounter could be carved up in different ways (e.g., Ong et al. identify creating a good inter-personal relationship, exchanging information, and making treatment-related decisions as the three purposes of clinical communication) (Ong et al. 1995). Here, I have tried to simply be responsive to the data in a way which illuminates the parallels between the literature concerned with placebo responses and the literature concerned with health inequalities, but I remain open to other nosologies, especially as the argument presented here is likely to be compatible with them as well.
IIIb. Beliefs and Expectations Related to Treatment

As the role of expectations in generating placebo responses was already introduced above, I offer here just a few more examples of how individuals beliefs or anticipations may impact clinical outcomes. In one experiment, individuals received either real acupuncture or sham acupuncture to treat their pain after dental surgery. While there was no significant difference in pain relief between the two conditions, what did predict pain relief was whether participants believed they were in the real acupuncture condition; those that thought they were receiving real acupuncture experienced significantly more pain relief than those who believed they were in the sham condition (Bausell et al. 2005). Of course, these results might occur simply because those that felt greater pain relief, because of a natural reduction in pain over time, then surmised that they were in the real acupuncture condition as a result. However, other 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 six months after treatment (Kalauokalani et al. 2001, Linde et al. 2007). This suggests that expectations and beliefs related to treatment are playing a causal role in relation to clinical outcomes.

Words spoken in the clinical encounter can shape expectations and impact outcomes as well. One physician gave half of his patients, who were symptomatic but had no abnormal physical signs, a “firm diagnosis” and told them they would feel better in a few
days, while he told the other half that he wasn’t sure what was wrong with them or when they’d feel better. Of those in the first group, 64% later reported that they did indeed get better, while only 39% of those in the second group reported that they got better (Thomas 1987, 1200). In another 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 who’d 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 (Varelmann et al. 2010). 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 weren’t told reported any sexual side effects (Mondaini et al. 2007). Taken together, this evidence suggests that patient beliefs and expectations that are formed within the clinical encounter can significantly impact experiences and outcomes.

IIIc. Clinician Empathy and Communication Style

Emotional and communicative characteristics of the clinician have been shown to influence patient wellbeing as well. Recent research suggests that placebo effects derived from expectations may be mediated by the perceived warmth and competence of the clinician. Howe et al. 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 wheal) compared to other groups
with negative expectations and/or providers with low warmth and competence (Howe,
Goyer, and Crum 2017). 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 one day less than those who rated their
clinician as low on empathy (Rakel et al. 2009). In an experiment involving individuals
receiving physical therapy for chronic low back pain who were given either real or sham
treatment, and placed in either limited or enhanced therapeutic alliance conditions, results
demonstrated that the degree of therapeutic alliance was just as important for pain relief
as whether they were receiving real or sham therapy (Fuentes et al. 2014).

Relatedly, clinician communication style has shown to be predictive of patient outcomes.
A systematic review of experiments that reported on both the quality of communication
and clinical outcomes found that a higher quality of communication appeared to impact
“in descending order of frequency, emotional health, symptom resolution, function,
physiologic measures (i.e., blood pressure and blood sugar level) and pain control”
(Stewart 1995, 1423). 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 (Bass et al. 1986). Similarly, a working group
examining 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 (The et al. 1986). Finally, another systematic review considered both the amount of information and emotional support provided to surgical or coronary patients and found that those who received either form of support spent approximately two fewer days in the hospital than those who received neither (Mumford, Schlesinger, and Glass 1982).

**IIId. Patient Engagement and Participation**

A third aspect of the clinical encounter that appears to impact clinical outcomes is that of patient engagement and participation. Experiments suggest that simply engaging patients by giving them more information or tests leads to improved outcomes. Petrie et al. reported that when patients with chest pain were given information about the test and an explanation of normal test results before an exercise stress test, they showed both higher rates of reassurance and a lower likelihood of future reports of chest pain than those not given the information (Petrie et al. 2007). Another study found that when patients with nonspecific chest pain were given two routine tests, but no additional treatment, 20% reported short-term disability, while in matched patients who received the same treatment but no tests, rates of short-term disability rose to 46% (Sox, Margulies, and Sox 1981). Similarly, when patients were told about post-operative pain and how they might deal with it the day before their operation, they requested significantly less narcotics after the surgery and stayed in the hospital for a shorter time (Egbert et al. 1964).

---

19 It should be noted that the degree of patient participation results both from clinician and patient behaviours and preferences, and I do not mean to specify that the patient has no impact here.
Patient participation in care has been shown to correlate with improved outcomes as well. After heart surgeons were trained in communication skills that emphasize patient empowerment, their patients had shorter hospital stays (one day less on average) than the patients of physicians who were not trained in communication skills (Trummer et al. 2006). Another intervention developed to increase patient involvement in care was taught to half of a group of physicians, all of whom then saw patients with ulcer disease. Patients of physicians who had completed the intervention were more likely to demonstrate involvement during a clinical visit, and were less likely to report functional limitations resulting from their disease (Greenfield, Kaplan, and Ware 1985). Similarly, analysis of conversations between patients and physicians that were rated as higher in patient control correlated with better outcomes for patients with diabetes (Kaplan, Greenfield, and Ware 1989). Additionally, patients who were given a choice of which painkiller they could use reported more pain relief than those who were assigned one (Rose et al. 2012).

Upon reflection, there seems little room to doubt that the clinical encounter is a fruitful realm when it comes to placebo effects. There are multiple avenues that might influence clinical outcomes, beyond those that are ordinarily considered. These include the thoughts and feelings within the patient, the tone and manner of the clinician, and the nature and length of the interaction between them. Keeping in mind these important causal pathways, I now turn to a consideration of who is most likely, within the clinical encounter, to be treated warmly, asked to participate, and to walk away with positive expectations.
IV. Evidence of Inequality in the Clinical Encounter

The evidence described above in relation to health disparities describes differential patterns of referrals, diagnostics, and treatment for minorities, all well-documented contributors to health disparities. The concern here, however, is how subtle aspects of clinical care also have real import when it comes to patient’s health, both in the short term and the long term. Aspects of the clinical encounter such as communication style, patient engagement, and setting patient expectations, are often thought of as integral to the ‘art of medicine’, but as dispensable when it comes to objective outcomes. As demonstrated above, this is not the case. Therefore, it is worth taking a closer look when a meta-analysis on patient physician communication concludes that minority patients “are less likely to engender empathic response from physicians, establish rapport with physicians, receive sufficient information, and be encouraged to participate in medical decision making” (Ferguson and Candib 2002, 353). In the following three sections, I present data from research related to inequalities in health care, mirroring each of the categories discussed above: (a) beliefs and expectations related to treatment, (b) clinician empathy and communication style, and (c) patient engagement and participation.

IVa. Beliefs and Expectations Related to Treatment

While there is little to no data documenting beliefs and expectations related to treatment according to race or ethnicity, there is a significant amount of evidence related to differences in trust in clinicians among different populations. This body of research, in
part, seeks to investigate the scars left behind by a history of racism within biomedical research, including such atrocities as the Tuskegee Syphilis Experiment. This experiment tracked for 40 years the natural progression of untreated syphilis among poor, illiterate African American men in Macon County, Alabama. The men were untreated even after penicillin was found to be an effective cure, contributing to many deaths and disabilities in the participants, and the infection of many of their partners and children (Beecher 1966). Evidence suggests that Blacks and Latinos trust health care professionals less than whites (Sewell 2015, Boulware et al. 2003), and qualitative data suggests that lower levels of trust in Blacks may be related to Tuskegee, while lower levels of trust in Latinos may be based on experiences of mistreatment and discrimination relating to language barriers (Jacobs et al. 2011). Another 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 (Gordon et al. 2006).

While not related to trust directly, a survey conducted in Cincinnati reported that both Blacks and individuals of low socioeconomic status were more likely than whites or individuals of high socioeconomic status to agree that positive self-presentation is important for them to get the best medical care, suggesting that the participants felt that bias or stigma could influence the quality of care they receive (Malat, van Ryn, and Purcell 2006). Similarly, another survey found that the quality of clinical interactions was rated significantly lower by non-white patients, especially by Hispanic and Asian patients, by an even greater margin than that between those with and without health insurance. The authors report that part of the difference was explained by differences in
the cultural sensitivity of clinicians and in the health literacy of patients (Saha, Arbelaez, and Cooper 2003).

As none of these experiments directly measure patient beliefs and expectations related to treatment, they should not be taken as sufficient to support the claim that racial and ethnic minorities differ from whites when it comes expectations of clinical outcomes. These differences of trust, experiences of quality of care, and expectations of good care being based on self-presentation are important findings though, and ought to motivate us to dig deeper into how these differences may or may not impact placebo effects within the context of care.

IVb. Clinician Empathy and Communication Style

In terms of empathy and communication, disparities also appear to exist. In an experiment involving breast cancer patients, it was found that physicians spent significantly less time engaging in relationship building behaviors with Black patients as compared to white patients (Siminoff, Graham, and Gordon 2006). Another study had independent observers watch patient physician interactions through a one way mirror and rate behaviors related to interviewing, nonverbal attention, courtesy, information giving, and empathy. It was found that physicians spent more time with white patients and scored higher on both interviewing and empathy in relation to their encounters with Latino patients (Hooper et al. 1982). Another study found that physicians used significantly fewer positive expressions when engaging with Latino patients as compared to non-Latino patients, but that levels of empathy were similar in both groups (Sleath, Rubin,
According to an analysis of ratings by independent coders who listened to audio-recordings of patient visits, physicians were rated as more contentious with Black patients than white patients, while Black patients were rated as less satisfied with the care received and less effective at communicating (Street, Gordon, and Haidet 2007). After meeting with a number of patients and then completing short surveys about each of them, it was found that clinicians were likely to see Black patients as eliciting less feelings of affiliation, as less intelligent, as more likely to engage in risky behavior, and as less likely to adhere to medical advice, when compared to white patients (van Ryn and Burke 2000). Further investigations of communication styles of clinicians have also revealed that high scores on implicit racial bias, as determined by a test derived from the Implicit Association Test (IAT), correlated with lower ratings of positive affect in patients and higher ratings of clinician-dominated dialogue during the encounter. Similarly, high scores on a test of implicit racial stereotyping, also derived from the IAT, correlated with lower ratings of patient-centered dialogue (from independent coders) and lower ratings of trust from patients (Cooper et al. 2012).

The IAT is a favored tool within the literature on inequalities in health care and was designed to measure levels of implicit associations that individuals may have, despite their explicit beliefs (e.g. One may explicitly believe that gender makes no difference to one’s scientific capacity, but still hold an implicit association between men and science) (Greenwald, McGhee, and Schwartz 1998). 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 (Blanton et al. 2007, Blanton et al. 2006, Rothermund and Wentura 2001, Karpinski and Steinman 2006). That said, according to this test, clinicians appear to be no different than the rest of us, displaying substantial implicit bias in relation to minority groups, while reporting little explicit bias towards these same groups (Green et al. 2007, Sabin et al. 2009). There is also conflicting evidence related to how this evidence translates into practice however, as some data suggests that IAT scores are not significantly associated with clinical decision making (Haider et al. 2015), while other
IVc. Patient Engagement and Participation

Finally, differences also appear in relation to patient engagement and participation. It’s been 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. Black patients, reflecting on the same encounters, saw clinicians as less supportive, less partnering, and less informative than white patients (Gordon et al. 2006). Corroborating this evidence, Cooper-Patrick et al. found in a telephone survey that Black patients tended to rate their medical visits as significantly less participatory than their white counterparts (Cooper-Patrick et al. 1999). Independent raters of audio tapes of patient visits reported that when clinicians were engaging with Black patients, they showed less positive affect and were 23% more verbally dominant and engaged in 33% less patient-centered communication than when they were speaking to white patients (Johnson et al. 2004). Finally, it was found that Black patients tended give worse ratings for patient-centered care to clinicians with greater implicit racial biases, as measured by the IAT (Blair et al. 2013).

V. Ethical Implications

Taking these two bodies of literature together, it appears that differences in placebo effects resulting from the clinical encounter may be occurring as a result of patient race research demonstrates that IAT scores accurately predict patient perceptions of clinicians (Penner et al. 2010, Blair et al. 2013, Cooper et al. 2012).
and ethnicity. While white patients are more likely to be benefitting frequently from placebo effects that are mediated by interactions with clinicians, these beneficial effects are likely to be occurring less often among racial and ethnic minorities. Either through beliefs and expectations of individuals, through expressions of empathy and communication styles, or through the form and degree of patient engagement and participation during the clinical encounter, the evidence presented above implies that minorities are likely to be receiving less benefit and experiencing more harm as a result of direct effects of therapeutic communication. This is especially worrisome because minorities already fare far worse than whites when it comes to health outcomes, suggesting that clinicians may be, largely without their knowledge, directly contributing to an increase in health inequalities.

What can we take away from this? While this chapter is simply a first attempt to draw connections between inequality in health care and placebo effects, a brief discussion of the implications of this connection is warranted. While there are many directions such a discussion could be taken, I will focus here on just three: whether the standard of care ought to be expanded, the task of reducing implicit biases, and other ways in which inequality might be increasing as a result of direct effects of therapeutic communication.

**Va. 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 aren’t
typically taught is the way in which the manner they administer an intervention can impact clinical outcomes. The evidence above raises a question with regards to whether, at least for some conditions, what’s considered 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 the placebo-maximizing aspects of the clinical encounter can truly be taught, and, in some countries, how to bill for the manner in which a treatment is delivered. While more research is surely needed before such a shift could be implemented, it’s worth taking a first look at some of these questions.

Importantly, if the standard of care were to expand to include not just what, but how medical interventions are delivered, it will 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 appear unresponsive. Experiences of pain are highly susceptible to placebo treatments, as are some psychiatric disorders, Parkinson’s disease, and several functional somatic syndromes, so these might be better candidates for expanded treatment models than others (Benedetti 2009, Kirsch et al. 2008). Then again, it’s likely that anyone in poor health can stand to benefit from positive direct effects of therapeutic communication.
While tumor growth may be unaffected by the clinical relationship, cancer related fatigue has been shown to be responsive to placebo treatments (de la Cruz et al. 2010).

Once it is acknowledged that aspects of the clinical encounter such as communication, participation, and empathy impact clinical outcomes, it appears that treatment (whether positive or negative) is always occurring in some sense. If the standard of care were 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 (Miller and Colloca 2011). It has been observed that a tension that arises between commitments to transparency that are commonly embraced within medical codes of ethics’, and the way in which direct effects of therapeutic communication remain unacknowledged in the clinical setting (Blease 2012). 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? This question becomes even more troubling if we try to picture what transparency might look like in terms of the differential treatment of racial and ethnic minorities, especially since telling patients that they could be harmed by their clinical visit may increase the likelihood of nocebo effects occurring.

Translating these findings into improved outcomes in practice is no easy task. In a fee-for-service models of health care, where clinicians are reimbursed for components of treatment piece by piece, it may be necessary to bill for placebo-maximizing 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 20 seconds 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 post-surgical days spent in the hospital (Trummer et al. 2006, Mumford, Schlesinger, and Glass 1982).

Another question arises in terms of whether the aspects of the clinical encounter that make a real difference are aspects that can really be taught to clinicians. While some factors, such as the length of time spent with a patient and the number of tests run, may be easy to increase, others, such as the degree of empathy expressed and the participatory style of communication, might be harder to teach. One might argue that no chit chat is better than inauthentic or forced chit chat. However, the robust reductions in days spent at the hospital after surgery just mentioned were the result of short courses focused on teaching surgeons how to increase patient empowerment and communicate better (Trummer et al. 2006, Mumford, Schlesinger, and Glass 1982). This suggests that, at least to a certain degree, placebo-maximizing behaviors can be taught. Perhaps more important, however, is unlearning that which leads to differential treatment of minority patients in the first place.

Vb. Reducing Implicit Bias
Of immediate concern is the question of how we can reduce differences aligning with race and ethnicity within the clinical encounter. Most researchers agree that these differences are likely to be a result of stereotypes and biases held by providers, although there is no direct evidence for this causal claim (Dovidio et al. 2008). These biases are unlikely to be explicit and overt, since such expressions and beliefs have significantly declined over the past several decades, but are more likely to be implicit, unconscious, and possibly unknown to the clinician, posing a challenge in terms of both identification and reduction (Burgess et al. 2007, Dovidio et al. 2008). Understanding the role of biases in the clinical setting is especially important, since evidence shows that reliance on stereotypes tends to increase with cognitive load (Wigboldus et al. 2004, Van Knippenberg, Dijksterhuis, and Vermeulen 1999), suggesting that health care professionals, who are typically engaging in many tasks while under time pressures, are more likely than others to fall back on such stereotypes (Burgess 2009). Some have also hypothesized that the culture of medicine may exacerbate tendencies to frame one’s experience through stereotypes, either through derogatory humor (Wear et al. 2006) or through the ‘ethical erosion’ that happens to medical students during their training (Feudtner, Christakis, and Christakis 1994).

Fortunately, a wealth of evidence from social psychology points towards ways in which implicit biases and stereotypes might be reduced. Some techniques that have been shown to be effective include repeated exposures to counter-stereotypes (Kawakami et al. 2000), increased contact with those which are the target of one’s biases (Pettigrew and Tropp 2006), as well as experiencing empathy in both its cognitive and emotional dimensions,
through practicing perspective taking and empathic affect (Burgess et al. 2007). In the context of health care, providing medical students with positive role models and safe spaces to reflect on role model behaviors and communication styles has produced positive results (Wear et al. 2006), as have exercises designed to challenge the outgroup bias that physicians might feel towards patients who are unlike them by emphasizing the collaborative nature of the patient-physician relationship (Dovidio et al. 2008).

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 (Saha et al. 1999, Cooper et al. 2003, Cooper and Powe 2004, Van Wieringen, Harmsen, and Bruijnzeels 2002, Johnson-Jennings, Tarraf, and González 2015). 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 (Meghani et al. 2009). 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\textsuperscript{21}.

\textit{Vc. 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 health care 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 (Wear et al. 2006, Ferrante et al. 2016, Dabby, Tranulis, and Kirmayer 2015, van Boekel et al. 2013, Willems et al. 2005, Avendano et al. 2009, Greenfield et al. 1987, Jaffee, Shires, and Stroumsa 2016, Sabin, Riskind, and Nosek 2015, Minerva 2016, Frank et al. 2014, Skosireva et al. 2014, Silliman et al. 1997, Mahajan et al. 2008). This suggests that minority individuals from any of these groups may be less likely to experience placebo effects during health care interactions, further increasing inequality in health outcomes, along countless other dimensions. Furthermore, for those in which two or more of these identities may intersect, negative experiences within health care are even more likely (Skosireva et al. 2014, Peterson-Besse et al. 2014, Kinsler et al. 2007).

\textsuperscript{21} Thank you to Mira Schneiders for encouraging me to emphasize this point.
Recognizing the ubiquity of discrimination within health care 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, it appears that priority should be given to those who are most likely to face stigma in a health care setting. Concerns arise, however, regarding whether flagging patients at risk for discrimination and intentionally treating them differently, is the right solution to reducing 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 this occurs, and the ways in which we can ameliorate these effects is urgently required.

Finally, 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 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 (Colloca and Benedetti 2009, Hahn 1997). This suggests that both harnessing placebo effects and counteracting nocebo effects is possible outside of the clinical encounter, and we’d 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 (Sandler and Bodfish 2008, Kam-Hansen et al. 2014, Kaptchuk et al. 2010, Park and Covi 1965), and there is also hope that placebo conditioning may allow for reductions in medication dosages which will thereby minimize harmful side effects (Enck et al. 2013).

VI. Conclusion

While bioethical discussions of the placebo effect have long focused on conflicts raised between patient autonomy and beneficence, the intersection of placebo responses and injustice deserves sustained philosophical treatment as well. I have argued here that an important and unacknowledged route by which disparities in health status may be exacerbated is through differences in the distribution of placebo effects. Several aspects of the clinical encounter, including explicit beliefs and expectations of patients, the tone and emotional presence of the clinician, and the participatory nature of clinical decision making, all have been found to directly shape clinical outcomes, and these aspects of the clinical encounter are experienced differently by different racial and ethnic groups. A closer look at the relationship between inequality and placebo effects is long overdue.

Final Remarks
Within this dissertation, I have offered a novel philosophical analysis of the placebo effect. Beginning with a critical analysis of the accounts of the placebo effect that have been put forward in relation to recent scientific evidence concerning the phenomenon, I argued that there is currently no account of the placebo effect that can adequately capture what we know of the phenomenon. In response, with the aim of working towards the goals of demarcation, explanation, and direction, I offered a novel account of the placebo effect, which divides the phenomenon into conditioned, cognitive, and network placebo responses, tracking distinct mechanisms that appear to underlie these responses. While I have offered some empirical evidence for this account within the chapter, there are several empirical research projects that fall out of these proposal that have yet to be completed. The first is to investigate the link between functional somatic syndromes and the symptom network model of illness. While this model has been applied to psychiatric disorders with success, there has been no work by psychometricians to date that considers whether this model applies well to other realms. If this were the case, it would provide support for the account of the placebo effect I have offered here.

In the third chapter, I explored the ways in which the role of the placebo effect within complementary and alternative medicine (CAM) challenges theoretical work on the question of demarcation within philosophy of science. I argued that CAM practices have harnessed the placebo effect for their benefit, demonstrating an ability to manipulate and make successful predictions regarding a scientifically interesting phenomenon, and that this sets them apart from other prototypical sciences. I argued that CAM is better thought of as a protoscience, and offered an account of protoscience as an epistemic project that is
able to make successful predictions, but that still has pseudoscientific features. More empirical investigation on whether and how CAM practices shape placebo responses would contribute to this discussion, as would the application of the theory of protoscience proposed here to other epistemic projects.

Finally, I explored evidence related to inequalities in the clinical encounter alongside evidence related to the placebo effect, and argued that focusing merely on interventions and not the ways in which interventions are delivered within medicine may be contributing to an increase in racial and ethnic health disparities. As mentioned at the end of this chapter, while I have only considered a link between placebo effects and health disparities along the lines of race and ethnicity, there are countless other identity features that form the basis of unequal treatment within clinical settings. To extend this link, both through empirical investigations and through bioethical analysis, would be a worthwhile project. Similarly, while the ethical implications of the connection between placebo effects and health disparities are briefly discussed in this chapter, a more detailed applied ethical analysis of this link would be most welcome.

Given how few philosophical investigations of the placebo effect exist, there are several other philosophical aspects of the phenomenon that would be worth exploring, two of which I will outline in some detail here, and three of which I will mention only briefly. First of all, while writing the third chapter on the demarcation question within philosophy, I began to reflect on the resistance of proponents of CAM to the process of demarcation that exists within medicine, and how this resistance might connect to the role
of the placebo effect within CAM. I offer a brief summary of what an exploration of this
topic might look like here.

I. Demarcation within Evidence Based Medicine: The RCT

Medicine has its own criterion of demarcation, which is meant to sort novel interventions
that work from those that do not work. This criterion is the randomized control trial
(RCT), ideally one that is double-blind (neither the practitioner nor patient knows who
has been assigned to which condition) and placebo-controlled (a placebo control
condition that is identical to the intervention condition except with regards to the specific
therapeutic component(s) being tested is included). The RCT lies at the heart of evidence
based medicine (EBM), and plays a significant role in determining which treatments gain
regulatory approval and are covered by insurance.

The importance that has been placed on RCTs to demarcate between effective and
ineffective medicine has received a significant amount of criticism from proponents of
CAM. As Christine Barry puts it, “calls for ‘gold standard’ randomised controlled trial
evidence, by both biomedical and political establishments, to legitimise the integration of
alternative medicine into healthcare systems, can be interpreted as deeply political”
(Barry 2006, 2646). Interestingly, much of the push-back from proponents of CAM
against the notion of measuring CAM according to the conventions of EBM only serves
to underline the importance of placebo responses in these forms of treatments. Arguments
against measuring CAM treatments within RCTs hold that one cannot simply measure
one piece of these interventions alone, but must examine the ‘whole system’ of the
practice (Verhoef et al. 2005). They also suggest that blinding the practitioner or patient will negatively impact the treatment effect, that randomizing patients who may not be interested in either conventional or complementary medicine is damaging, and that the therapeutic relationship will be harmed within the format of the RCT (Barry 2006, Carter 2003, Margolin, Avants, and Kleber 1998, Miller et al. 2004)

While most proponents of CAM make no mention of the placebo effect in these arguments, and primarily highlight the holism of the treatment they favour or the role of the therapeutic alliance, the resistance to measurement according to the principles of EBM aligns well with a view that sees CAM practices as exceptionally capable of producing placebo responses in patients. The reason for this is that the ideal RCT measures a therapeutic intervention’s efficacy over and above the placebo effect. This means that if a particular intervention produces an especially robust, clinically significant, placebo effect in an RCT, the treatment will be deemed worthless. In most cases, the result will not even be noticeable from a statistical perspective, since the placebo control arm is likely to also produce the same placebo effect, since it will be similar in all aspects except what is seen as fundamental to the treatment (e.g. in an RCT of homeopathy, the consultation will be identical in both arms, but the content of the remedies will be different). Sometimes, although it is uncommon for both ethical and economic reasons, a no treatment control arm will also be added, so that one can clearly see the difference between the no treatment control condition on the one hand, and the placebo control condition and intervention condition on the other hand; in these cases, the impact of the placebo effect is much more obvious. While these are often the results one
sees in RCTs of CAM (e.g. acupuncture and homeopathy – see (Ernst 2002b, Madsen, Gøtzsche, and Hróbjartsson 2009)), such effects are considered meaningless within EBM, as there is no improvement over and above the placebo control arm22.

The structure of demarcation through RCTs within medicine offers some explanation of what Fønnebø and colleagues have called the “gap between published studies showing little or no efficacy of CAM, and reports of substantial clinical benefit from patients and CAM practitioners” (Fønnebø et al. 2007, 2). Of course, RCTs are structured the way they are for a reason: we want to know precisely which specific factors of an intervention are contributing to a treatment effect. Additionally, in principle, RCTs can be built to measure any therapeutic factor of interest, including placebo-inducing treatments, as has been shown in previous chapters. In practice, however, RCTs tend to reward treatments like pharmacological agents, that work either in isolation from context or produce an additional placebo effect because of their felt side effects, while interventions that induce placebo responses in patients tend to be considered inefficacious.

Proponents of CAM have put forth many alternative forms of evidence that they argue are downplayed or dismissed within EBM, but that are likely to better capture the factors that contribute to positive clinical outcomes within CAM. These include preference trials, n of 1 trials, pragmatic trials, factorial designs (Verhoef et al. 2005), ethnography (Barry

22 It is worth noting that RCTs also exclude the consideration of any causal or explanatory factors related to clinical outcomes, so even if a CAM treatment leads to a positive clinical outcome, the causal factors involved are unlikely to be explored (Brody 2001, Verhoef, Casebeer, and Hilsden 2002).
2006), qualitative research (Verhoef, Casebeer, and Hilsden 2002), and whole systems research (Weatherley-Jones, Thompson, and Thomas 2004, Verhoef et al. 2005, Ritenbaugh et al. 2003). While none of these suggestions have been taken up within EBM, there does seem to be a general push towards adopting a more pluralistic approach to evidence within medicine (Jonas 2005). In a discussion of research and CAM, Kenneth Schaffner suggests that the pluralism that has been making waves within philosophy of science may soon find its way into medicine and better accommodate CAM, although he still holds out hope for the ability of the RCT to tell us ‘what works’ (Schaffner 2002). At the very least, I agree with Segal that “shedding the moral baggage attached to much of the discussions about CAM which seek to portray these therapies as either ‘fake’ or ‘real’ would allow more fruitful lines of enquiry” (Segar 2011).

II. The Unique Features of Pseudoscience in CAM

A second potential project that came to mind while I was writing the third chapter considers several unique features of medicine that ought to inform a theory of demarcation, given their links with pseudoscientific medical practice. Because of these unique features, it may be the case that a theory of demarcation that is successful in the field of physics may not be successful in the field of medicine. These features include: the preponderance of practitioners, the significance of profit, the role of the placebo effect, and the limitations of evidence based medicine (EBM).

The majority of those working in the realm of CAM are practitioners, not researchers. This abundance of practitioners is unique to medicine, in that arguably, the primary goal
within the field is to effectively heal those who are suffering, and perhaps only secondarily to understand why and how treatments work. No equivalent role exists within fields such as physics, ufology, or biology, which, despite having applications, are centrally concerned with understanding. This also puts the field of medicine at more risk for being labeled a pseudoscience, since there are many practitioners offering treatments, but not engaging in research.

The practical aim of treatment also makes space for the overwhelming role that profit plays in the enterprise of medicine, both in the clinical realm and in the research setting. As evidenced by the $60 Body Vibes stickers being sold by Gwyneth Paltrow, profit is a significant motivator within the field of CAM. Because regulation is patchy with regards to the claims that practitioners or businesses can make in terms of their ‘medical’ products, many false or deceptive claims are made, especially within the realm of CAM. Profit also plays a significant role in clinical decision making in conventional medicine, however, especially in countries like the United States where health care is not provided universally.

Given its reputation as a pseudoscience, “research funds for CAM are rare as gold-dust and the infrastructure or culture for CAM research is largely non-existent” (Ernst 2001, 532). This is in part because the majority of medical research being conducted within the field of medicine is funded by the pharmaceutical industry, which has little interest in investigating the time-consuming practices that are common to CAM. The profit motive can also lead to distorted epistemic practices within mainstream medicine, where a
connection between industry funding and favourable results of clinical trials has been established for years (Lundh et al. 2017). Additionally, because of the requirements of EBM, RCTs involving CAM practices are more expensive than those involving conventional treatments and require particular expertise (Ernst 2001). Since such expertise is often not available, the research that has taken place in order to investigate CAM frequently involves methodologies issues (Linde et al. 2001, Margolin, Avants, and Kleber 1998, Jakel and von Hauenschild 2012).

Strangely, given the role of the placebo effect in CAM, it seems that the more one engages in pseudoscience, by dressing up one’s practice in scientific language and confidently boasting of the effects it may have, the more one might contribute to positive clinical effects in one’s clients. This suggests that, ironically, the more one acts like a pseudoscience in medicine, the less one might be one. While James Ladyman suggests that “the pseudoscientist, like the bullshitter, is less in touch with the truth and less concerned with is than either the fraudster or the liar”, this might be both true and untrue in the realm of medicine (Ladyman 2013, 45). It is likely that users of CAM also engage in self-deception and thereby, increase the efficacy of the treatment by way of placebo responses, either by ignoring conflicting evidence or by seeking out confirmatory evidence of the practice. In her research on homeopathy, Barry found that users “did not see a need for scientific testing and were happy with their own judgement of whether the treatment was working for them” (Barry 2006, 2654). This tension between honesty and beneficence reflects many ethical debates that have arisen in bioethics in relation to the placebo effect (Brody 1982, Foddy 2009, Kolber 2007).
Finally, a unique feature within the practice of medicine is the process of demarcation that is currently dominant within the field: EBM. As discussed above, this system of evaluation raises challenges for treatments that primarily manipulate placebo responses in order to produce clinical benefit. For this reason, it has even been said to “involve an element of quackery”, because in its attempts to exclude placebo responses, it “sometimes obscures the translation of treatments efficacy into effectiveness” (Naudet et al. 2015, 5). Ideally within medicine, however, there will be space for an evidence base that allows for understanding not just of the impact of pharmacological agents, but also of the role of placebo effects in clinical outcomes. As Ernst has expressed:

“If patients are helped by treatment X, which is entirely devoid of risks but not better than a placebo, these patients are obviously benefiting from a placebo effect. And there is nothing wrong with that. However, instead of perpetuating the myth that treatment X has specific effects, we should be honest and endeavour to understand its non-specific placebo effects. The aim here is to arrive at a state of knowledge and know-how about placebo-effects where not just patients using treatment X profit from the power of placebo but all patients seeking medical treatment under similar conditions” (Ernst 2002a)

These four features: the number of practitioners, the role of profit, the impact of the placebo effect, and the limits of EBM, suggest that the project of demarcating between sciences, pseudosciences, and protosciences might look different within the realm of medicine than within other epistemic fields. The role of profit, the significant number of practitioners in medicine, and the presence of the placebo effect encourage the domain to engage in pseudoscientific behaviors in order to make money and benefit their patients. On the other hand, the placebo effect also lends some legitimacy to practices within medicine that may not have efficacy according to the mechanisms being given credit by their proponents. However, the gateway for being deemed an “evidence-based” treatment
within the realm of medicine excludes interventions that harness the placebo effect, so is unlikely to bring the effective elements of these practices to light any time soon. All this suggests that we might need a theory of demarcation that is unique to medicine, and that can help us distinguish between epistemic practices that need nurturing, and those that need oversight.

Finally, there are three additional projects at the intersection of philosophy and placebo studies that I would like to pursue. First, a philosophical analysis of how recent evidence related to placebo analgesia can inform the debate related to the existence of cognitive penetration would be worthwhile, and is something that I am in the midst of writing along with Henry Shevlin. Secondly, a detailed consideration of whether placebo phenomena provides support for different proposals within philosophy of mind (e.g. a Bayesian model of the mind, extended cognition) would make a substantial contribution to the literature and would be likely to generate discussion. Finally, in the realm of bioethics, the development and success of open label placebo treatments makes for rich ethical terrain. I hope to soon write a manuscript that considers the ways in which placebo effects can contribute to patient autonomy, as opposed to merely violating autonomy (as is usually the focus within bioethical literature on the placebo effect). This project could draw on novel evidence related to open label placebo effect as well as early successes related to classical conditioning as a tool to ween individuals off psychopharmacological agents while retaining their effects.
Appendices

Appendix A. Open versus hidden administration of morphine

Figure 1. and description from (Colloca et al. 2004): Top: Open versus hidden administration of morphine treatment (10 mg) for postoperative pain. The broken line indicates time of injection. Whereas the open group knew when they received their morphine, the hidden group did not know when morphine was given. Note the slower decrease in pain intensity in the hidden group compared with the open one, suggesting that most of the initial benefit in the open group is attributable to a placebo effect. Bottom: Open versus hidden interruption of a morphine treatment. The broken line shows the time of morphine interruption. Note the early relapse of pain in the open group but not in the hidden one. NRS=numerical rating scale.
**Appendix B. Immune parameters affected by behavioral conditioning paradigms**

Table from (Pacheco-Lopez et al. 2006):

<table>
<thead>
<tr>
<th>Conditioned stimulus</th>
<th>Unconditioned stimulus</th>
<th>Conditioned response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taste/odor</td>
<td>Immunosuppressant drugs</td>
<td>Antibody production</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lymphocyte proliferation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hypersensitivity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Allergic response</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Allograft rejection</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NK-cell activity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cytokines</td>
</tr>
<tr>
<td>Taste/odor</td>
<td>Immunostimulating drugs/antigens</td>
<td>Skin hypersensitivity</td>
</tr>
<tr>
<td>Auditory/visual</td>
<td></td>
<td>NK-cell activity</td>
</tr>
<tr>
<td>Touch</td>
<td></td>
<td>CTL activity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Neutrophil activity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Antibody production</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Histamine release</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anaphylaxis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Complement</td>
</tr>
</tbody>
</table>

**Appendix C. Categorization of complementary and alternative medicine therapies**

Table by (Frass et al. 2012):

<table>
<thead>
<tr>
<th>Whole Medical Systems</th>
<th>Biologically Based Therapies</th>
<th>Energy Medicine</th>
<th>Manipulative and Body-Based Therapies</th>
<th>Mind-Body Therapies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acupuncture</td>
<td>Aroma therapy</td>
<td>Healing</td>
<td>Acupressure</td>
<td>Anthroposophical</td>
</tr>
<tr>
<td>Ayurveda</td>
<td>Chelation therapy</td>
<td>Light therapy</td>
<td>Alexander technique</td>
<td>medicine</td>
</tr>
<tr>
<td>Homeopathic treatment</td>
<td>Diet-based therapies</td>
<td>Magnetic therapy</td>
<td>Bowen technique</td>
<td>Autogenic training</td>
</tr>
<tr>
<td>Naturopathy</td>
<td>Folk medicine</td>
<td>Millimeter wave therapy</td>
<td>Chiropractic manipulation</td>
<td>Biofeedback</td>
</tr>
<tr>
<td>Traditional Chinese medicine</td>
<td>Megavitamin therapy</td>
<td>Qi gong</td>
<td>Feldenkrais method</td>
<td>Bioresonance</td>
</tr>
<tr>
<td>medicine</td>
<td>Neural therapy</td>
<td>Reiki</td>
<td>Massage</td>
<td>Cognitive-behavioral therapies</td>
</tr>
<tr>
<td></td>
<td>Phytotherapy/herbal medicine</td>
<td>Sound energy therapy</td>
<td>Osteopathic manipulation</td>
<td>Deep-breathing exercises</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Reflexology</td>
<td>Group support</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Rolfing</td>
<td>Hypnosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Trager bodywork</td>
<td>Imagery</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Tui na</td>
<td>Meditation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Prayer</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Relaxation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Qi gong</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Tai chi</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Yoga</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Shiatsu</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Spiritual healing by others</td>
</tr>
</tbody>
</table>
Appendix D. Effective elements in homeopathic communications

Table by (Hartog 2009):

<table>
<thead>
<tr>
<th>Description</th>
<th>Homeopathic consultation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of consultation</td>
<td>Between one and several hours</td>
</tr>
<tr>
<td>Physician empathy</td>
<td>Present throughout the whole encounter</td>
</tr>
<tr>
<td></td>
<td>Essential tool to acquire data for clinical decision-making</td>
</tr>
<tr>
<td></td>
<td>Appears genuine to patients</td>
</tr>
<tr>
<td>Hopefulness and enablement</td>
<td>Enables patients to present emotional, social and other data from their lifeworld</td>
</tr>
<tr>
<td>Narrative competence</td>
<td>Focus on self-healing powers and individual coping strategies</td>
</tr>
<tr>
<td>Collaboration</td>
<td>Patient-controlled communication</td>
</tr>
<tr>
<td></td>
<td>Patient is encouraged to use own words and present his/her full agenda</td>
</tr>
<tr>
<td></td>
<td>Mutual process of making sense and pointing out solutions by narration</td>
</tr>
<tr>
<td></td>
<td>Assertiveness of patient is encouraged</td>
</tr>
<tr>
<td></td>
<td>Individuality of patient is respected</td>
</tr>
</tbody>
</table>
Bibliography


Fredrikson, Mats, CJ Furst, Mats Lekander, Samuel Rotstein, and Henric Blomgren. 1993. "Trait anxiety and anticipatory immune reactions in women receiving

Friesen, Phoebe, and Charlotte Blease. 2018. "Placebo effects and racial and ethnic health disparities: an unjust and underexplored connection." *Journal of Medical Ethics*.


Copyright 2002 by the National Academy of Sciences. All rights reserved.


Naudet, Florian, Bruno Falissard, Remy Boussageon, and David Healy. 2015. "Has evidence-based medicine left quackery behind?" *Internal and emergency medicine* 10 (5):631-634.


van Boekel, Leonieke C., Evelien P. M. Brouwers, Jaap van Weeghel, and Henk F. L. Garretsen. 2013. "Stigma among health professionals towards patients with


