Title: The Population Dynamics of Placebo Effect and Its Role in the Evolution of Medical Technology

Author: Ze Hong [a1]

Author Affiliations:

[a] Department of Human Evolutionary Biology, Harvard University, 11 Divinity Avenue, 02138, Cambridge, MA, United States

[1] To whom correspondence should be addressed: ze_hong@g.harvard.edu

Abstract

The placebo effect, though today used as the benchmark to evaluate treatment efficacy in modern medical settings, likely played a major functional role in traditional medical practices. To better understand its effect at the population level, I use a formal modeling approach to examine the population dynamics of placebo effect and show a reciprocal causal relationship between belief and efficacy: belief in the efficacy of treatments enhances their realized efficacy, which in turn increases people's confidence in their therapeutic power. A unique equilibrium for subjective belief and realized efficacy always exists, whose magnitude depends on how beliefs are constructed (relative weight on observed action vs. observed outcome). I further investigate how placebo effect affects the maintenance of existing medical technologies and the invasion of new technologies by explicitly modeling a belief construction process. Analytic and simulation results show that although placebo effect mostly suppresses the spread of new technologies, it may occasionally enhance the adoption of superior technological variants under specific parameter combinations.

Keywords

Placebo effect, Technological evolution, Cultural evolution, Social learning

Declarations

Funding

Not Applicable.

Conflicts of interest

None.

Availability of data and material

Not Applicable.

Code availability

Code used for simulation is available at https://github.com/kevintoy/placebo_effect

Acknowledgements

I thank Dr. Joseph Henrich for his helpful suggestions and feedback in developing this project, and Graham Noblit for providing constructive comments for an earlier version of the paper.

"What he believes he therefore sees; and what he sees he therefore believes."

—Edward Tylor, *Primitive Culture*

1. Introduction

The suggestive power of the human mind has long fascinated people across cultures and historical times (Kaptchuk 1998). Under the influence of psychological suggestion, subjective experience often profoundly shapes our perception of reality. Such subjective experience can be self-induced (e.g. psychedelic substances) or by the active manipulation from others (e.g. hypnotism). Importantly, our inner experience can also be affected by the perceived reality. This interesting reciprocal causal relationship is nicely illustrated by Sir Edward Tylor's example on dreams in his seminal work *Primitive Culture* (1871), in which he describes indigenous people's conception of dreams as a "vicious circle": one's beliefs about the world influences what he dreams, which in turns is used to confirm his beliefs.

Tylor's discussion on dreams primarily occurs in the context of animism, but his point of the reciprocal nature of belief and reality is relevant for many psycho-physio phenomena. Placebo effect, for instance, is a typical case of belief and reality reinforcing each other: certain treatments "work" because their efficacy is believed, and their efficacy is believed because they are perceived to "work". The term "placebo effect" which is frequently used in contemporary medical setting owes its modern meaning in the 18th century medical context (De Craen et al. 1999) and has become part of the gold standard for evaluating treatment efficacy (Misra 2012). To date, much research has been devoted to understanding psychological, sociological, and cultural factors that contribute to its potency. At its core, placebo effect relies on patients' expectation that certain therapeutic interventions will be effective. As such, anything that contributes to the belief in therapeutic efficacy will likely induce placebo effect. For example, the optimism/enthusiasm (Shapiro 1969) as well as the perceived authority (Kirmayer 1994) of the physician, elaborate procedures and devices (De Craen et al. 2000; Kaptchuk et al. 2000), costliness of the intervention (Waber et al. 2008) have all been shown to enhance therapeutic efficacy through placebo effect. In addition to the specific features of the physician and therapeutic practice themselves, observing other patients improve after taking some drug increases one's own recovery under the same drug treatment (Faasse and Petrie 2016). Though not the prime focus of the current placebo research, this last point illustrates the possibility where reality (drugs observed working) shapes subjective belief (drug is efficacious), which then enhances the realized therapeutic effect in a medical setting.

At the population level, the belief-efficacy feedback loop likely plays a non-negligible role in the maintenance of traditional healing practices. Such feedback loop may be due to personal experience: one may undergo some medical treatment and recovers, which increases her confidence in the efficacy of the treatment and makes her more likely to recover from illness the next time using the same treatment. It can also occur as a result of social learning: she can have confidence in some treatment because others have told her that the treatment had worked for them; she then tries the treatment and in the case of recovery, advertises the effectiveness of the treatment and such testimony may further increase people's confidence in the treatment. In

101 reality, the efficacy information of medical treatments and interventions primarily transmits
102 through social learning, because 1) individuals often lack first-hand experience of these
103 treatments and their efficacy outcomes, and 2) even when they do have such personal experience,
104 culturally-acquired efficacy information may trump it, as occasional failures of medical
105 treatments can be easily explained away (Evans-Pritchard 1937; Smith and Dale Andrew Murray
106 1920; Turnbull 1965).

107 The large literature on cultural evolution has amply shown the importance of social
108 learning of beliefs, values, and cultural practices (Boyd and Richerson 1985; Joseph Henrich and
109 McElreath 2003). In traditional, small scale societies, knowledge transmission is largely de-
110 centralized (Lancy et al. 2010) and individuals most likely obtain the efficacy information of
111 some medical treatment from observation and inference of others' action and associated
112 outcomes. Therefore, examining the population dynamics of placebo effect offers important
113 insights regarding the process via which these practices are transmitted and maintained. In this
114 paper, I will first briefly describe illness and treatment in small scale societies as well as the role
115 of placebo effect, and then formally model the mutual reinforcement of belief and treatment
116 efficacy as well as how the adoption of new medical practices may be affected in a cultural
117 evolutionary framework.

118 2. Placebo effect in the context of traditional healing practices

119 Theories of illness in most traditional societies are often supernatural where people attribute
120 causes of illness to soul loss, spirit aggression, sorcery and witchcraft (Murdock 1980). Even the
121 more "natural" theories such as balance of humors or *qi* (Sigerist 1951) usually lack sound
122 scientific basis. Given these theories, the treatments such ritualized sacrifice/offering or
123 bloodletting are often intuitive responses to address the presumed causes. From our modern
124 scientific perspective, these forms of traditional healing practices seem utterly ineffective. Yet, it
125 should be kept in mind that this modern conception of effectiveness is defined in opposition to
126 placebo effect (Kaptchuk and Miller 2015). In other words, a medical treatment is only
127 considered effective if it can be shown through randomly controlled trials (RCT) that it has a
128 therapeutic effect on top of the placebo component. Therefore, many forms of traditional and
129 alternative medicine are often dismissed as "just placebo". The implication here, however, is
130 that patients do get better under such treatment compared to no treatment precisely due to the
131 presence of placebo effect, and the eventual therapeutic outcome depends on the degree to which
132 the patient believes in the efficacy of the treatment.

133 But what makes people believe in these seemingly ineffective practices in the first place?
134 Evolutionarily minded anthropologists tend to focus on the intuitive plausibility of treatments
135 due to evolved psychological biases; for example, the prevalence of bloodletting has been
136 attributed to some universal cognitive mechanisms that makes "letting go of bad blood" appear
137 an attractive cure (Miton et al. 2015). Such cognitive biases certainly play a role, yet another
138 important reason for people to believe in the efficacy of these treatments has to do with people
139 trusting culturally transmitted information. Ethnographically, plenty of anecdotal evidence
140 suggests that people believe in the efficacy of some treatment because they were told anecdotal

141 stories in which these treatment yield positive results[1] (Harrell 1983). My own fieldwork in
142 southwest China also shows that people frequently use observed positive outcomes from others
143 ("it worked on my friend") to justify their own belief in the efficacy of some culturally
144 transmitted medical treatment. In fact, some even acknowledge that they were initially skeptical
145 of some medical treatment but became convinced after some closer relative or friend was
146 successfully treated (Hong, unpublished).

147 Intuitive plausibility, trust in social information sources, and a range of other cultural
148 factors such as positive physician-patient relationship likely collectively contribute to the
149 placebo effect of medical treatments. In a recent comprehensive review, Hróbjartsson and
150 Gøtzsche (2010) show that placebo effect most prominently manifests itself in subjectively
151 reported pain reduction, which is especially relevant in small scale societies as the feeling of pain
152 is often a major indicator by which people tell whether the illness is getting better or worse. The
153 magnitude of placebo effect can be substantial; some recent estimates of its effect size in
154 contemporary medical settings range from d=0.28 to d=0.64 (Hunsley and Westmacott 2007;
155 Wartolowska et al. 2016), and it is likely that culturally trusted medical practices such as
156 acupuncture may have an even larger placebo effect (Vickers et al. 2018). In some traditional
157 societies, the effect of belief on realized therapeutic efficacy is well recognized; for example, the
158 Karanga in Zimbabwe know that the effectiveness of some medical treatment depends on the
159 belief of the patient, and the curing procedure is specifically designed to induce the patient's
160 confidence, such as having the patient's relatives testify their trust in the doctor and his treatment
161 method (Aschwanden and Cooper 1987).

162 3. Model

163 Here I take a modelling approach to more rigorously examine the population level dynamics of
164 the placebo effect. I present two models that share the same set of assumptions but aim to
165 address different questions. The first model formalizes the verbal argument of the feedback
166 relationship between subjective belief and efficacy; specifically, it aims to describe the temporal
167 evolution of belief and efficacy, and I am particularly interested in whether some equilibrium
168 states will be obtained in the population, that is, whether the belief and efficacy of some medical
169 technology will reach stable values and resist further change. The second model examines the
170 situation where there are two technological variants (one existing, the other invading) that are
171 susceptible to placebo effect in a population, and individuals need to decide which variant to
172 adopt. This dynamic is explicitly modeled in a general cultural evolutionary framework (Boyd
173 and Richerson 1985) where naive individuals acquire information regarding the efficacy of these
174 technological variants from observing other individuals' actions (i.e. which technological variant
175 did that person possess/perform?) as well as the outcomes of the technological variants (i.e. did
176 this technological variant work for that person?). Special attention will be paid to the role of
177 placebo effect in the adoption of novel, potentially superior technological variants. Note that in
178 contrast with classic models in the cultural evolution literature where individuals "copy" cultural
179 variants from others, my model takes a more cognitive approach in the sense that various types

[1] On the other hand, people may become skeptical of the treatment if it doesn't yield positive results (Bianchi 1989).

180 of information are first translated into subjective belief in the efficacy of the technology (Hong
181 and Henrich 2021), which affects the realized efficacy (through placebo effect) and subsequent
182 trait adoption decisions.

183 3.1. Modeling the feedback between belief and efficacy of medical technology

184 I assume that the outcome of some treatment practice is a binary variable and can either be
185 positive or negative, and define its efficacy as the proportion of time that the practice yields
186 positive outcome. The assumption that technological practices yield binary outcomes is based on
187 the historical evidence that the outcome of many forms of medical treatments are recorded in a
188 binary fashion, i.e. success or failure (Hong, unpublished). Additionally, given that testimony is
189 often the primary transmission channel for efficacy information, such information is unlikely to
190 be properly quantified.

191 Each treatment practice has a "baseline efficacy" of E_b, which refers to the efficacy that
192 is independent of the placebo effect (i.e. the effectiveness rate when the patient is completely
193 skeptical of the efficacy of the treatment), and the "realized efficacy" E_r is the numeric sum of
194 the baseline efficacy and the additional efficacy due to the patient's confidence in the treatment.
195 For a particular individual, the relationship between realized efficacy and baseline efficacy of
196 some treatment *T* is defined as

$$E_r = \begin{cases} E_b + \beta \cdot p + \beta_1 \cdot E_b \cdot p & if\ E_b + \beta \cdot p + \beta_1 \cdot E_b \cdot p\ \le 1 \\ 1 & if\ E_b + \beta \cdot p + \beta_1 \cdot E_b \cdot p\ > 1 \end{cases} \quad (1)$$

197 where p denotes the individual's subjective belief ($0 \le p \le 1$) of the *T*'s efficacy, and placebo
198 effect is modeled as having two components: $\beta \cdot p$ represents the additive component of placebo
199 effect, and $\beta_1 \cdot E_b \cdot p$ represents the interactive component to account for potential drug-placebo
200 interaction (Hammami et al. 2010). The difference between these two terms is that while in the
201 first term β is the only multiplier that controls the extent to which belief contributes to realized
202 efficacy, in the second term β_1's effect also depends on baseline efficacy E_b. In other words, the
203 second term ($\beta_1 \cdot E_b \cdot p$)'s contribution to overall realized efficacy would be relatively small if
204 baseline efficacy is low.

205 Because E_b and p are strictly non-negative, positive β and β_1 will increase realized
206 efficacy of T. Equation (1) thus captures the intuition that the more one believes in the
207 effectiveness of some treatment, the more likely the treatment yields positive outcome for her.
208 Note that because E_r may be numerically larger than 1 if either E_b, β, β_1, or p is sufficiently
209 large, E_r is set to be 1 when $E_b + \beta \cdot p + \beta_1 \cdot E_b \cdot p\ > 1$ to ensure that it meaningfully
210 represents the probability of treatment success (this condition applies to all subsequent analysis).
211 Regarding the transmission of efficacy information I consider two sources: observed action and
212 observed outcome (payoff information of treatment variants) from other individuals. In other
213 words, one may believe that some treatment *T* is effective because he observes other people
214 practicing *T* or he observes (or is told by others) that *T* yields positive outcomes. Suppose the
215 focal individual is trying to evaluate the efficacy of some technology to form a subjective belief.
216 To do so she samples n individuals from the population, all of whom have performed the
217 technology exactly once, and constructs her belief p according to the following equation:

$$p = \frac{n \cdot w_a + T_{pos} \cdot w_o}{n \cdot w_a + n \cdot w_o} \quad (2)$$

218 where w_a denotes the weight attached to observed action, w_o denotes weight attached to
219 observed outcome, and T_{pos} denotes the number of positive outcomes. From an epistemic
220 perspective, the denominator ($n \cdot w_a + n \cdot w_o$) can be viewed as the total amount of information
221 available to the observer, and the numerator ($n \cdot w_a + T_{pos} \cdot w_o$) represents the amount of
222 information/evidence that is confirmatory regarding the efficacy of *T*. As such, their ratio
223 ($\frac{n \cdot w_a + T_{pos} \cdot w_o}{n \cdot w_a + n \cdot w_o}$) is simply the proportion of evidence that is in favor *T* being effective. The weight
224 terms (w_a *and* w_o) can be viewed as the individual's subjective evaluation of the importance of
225 different kinds of information (i.e. action vs. outcome). For example, someone with small w_a and
226 large w_o pays little attention to observed action (whether the treatment is being used) but takes
227 observed outcome (whether the treatment works on other people) very seriously. In both models
228 presented here these internal weightings are assumed to be fixed and given; in other words, all
229 individuals in the population have the same w_a and w_o which remain constant. Elsewhere I have
230 explicitly modeled the evolution of these epistemic weights and show that natural selection
231 should favor w_a, though w_o is likely to be substantial as well in a domain-specific way (Hong,
232 unpublished). To sum up, equation (2) represents the belief formation process where the focal
233 individual takes both observed action and observed outcome into consideration. This particular
234 way of constructing belief p is informed by two well-recognized transmission biases in the
235 cultural evolution literature, frequency dependent transmission (Henrich and Boyd 1998) and
236 payoff biased transmission (Vale et al. 2017). In this first model although individuals are not
237 picking amongst multiple cultural variants, they take into account both the relative amount of
238 individuals possessing a cultural variant in a population and the payoff of cultural variants in
239 forming a belief, which serves as the basis for variants adoption when multiple treatment variants
240 are available in the second model.

241 Equation (2) essentially partitions the belief into two components whose relative
242 importance are modulated by w_a and w_o. In the extreme case of $w_a = 0$, belief p is determined
243 entirely by the proportion of positive outcomes among sampled individuals $p = \frac{T_{pos}}{n}$; on the other
244 extreme end when $w_o = 0$, outcome information is completely ignored and therefore $p = 1$.

245 Since we are interested in the evolutionary dynamics of p at the population level, in
246 particular potential equilibrium states, we now introduce a temporal dimension. For the sake of
247 analytic convenience, I employ the typical assumptions in theoretical biology of non-overlapping
248 generations (Day and Bonduriansky 2011). Suppose the subjective belief of the focal individual
249 at time $t + 1$ is $p_{(t+1)}$, we have

$$p_{(t+1)} = \frac{n \cdot w_a + T_{pos(t)} \cdot w_o}{n \cdot w_a + n \cdot w_o} \quad (3)$$

250

251

252 where $T_{pos(t)}$ refers to the number of sampled individuals who have positive outcomes at time t.
253 Using equation (1), we now construct the realized efficacy of T at time $t + 1$:

$$E_{r(t+1)} = E_b + \beta \cdot p_{(t+1)} + \beta_1 \cdot E_b \cdot p_{(t+1)} \\ = E_b + \beta \cdot \frac{n \cdot w_a + T_{pos(t)} \cdot w_o}{n \cdot w_a + n \cdot w_o} + \beta_1 \cdot E_b \cdot \frac{n \cdot w_a + T_{pos(t)} \cdot w_o}{n \cdot w_a + n \cdot w_o} \quad (4)$$

254 To find the equilibrium state, set $E_{r(t+1)} = E_{r(t)}$, meaning that the realized efficacy no longer
255 changes with time. Recall that the expected number of sampled individuals with positive
256 outcome is numerically equivalent to the product of realized efficacy at t and total number of
257 sampled individuals ($T_{pos(t)} = E_{r(t)} \cdot n$). We thus have

$$E_b + \beta \cdot \frac{n \cdot w_a + n \cdot E_{r(t)} \cdot w_o}{n \cdot w_a + n \cdot w_o} + \beta_1 \cdot E_b \cdot \frac{n \cdot w_a + n \cdot E_{r(t)} \cdot w_o}{n \cdot w_a + n \cdot w_o} = E_{r(t)} \quad (5)$$

258

259 Solving for the equilibrium value of $E_{r(t)}$ (denoted by E_r^*), we have

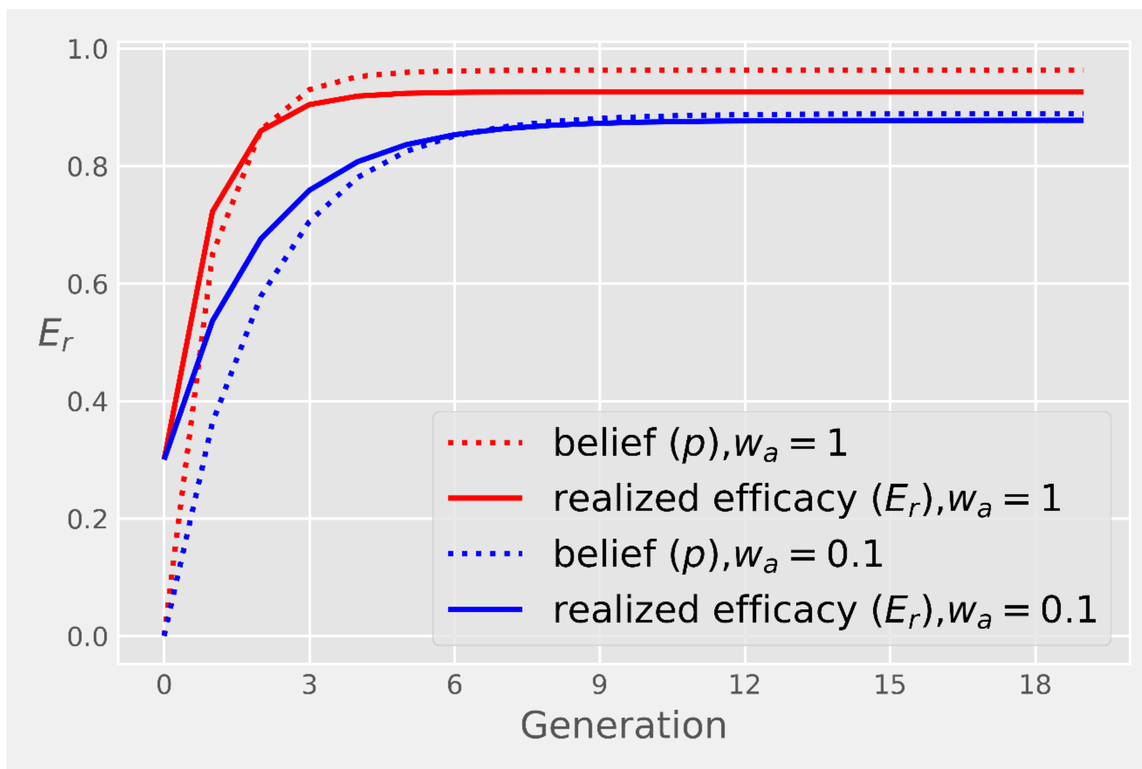
$$E_r^* = \frac{w_a \cdot (E_b + \beta + \beta_1 \cdot E_b) + w_o \cdot E_b}{w_a + w_o \cdot (1 - \beta - \beta_1 \cdot E_b)} \quad (6)$$

260

261 Equation (6) has some interesting properties. The number of sampled individuals n drops
262 out, and the magnitude of placebo effect (β, β_1) as well as baseline efficacy (E_b) both contribute
263 to realized efficacy at equilibrium positively as long as the denominator $w_a + w_o \cdot (1 - \beta - \beta_1 \cdot$
264 $E_b)$ is larger than zero. Reassuringly, the interaction term β_1 matters more when E_b is large. In
265 the extreme case where $w_o = 0$ (agents ignore outcome information completely), $E_r^* = E_b + \beta +$
266 $\beta_1 \cdot E_b$, which is simply substituting $p = 1$ into equation (2), as all individuals fully believe in
267 the efficacy of the treatment.

268 Figure 1 provides a graphical illustration of the temporal evolution belief (p) and realized
269 efficacy (E_r). In both conditions, the initial beliefs are set to be 0, meaning that individuals are
270 completely skeptical of the technology (but adopt the treatment nonetheless as there is no other
271 alternative), and the baseline efficacies are set at 0.3. Notice that both belief and realized efficacy
272 quickly increase and reach equilibrium, especially when w_a is large. From an epistemic
273 perspective, observed action provides unambiguous evidence for the efficacy of the treatment as
274 all sampled individuals utilizes the treatment (whereas observed outcome may be either positive
275 or negative). Weighing more on action thus increases individuals' confidence and consequently
276 realized efficacy.

277



278 Figure1. Numerical illustration of the temporal evolution of belief and realized efficacy of some technology under
279 two weight conditions ($w_a = 0.1$ and $w_a = 1$). w_a is fixed at 1. Other parameter values: $E_b = 0.3$, $\beta = \beta_1 = 0.5$.

280 Figure 2 shows the realized efficacy at equilibrium under various parameter
281 combinations. In the absence of any placebo effect ($\beta = \beta_1 = 0$, top left graph), realized efficacy
282 is always the same as baseline efficacy regardless of w_a (note that the three w_a conditions
283 completely overlap). This makes intuitive sense: when there is no placebo effect, realized
284 efficacy does not depend on what people believe. When there is placebo effect, however,
285 realized efficacy is always larger than baseline efficacy as placebo effect adds to the therapeutic
286 effect of treatment, and the more weight placed on observed action, the larger the difference,
287 especially when baseline efficacy is low. The intuition here is that in order to benefit from
288 placebo effect, individuals need to first increase their belief in the efficacy of the treatment, and
289 as already pointed out, weighing more on observed action to construct belief is a better way than
290 to weighing on observed outcome, because most outcomes may turn out to be negative
291 (especially when E_b is small) while everyone in the population performs the action.

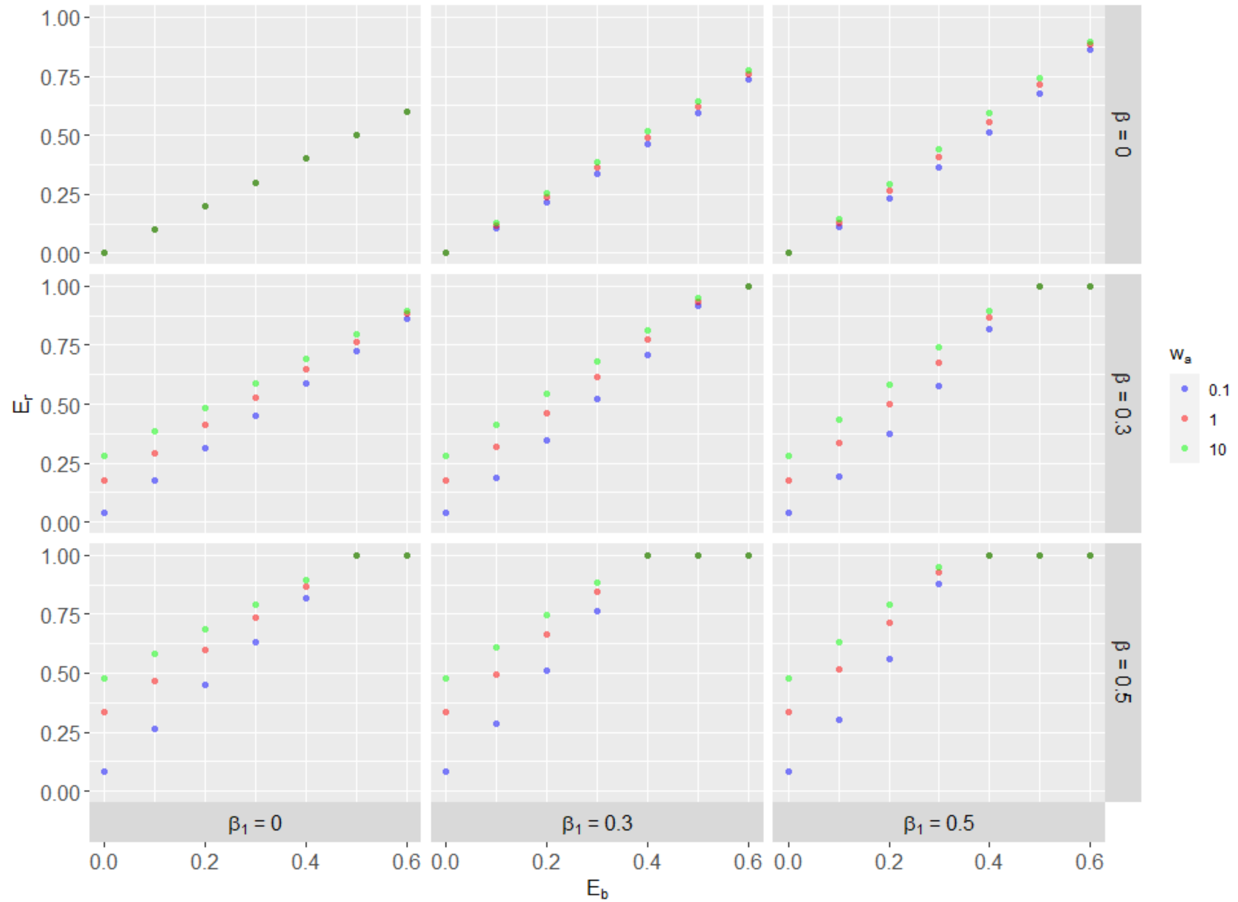


Figure 2: Relationship between β, β_1, E_b, $w_a$and E_r at equilibrium. Weight for observed outcome w_o is fixed at 1.

Note that in figure 2, all E_r^* values that are larger than one are transformed into 1. As mentioned, although an equilibrium value of realized efficacy always exists in theory, equation (6) itself doesn't constrain E_r^* within 0 and 1. In reality, of course, E_r^* is a probability and is always bound within 0 and 1. This suggests that there is a ceiling effect of placebo effect when E_b is sufficiently large: when the treatment already works 100% of the time, additional trust in the treatment does not affect realized efficacy.

Two conclusions may be drawn from the above model. First, the belief-efficacy feedback loop can significantly drive up both individuals' subjective belief in the efficacy of some treatment and its actual (realized) efficacy. Second, when realized efficacy is influenced by agents' subjective belief, a unique stable equilibrium always exists, and its value is determined by not only the parameters that directly control the magnitude of placebo effect (β and β_1) but also how much individuals trust different sources of information (w_a and w_o). Both subjective belief and realized efficacy can be maintained at high levels when individuals weigh more on observed action in constructing their beliefs. The implication here is that the overall belief in the efficacy of some newly introduced treatment may quickly increase when it is the only game in town, and when people have some confidence in the treatment, the realized efficacy may be substantially higher than baseline efficacy.

311 ## 3.2 Modeling the adoption of different treatment variants and the role of placebo
312 effect

313 In the second model I use a combination of analytic modeling and agent-based simulation to
314 examine the conditions under which a new treatment variant may be able to "invade" a
315 population where there is already an existing treatment. I assume that individuals evaluate the
316 efficacy of both treatment variants through social learning, but they can only adopt one variant at
317 a time. We are particularly interested in the role of placebo effect: if the existing treatment
318 dominates the population, how does placebo effect influence the invasion of a new, potentially
319 superior (higher baseline efficacy) treatment? One intuition may be that placebo effect prevents
320 new treatment variants from spreading because they do not enjoy its full benefit as the existing
321 treatment does. Below we examine such intuition formally.

322 ### 3.2.1. Agent construction and life cycle

323 Each agent is represented as a list $[T, p]$ where T denotes the treatment variant that the agent
324 possesses, and p denotes the agent's subjective belief about the efficacy ($0 < p < 1$) of the
325 treatment variant that he possesses. Let T_1 be the existing treatment variant and T_2 be the
326 invading treatment variant.

327 To set up the initial condition, we create a starting population of N agents (hereafter
328 referred to as F1 agents), with the majority of agents possessing treatment 1 (T_1) and the rest
329 possessing treatment 2 (T_2). Assuming that the realized efficacy of T_1 has reached equilibrium in
330 the population ($E_{r1}^{*} = \frac{w_a \cdot (E_{b1} + \beta + \beta_1 \cdot E_{b1}) + w_o \cdot E_{b1}}{w_a + w_o \cdot (1 - \beta - \beta_1 \cdot E_{b1})}$, equation (6)) prior to the invasion of T_2, where
331 E_{b1} and E_{r1}represents the baseline efficacy of T_1 and realized efficacy of T_1 respectively.
332 Individuals' belief of T_1's efficacy is therefore $p_1 = \frac{w_a + w_o \cdot E_{r1}^{*}}{w_a + w_o}$. Agents with T_2, on the other hand,
333 have belief of 0 regarding the efficacy of T_2, meaning that since it is the new treatment and these
334 agents have no prior experience with it, they do not believe it will work at all. Therefore, the
335 realized efficacy of treatment 2 (E_{r2}) initially is the same as baseline efficacy (E_{b2}).

336 The life cycle of the agents is as follows:

337 1) In the first generation, each F1 agent will "use" the treatment variant she possesses and
338 generates either a "positive" or "negative" outcome probabilistically based on the
339 treatment's realized efficacy.

340 2) A F2 generation is created with the same size N (no population growth). Each F2
341 agents will sample a number of F1 agents as their models. Note that these models could
342 all have T_1, all have T_2, or a mixture of the two treatments, along with the outcomes of
343 the treatments. The focal F2 agent will then construct her belief regarding the efficacy of
344 T_1 and T_2 using the following formula based on equation (2):

$$p_1 = \frac{n_1 \cdot w_a + T_{1pos} \cdot w_o}{(n_1 + n_2) \cdot w_a + n_1 \cdot w_o} \tag{7}$$

345

$$p_2 = \frac{n_2 \cdot w_a + T_{2pos} \cdot w_o}{(n_1 + n_2) \cdot w_a + n_2 \cdot w_o} \quad (8)$$

346

347 where n_1 and n_2 represent the number of models in the sample that have T_1 and T_2
348 respectively ($n_1 + n_2 = n$), T_{1pos} and T_{2pos} represent the number of positive outcomes of
349 T_1 and T_2, and w_a and w_o represent the weights associated with observed action and
350 observed outcomes.

351 3) The focal agent then makes a decision regarding which treatment variants to adopt. If
352 all models possess T_1 or T_2, then the focal F2 agent will adopt T_1 or T_2 with probability 1.
353 If the models possess a mixture of T_1 and T_2, then she will adopt T_1 or T_2 with probability
354 proportional to the relative magnitude of the agent's subjective belief p_1 and p_2, that is,
355 she will adopt T_1 with probability $\frac{p_1}{p_1+p_2}$, and T_2 with probability $\frac{p_2}{p_1+p_2}$.

356 4) After all agents in F2 have adopted a treatment variant and constructed the
357 corresponding belief, they become the parent generation and the cycle continues.

358 ### 3.2.2. Analytic result for probability of adopting technological variants

359 We will first derive some analytic result based on the above setup. Let r denote the proportion of
360 T_1 individuals in the parental generation a given time; because each naive individual picks n
361 models from the parental generation, the expected value of n_1 and n_2 (number of models with T_1
362 and T_1, respectively) is thus $r \cdot n$ and $(1 - r) \cdot n$, and the expected value of T_{1pos} and T_{2pos}
363 (number of models with T_1/T_2 who have positive outcome) is $r \cdot n \cdot E_{r1}$ and $(1 - r) \cdot n \cdot E_{r2}$. Let
364 q denote the probability of picking T_1 when there is a mixture of models with T_1 and T_2, and
365 substitute the above expressions into equation (1) and (2), we have

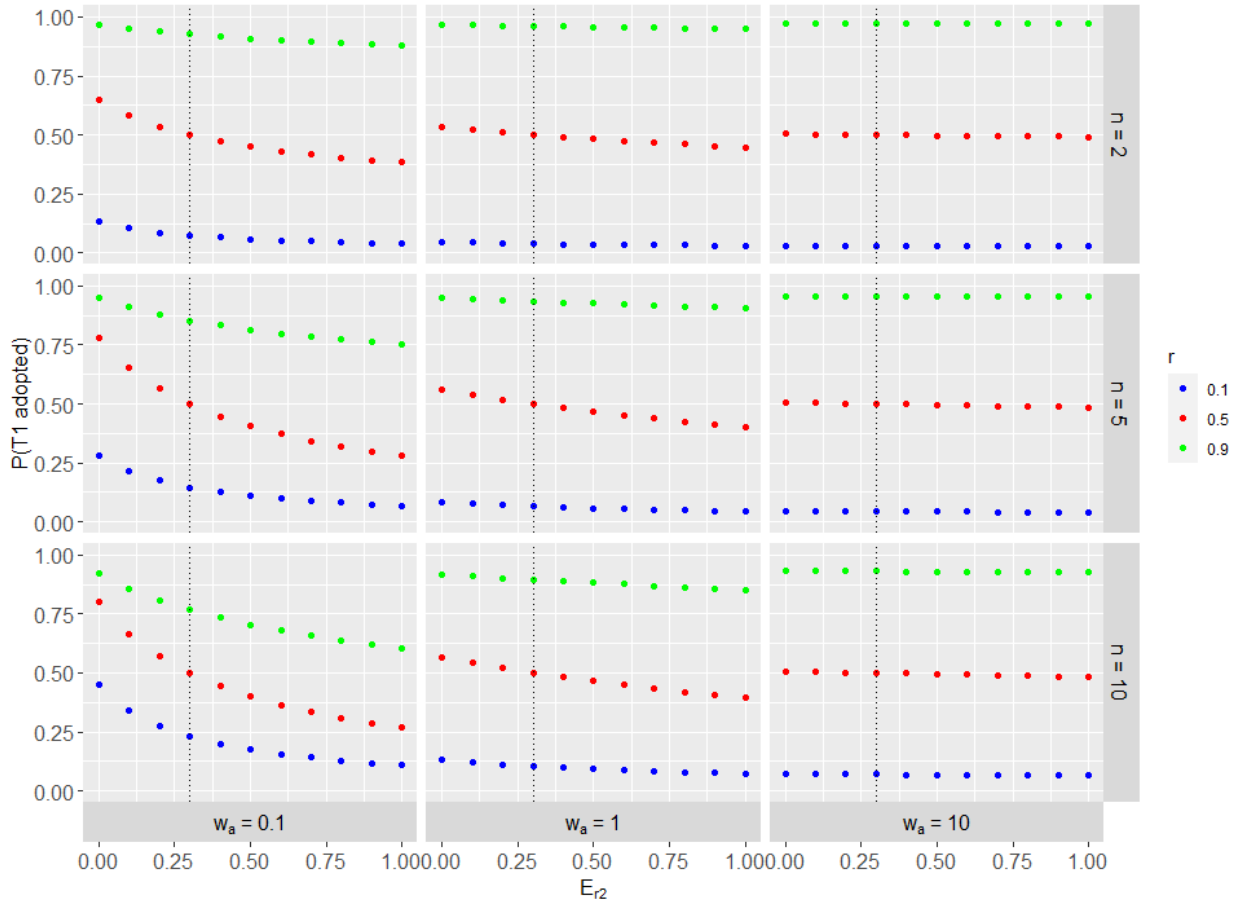
$$q = \frac{p_1}{p_1 + p_2} = \frac{\frac{r \cdot w_o + r \cdot E_{r1} \cdot w_a}{w_o + r \cdot w_a}}{\frac{r \cdot w_o + r \cdot E_{r1} \cdot w_a}{w_o + r \cdot w_a} + \frac{(1-r) \cdot w_o + (1-r) \cdot E_{r2} \cdot w_a}{w_o + (1-r) \cdot w_a}} \quad (9)$$

366

367 The overall probability that a naive agent adopts T_1 at a given time is thus

$$\begin{aligned} P(T_1 \text{ adopted}) &= 1 \cdot r^n + 0 \cdot (1-r)^n + (1 - r^n - (1-r)^n) \cdot q \\ &= (1-q) \cdot r^n - q \cdot (1-r)^n + q \end{aligned} \quad (10)$$

368 The obvious special cases here, $r = 0$ (no T_1 individuals in the parental generation) and
369 $r = 1$ (no T_2 individuals in the parental generation) yield 0 and 1 respectively. It is difficult,
370 however, to obtain general insight from equation (4) due to the unwieldy nature of q. The
371 relationship between $P(T_1$ adopted) and various parameters are thus explored using a numerical
372 method, as shown in Figure 3.



373

374 Figure 3: Relationship between E_{r2}, w_a, r, n and the probability of adopting T_1. The realized efficacy of T_1 (E_{r1}), is
375 fixed at 0.3 (dotted line) and weight for observed outcome w_o is fixed at 1.

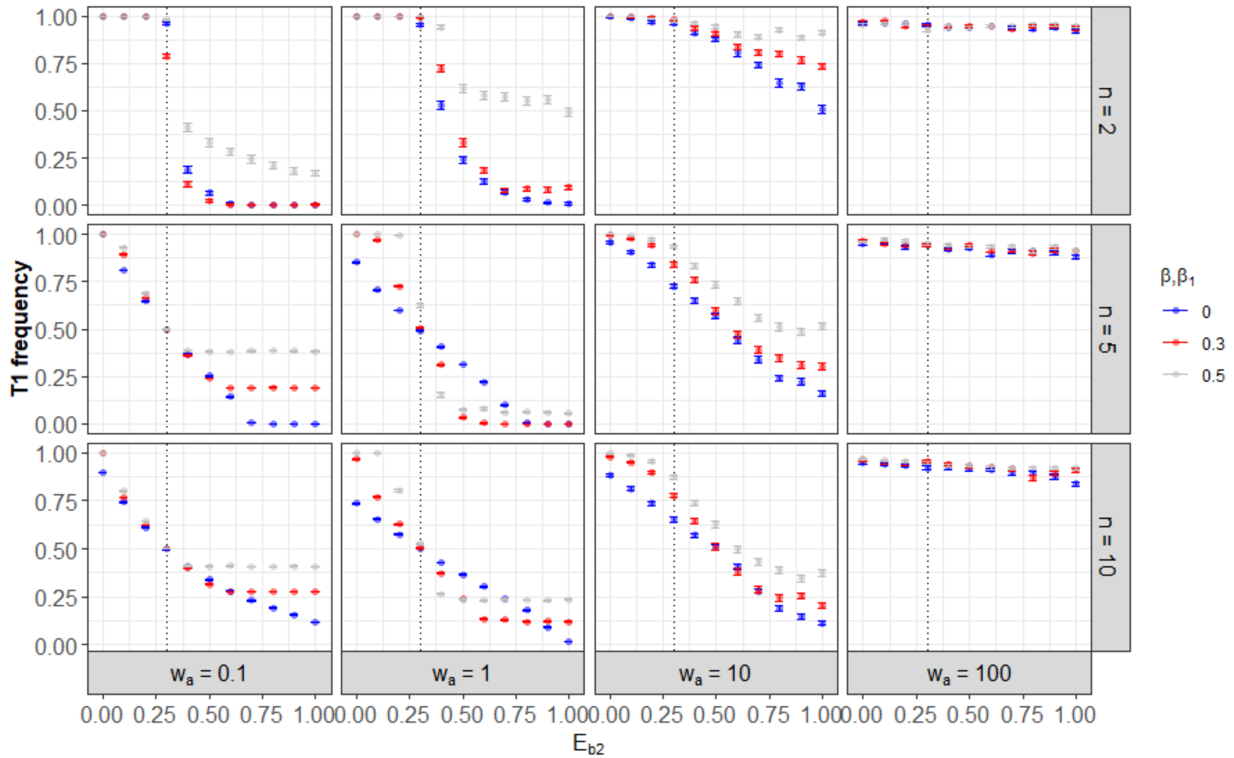
376 The following observations are noted. First, reassuringly, the probability of adopting T_1 is
377 higher when the parental population have more T_1 individuals (larger r), as it is more likely that
378 T_1 individuals are selected as models.

379 Second, as the realized efficacy of T_2 (E_{r2}) increases, the probability of adopting T_1
380 decreases, but the rate of decrease is slow when the weight of observed technological practice is
381 large, which makes sense, because a large w_a means a relatively small w_o, or the weight of
382 observed outcome; if naive individuals don't pay much attention to outcome, efficacy won't
383 matter very much.

384 Third, when individuals weigh more on observed outcomes ($w_a = 0.1$), the probability of
385 adopting T_1 has a nuanced relationship with n. If we only consider cases where T_1 is superior
386 ($E_{r1} > E_{r2}$), $P(T_1$ adopted) decreases with n when most individuals in the parental generation
387 possess T_1 ($r = 0.9$) yet increases with n when T_2 individuals are the majority ($r = 0.1$). This
388 suggests that the suppression of inferior treatment depends on both the population composition
389 and the number of models picked. We will return to this point and the role of n in the next
390 section.

391 ### 3.2.3. Simulation of technological adoption dynamics with placebo effect

392 The above analytic results assume that the realized efficacy of treatments is given and fixed. The
393 population dynamics would be more interesting once we include placebo effect and allow
394 realized efficacy to be endogenously determined. That is, individuals' treatment outcomes are a
395 function of not only the treatment's baseline efficacy E_b but also the the magnitude of placebo
396 effect. To this end, I construct an agent-based simulation with agents' life cycle specified in
397 section 2.3., and examine the relative frequency of T_1 individuals after a certain time period
398 under various parameter combinations.



399

400 Figure 4: Frequency of T_1 individuals at generation 200 under different parameter settings. Initial population ($N =$
401 200) consists of 95% T_1 individuals and 5% T_2 individuals and is kept at constant size. Baseline efficacy of the
402 existing technology (E_{b1}) is fixed at 0.3 (dotted line) and weight for observed outcome w_o is fixed at 1. β and β_1 are
403 set to be the same to represent the overall magnitude of the placebo effect. Error bars represent 95% confidence
404 interval for 500 independent simulation runs.

405 A full exploration of parameter space is shown in Figure 4. Note that because the
406 population size is relatively small, fixation of either T_1 or T_2 occurs rather often, and therefore
407 "T_1 frequency" on y axis can also be viewed as the probability that T_1 or T_2 reaches fixation (if
408 T_1 reaches fixation in a given run, it will have a T_1 frequency of 1).

409 The most obvious pattern, of course, is that the end-point frequency of T_1 individuals at
410 generation 200 decreases as the baseline efficacy of the invading treatment increases across all
411 conditions. This result makes intuitive sense; the more the invading treatment is objectively
412 better (i.e. larger E_{b2}), the more likely it will spread in the population. This pattern is least
413 pronounced, however, when w_a is extremely large ($w_a = 100$), as when agents entirely rely on

414 observed action and ignore outcome, the efficacy of the invading treatment does not matter. The
415 role of placebo effect, on the other hand, is subtle and more dependent on specific parameter
416 combinations. First, placebo effect always makes the adoption of new technology less likely
417 when it has lower baseline efficacy than that of the existing treatment ($E_{b1} < 0.3$), as indicated
418 by the relatively high frequency of T_1 individuals. This is because the degree to which a belief
419 may benefit from placebo effect depends on its initial magnitude, and since the initial belief for
420 the invading treatment is 0, existing treatments benefit more from placebo effect. Additionally,
421 the disadvantage of the invading treatments is exacerbated by the fact that they are objectively
422 inferior (small E_{b2}). Since most individuals in the starting population possess T_1, sampling more
423 individual as models and weighing more on action makes belief in the efficacy of T_1 even
424 stronger. Therefore, the suppression of inferior treatment is most pronounced when the number
425 of models picked n is large and the weight of observed action w_a is moderately large. As
426 mentioned, extremely large w_a renders placebo effect unimportant; on the other hand, when w_a
427 is very small (meaning w_o is relatively large), placebo effect also does not make noticeable
428 difference when the invading treatment has lower baseline efficacy. The intuition here is that a
429 strong reliance on observed efficacy already suppresses inferior technology and the addition of
430 placebo effect does not add much.

431 Second, when the invading treatment is objectively superior ($E_{b1} < E_{b2}$) the presence of
432 placebo effect may enhance the adoption of the invading treatment when n is large and w_a is of
433 intermediate magnitude, and the invading technology's baseline efficacy is only moderately
434 larger than that of the existing technology. For example, in the case of $n = 10$ and $w_a = 1$
435 (bottom middle graph), The frequency of T_1 individuals is lower in the presence of placebo effect
436 ($\beta = \beta_1 = 0.5$) compared to no placebo effect ($\beta = \beta_1 = 0$) when E_{b2} is within a particular
437 range, i.e, $0.3 < E_{b2} < 0.7$. Why is this? Recall that the superior invading treatment can also
438 benefit from placebo effect because individuals' subjective belief of its efficacy will gradually
439 increase and may eventually reach an equilibrium which is higher than that of the existing
440 treatment. In other words, a superior technology will quickly spread in the population in the
441 presence of large placebo effect once it gets over the initial hurdle. What we observe in the
442 simulation is that this occurs when agents weigh both observed action and observed outcome
443 similarly ($w_a = w_o = 1$). The intuition here is that weighing heavily on action makes the
444 evolutionary dynamics similar to the Hardy-Weinberg equilibrium situation and placebo effect
445 would play little role; on the other hand, weighing heavily on outcome paradoxically benefit the
446 existing technology as agents' initial belief in it is high and therefore has higher realized efficacy
447 under placebo effect. The ceiling effect occurs, however, when the magnitude of placebo effect
448 and baseline efficacy of the invading technology gets sufficiently large and the probability of the
449 invading technology spreading (lower T_1 frequency) does not further increase with increasing
450 E_{b2}.

451 Lastly, there is a very noticeable effect of number of models picked (n) on the adoption
452 of superior invading technology. When agents heavily weigh observed outcomes (left column in
453 Figure 4), large n neither suppresses inferior technology nor enhances the adoption of superior
454 technology to the same degree as small n. This is the direct result of how agents construct their
455 belief (see equation (7) and (8)) regarding the efficacy of T_1 and T_2; when observed outcomes

456 dominates belief construction, p_1 and p_2 are effectively the same as realized efficacy E_{r1} and
457 E_{r2}, and the proportion of models who practice T_1 and T_2 is largely ignored. When the number of
458 models picked is large, most agents will experience a mixture of T_1 and T_2 individuals in their
459 model set, and because agents don't pay much attention to observed action, the inferior
460 technology paradoxically enjoys an advantage: since action faithfully reflects belief (an agent is
461 more likely to practice T_1 if his subjective belief in T_1 is higher), exclusively focusing on
462 outcome loses much valuable information and increases the probability of adopting the inferior
463 treatment. There are two solutions: one is to decrease the number of models picked (reduce the
464 chance of having mixture of T_1 and T_2 models) and the other is to increase the weight attached to
465 observed action. This rather counter-intuitive result is independent of placebo effect and also of
466 particular importance from an evolutionary perspective, as it suggests that there may be an
467 optimal balance between weights of the two information sources, w_a and w_o (Hong,
468 unpublished). In order to maximize the probability of adopting the better treatment, the best
469 strategy is to take both action and outcome into belief construction.

470 # 4. Discussion

471 ## 4.1. The puzzle of ineffective medical treatment

472 As the French philosopher and essayist Michel de Montaigne famous claimed, "there are men on
473 whom the mere sight of medicine is operative." In fact, nearly all traditional medicine relied on
474 our minds' self-suggestive power to some degree (Hunter 2007). Therefore, our understanding of
475 pre-RCT medical practices and our conception of rationality for people in traditional societies
476 would be woefully incomplete without accounting for the existence of placebo effect. If we view
477 traditional healing practices as strictly ineffective, then their cross-cultural and historical
478 persistence presents an evolutionary puzzle. Why would people practice often costly rituals
479 which achieves no better than chance? Although people may engage in these healing practices
480 for a variety of social and religious reasons, these practices are still deeply puzzling from an
481 instrumental perspective. Horton (1967) forcefully argues against symbolistic interpretations of
482 these traditional practices; according to his argument, there is no fundamental difference between
483 a traditional healer and a western scientist with regard to the scope and objective of their
484 practices: both offer explanations, predictions, and control of worldly events. Although a general
485 theory of why people practice ineffective technologies may be difficult to achieve, a focus on
486 placebo effect in the domain of medical practice may render seemingly ineffective treatments
487 less puzzling. Many shamanistic healing practices, for example, are suggested to have a non-
488 trivial placebo component (Humphrey 2018). If we temporarily suspend our methodological
489 commitment to randomized, controlled trials, many of the healing practices do "work", and it is
490 to the patients' advantage to engage in these practices and believe in their efficacy.

491 As already mentioned, a range of factors contribute to the magnitude of placebo effect
492 and the eventual therapeutic outcome. In this paper I have focused on the cultural transmission of
493 efficacy information in the form of anecdotal stories and observed action, which creates a
494 reciprocal relationship between belief and efficacy. In my stylized model, I show that the
495 realized efficacy of some treatment may be higher than its baseline efficacy, and treatments in
496 which individuals do not have much initial confidence will experience an increase in realized

efficacy over time as individuals become more convinced of its effectiveness and eventually reach some equilibrium. In the model, transmission of cultural information occurs through distinct generations, yet depending on the frequency of the treatment practice, multiple belief-efficacy reinforcing cycles can occur within an individual's lifetime, and equilibrium may be reached even faster than the model suggests.

4.2. Transmission biases in technological adoption and the role of placebo effect

The population dynamics of technological adoption has been theoretically examined in classic cultural evolution literature (Boyd et al. 2013; Boyd and Richerson 1985). Like many other forms of cultural variants, technological practices are subjected to the same transmission biases as beliefs and values, yet they are distinct in that technologies are by definition means to some end. People use technologies to achieve various objectives, and it is very likely the outcomes of the technology affect the probability of their adoption. The existence of payoff biased transmission has ample empirical support: Human children have been shown to pay attention to their models payoffs when making copying decisions (Vale et al. 2017), and even pigeons were suggested to fail to copy their conspecific tutors' food-finding techniques if the tutors obtain smaller rewards than themselves (Giraldeau and Lefebvre 1987).

At the same time, frequency based social learning strategies may still play a role. Technologies that frequently yield negative results can still prevail in a society if the fact that they are practiced by many individuals in a community is taken as evidence for their validity. Many ethnographers have alluded to this factor to explain the persistence of magic and divination: failure to produce promised outcomes often do not disillusion either the practitioners or the observers (Culwick et al. 1935); rather, these failures may be explained away by appealing to incidental technical mal-function, unfulfilled-ritual requirements, or a lack of skill of the diviner (Annus 2010).

In reality, humans likely possess a suite of learning strategies. Though individual learning and different social learning rules are often portrayed as distinct strategies used in different contexts (Wood et al. 2013), they can be employed simultaneously (Laland 2004). In a way, the second model is an attempt to combine frequency dependent transmission and payoff biased transmission (see equation (9)) into a single decision-making process by explicitly modeling belief formation. The model shows that although placebo effect often creates an incumbent advantage and suppresses the invasion of new, potentially superior medical technologies, it can nonetheless enhance the adoption of new treatments when individuals weigh both observed action and observed outcome roughly equally. This result provides a more nuanced understanding of the conditions under which advantageous cultural variants may spread. For example, when placebo effect is present, existing treatment often have higher realized efficacy and thus an exclusive focus on outcome may make it difficult for the invading technology to overcome the initial disadvantage.

One implication here is that certain medical practice may "get stuck" in the population not because individuals do not care about efficacy, but because these practices do achieve substantial efficacy due to placebo effect. Therefore, successful invasion of new treatment may require special circumstances such as exceptionally high baseline efficacy or some boost in the

initial confidence of its efficacy induced by other socio-cultural factors and transmission biases such as prestige bias (Henrich and Gil-White 2001).

My model also highlights the importance of weighing both action and outcome in making optimal trait adoptions decisions. It is easy to understand why ignoring outcome information reduces the probability of adopting the better trait, but what is less obvious is that ignoring observed action also leads to sub-optimal decisions. Because both action and outcome carry useful information regarding the efficacy the technological variants, genetic and cultural selection likely favors substantial weight for both information sources. Note that as it stands, this paper only examines the population dynamics under specific assumptions, and do not analyze the evolutionarily stable strategies regarding what types belief updating and trait adoption decision rules maximize fitness. Previous authors have suggested that different learning strategies should be viewed as operating within a single inferential process (Heyes 1994; Plotkin 1988), and the weight that people attach to different information sources are subject to natural selection (Perreault et al. 2012). For example, Perreault and colleagues (2012) analyze a model where agents try to infer the correct environmental state based on social and nonsocial cues, and find that social cues are preferred when changes of the environment is slow. My model contributes to this literature by emphasizing the role of placebo effect and how the belief construction process affects the adoption of superior medical technology.

Finally, it should be noted that this paper does not provide evolutionary rationales for the existence of placebo effect and takes it as a given. Research on the evolution of placebo effect remains scant, but see Humphrey (2002)'s proposal that placebo effect evolved as a way to optimally allocate limited resource (our body's immune response is more likely to occur when the expectation of recovery is high), and Trimmer et al. (2013)'s formalization of this idea. My model, however, does suggest a new possibility for understanding the evolutionary benefit of placebo effect in the context of technological evolution: most obviously, placebo effect always suppresses the invasion of inferior medical technology, and may even enhance the adoption of superior treatment in certain situations. Future work may be devoted to exploring the evolutionary dynamics of placebo effect from this perspective.

References

Annus, A. (2010). *Divination and Interpretation of Signs in the Ancient World*. *Oriental Institute Seminars*.

Aschwanden, H., & Cooper, U. (1987). Symbols of death: an analysis of the consciousness of the Karanga. In *Shona heritage series* (p. 389). Gweru, Zimbabwe: Mambo Press. https://ehrafworldcultures.yale.edu/document?id=fs05-021

Bianchi, C. C. (1989). *Gubida illness and religious ritual among the Garifuna of Santa Fe, Honduras: an ethnopsychiatric analysis*. Ann Arbor, Mich.: University Microfilms International. https://ehrafworldcultures.yale.edu/document?id=sa12-016

Boyd, R., Richerson, P., & Henrich, J. (2013). The cultural evolution of technology: Facts and

577 theories. In P. J. Richerson and M. H. Christiansen (Ed.), *Cultural Evolution: Society,*
578 *Language, and Religion*. MIT Press. http://www2.psych.ubc.ca/~henrich/pdfs/Boyd
579 Richerson Henrich The cultural evolution of technology 7.pdf. Accessed 26 March 2019

580 Boyd, R., & Richerson, P. J. (1985). *Culture and the evolutionary process*. University of
581 Chicago Press.

582 Culwick, A. T. (Arthur T., Culwick G. M., M., & Kiwanga, T. (1935). *Ubena of the Rivers*.
583 London: G. Allen & Unwin, Ltd. https://ehrafworldcultures.yale.edu/document?id=fn31-
584 001

585 Day, T., & Bonduriansky, R. (2011). A Unified Approach to the Evolutionary Consequences of
586 Genetic and Nongenetic Inheritance. *The American Naturalist*.
587 https://doi.org/10.1086/660911

588 De Craen, A. J. M., Kaptchuk, T. J., Tijssen, J. G. P., & Kleijnen, J. (1999). Placebos and
589 placebo effects in medicine: Historical overview. *Journal of the Royal Society of Medicine*.
590 https://doi.org/10.1177/014107689909201005

591 De Craen, A. J. M., Tijssen, J. G. P., De Gans, J., & Kleijnen, J. (2000). Placebo effect in the
592 acute treatment of migraine: Subcutaneous placebos are better than oral placebos. *Journal*
593 *of Neurology*. https://doi.org/10.1007/s004150050560

594 Evans-Pritchard, E. (1937). *Witchcraft, oracles and magic among the Azande*. Clarendon Press.

595 Faasse, K., & Petrie, K. J. (2016). From Me to You: The Effect of Social Modeling on Treatment
596 Outcomes. *Current Directions in Psychological Science*.
597 https://doi.org/10.1177/0963721416657316

598 Giraldeau, L. A., & Lefebvre, L. (1987). Scrounging prevents cultural transmission of food-
599 finding behaviour in pigeons. *Animal Behaviour*. https://doi.org/10.1016/S0003-
600 3472(87)80262-2

601 Hammami, M. M., Al-Gaai, E. A., Alvi, S., & Hammami, M. B. (2010). Interaction between
602 drug and placebo effects: A cross-over balanced placebo design trial. *Trials*.
603 https://doi.org/10.1186/1745-6215-11-110

604 Harrell, S. (1983). *Belief and unbelief in a Taiwan village*. Ann Arbor, Mich.: Xerox University
605 Microfilms. https://ehrafworldcultures.yale.edu/document?id=ad05-011

606 Henrich, Joe, & Boyd, R. (1998). The Evolution of Conformist Transmission and the Emergence
607 of Between-Group Differences. *Evolution and Human Behavior*.
608 https://doi.org/10.1016/S1090-5138(98)00018-X

609 Henrich, Joseph, & Gil-White, F. J. (2001). The evolution of prestige: Freely conferred
610 deference as a mechanism for enhancing the benefits of cultural transmission. *Evolution and*
611 *Human Behavior*. https://doi.org/10.1016/S1090-5138(00)00071-4

612 Henrich, Joseph, & McElreath, R. (2003). The Evolution of Cultural Evolution. *Evolutionary*
613 *Anthropology*. https://doi.org/10.1002/evan.10110

614 Heyes, C. M. (1994). Social learning in animals: Categories and mechanisms. *Biological*

615 *Reviews of the Cambridge Philosophical Society*. https://doi.org/10.1111/j.1469-
616 185X.1994.tb01506.x

617 Hong, Z., & Henrich, J. (2021). The Cultural Evolution of Epistemic Practices. *Human Nature*,
618 1–30.

619 Horton, R. (1967). African Traditional Thought and Western Science. *Africa*.
620 https://doi.org/10.2307/1158253

621 Hróbjartsson, A., & Gøtzsche, P. C. (2010). Placebo interventions for all clinical conditions.
622 *Cochrane Database of Systematic Reviews*.
623 https://doi.org/10.1002/14651858.CD003974.pub3

624 Humphrey, N. (2002). Great expectations: the evolutionary psychology of faith- healing and the
625 placebo effect. In *The mind made flesh*.

626 Humphrey, N. (2018). Shamans as healers: When magical structure becomes practical function.
627 *The Behavioral and brain sciences*. https://doi.org/10.1017/S0140525X17002084

628 Hunsley, J., & Westmacott, R. (2007). Interpreting the magnitude of the placebo effect:
629 Mountain or molehill? *Journal of Clinical Psychology*. https://doi.org/10.1002/jclp.20352

630 Hunter, P. (2007). A question of faith. Exploiting the placebo effect depends on both the
631 susceptibility of the patient to suggestion and the ability of the doctor to instil trust. *EMBO*
632 *Reports*. https://doi.org/10.1038/sj.embor.7400905

633 Kaptchuk, T. J. (1998). Intentional Ignorance: A History of Blind Assessment and Placebo
634 Controls in Medicine. *Bulletin of the History of Medicine*.
635 https://doi.org/10.1353/bhm.1998.0159

636 Kaptchuk, T. J., Goldman, P., Stone, D. A., & Stason, W. B. (2000). Do medical devices have
637 enhanced placebo effects? *Journal of Clinical Epidemiology*. https://doi.org/10.1016/S0895-
638 4356(00)00206-7

639 Kaptchuk, T. J., & Miller, F. G. (2015). Placebo effects in medicine. *New England Journal of*
640 *Medicine*. https://doi.org/10.1056/NEJMp1504023

641 Kirmayer, L. J. (1994). Improvisation and authority in illness meaning. *Culture, Medicine and*
642 *Psychiatry*. https://doi.org/10.1007/BF01379449

643 Laland, K. N. (2004). Social learning strategies. *Learning and Behavior*.
644 https://doi.org/10.3758/bf03196002

645 Lancy, D. F., Bock, J., & Gaskins, S. (2010). *The anthropology of learning in childhood*.
646 Rowman Altamira.

647 Misra, S. (2012). Randomized double blind placebo control studies, the "gold Standard" in
648 intervention based studies. *Indian Journal of Sexually Transmitted Diseases*.
649 https://doi.org/10.4103/0253-7184.102130

650 Miton, H., Claidière, N., & Mercier, H. (2015). Universal cognitive mechanisms explain the
651 cultural success of bloodletting. *Evolution and Human Behavior*.
652 https://doi.org/10.1016/j.evolhumbehav.2015.01.003

653 Murdock, G. P. (1980). *Theories of Illness a World Survey*. University of Pittsburgh Press.
654 https://philpapers.org/rec/MURTOI. Accessed 28 March 2019

655 Perreault, C., Moya, C., & Boyd, R. (2012). A Bayesian approach to the evolution of social
656 learning. *Evolution and Human Behavior*.
657 https://doi.org/10.1016/j.evolhumbehav.2011.12.007

658 Plotkin, H. C. (1988). *The role of behavior in evolution*. MIT press.

659 Shapiro, A. K. (1969). Iatroplacebogenics. *International Pharmacopsychiatry*.
660 https://doi.org/10.1159/000468855

661 Sigerist, H. E. (Henry E. (1951). *A history of medicine.* Oxford University Press.
662 https://global.oup.com/academic/product/a-history-of-medicine-
663 9780195050790?cc=us&lang=en&. Accessed 30 March 2019

664 Smith, E. W., & Dale Andrew Murray, d. 1919. (1920). *Ila-speaking peoples of Northern*
665 *Rhodesia: vol. 1*. London: MacMillan and Co.
666 https://ehrafworldcultures.yale.edu/document?id=fq06-001

667 Trimmer, P. C., Marshall, J. A. R., Fromhage, L., McNamara, J. M., & Houston, A. I. (2013).
668 Understanding the placebo effect from an evolutionary perspective. *Evolution and Human*
669 *Behavior*. https://doi.org/10.1016/j.evolhumbehav.2012.07.004

670 Turnbull, C. M. (1965). *Wayward servants: the two worlds of the African Pygmies*. Garden City,
671 N.Y.: The Natural History Press. https://ehrafworldcultures.yale.edu/document?id=fo04-002

672 Tylor, E. B. (1871). *Primitive culture: researches into the development of mythology,*
673 *philosophy, religion, art, and custom* (Vol. 2). J. Murray.

674 Vale, G. L., Flynn, E. G., Kendal, J., Rawlings, B., Hopper, L. M., Schapiro, S. J., et al. (2017).
675 Testing differential use of payoff-biased social learning strategies in children and
676 chimpanzees. *Proceedings of the Royal Society B: Biological Sciences*.
677 https://doi.org/10.1098/rspb.2017.1751

678 Vickers, A. J., Vertosick, E. A., Lewith, G., MacPherson, H., Foster, N. E., Sherman, K. J., et al.
679 (2018). Acupuncture for Chronic Pain: Update of an Individual Patient Data Meta-Analysis.
680 *Journal of Pain*. https://doi.org/10.1016/j.jpain.2017.11.005

681 Waber, R. L., Shiv, B., Carmon, Z., & Ariely, D. (2008). Commercial features of placebo and
682 therapeutic efficacy. *JAMA - Journal of the American Medical Association*.
683 https://doi.org/10.1001/jama.299.9.1016

684 Wartolowska, K. A., Feakins, B. G., Collins, G. S., Cook, J., Judge, A., Rombach, I., et al.
685 (2016). The magnitude and temporal changes of response in the placebo arm of surgical
686 randomized controlled trials: a systematic review and meta-analysis. *Trials*, *17*(1), 589.

687 Wood, L. A., Kendal, R. L., & Flynn, E. G. (2013). Whom do children copy? Model-based
688 biases in social learning. *Developmental Review*. https://doi.org/10.1016/j.dr.2013.08.002

689

690