

Modern health care as a game theory problem

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I am addicted to [opioids], and it's doctors' fault because they prescribed them.

But, I'll sue them if they leave me in pain [1].

The clouds of a perfect storm are gathering over most healthcare systems around the world, the storm that will intensify the contrast between the interests of healthcare providers vs. those of individual patients. As treatment options proliferate and many of them are very expensive, patients are increasingly unable to get all treatments they demand or even need [2]. This is obvious in poor countries with limited resources, but even people in affluent societies increasingly feel that they do not get the health care they want. The access to and demands for health care have never been greater [3]. Given that 80% of all healthcare expenditures are affected by physicians' decisions [4,5], doctors are under increasing pressure not only to take care of patients but to be good stewards of resources [2,6–8]. Moreover, physicians are increasingly judged and even reimbursed based on how satisfied their patients are. But, struggling to satisfy their patients affects their decisions of what care they provide. Patients also fine-tune their interests according to the type of insurance coverage they have. Patients with more coverage may be more willing to seek aggressive, expensive care, as they do not have to pay for it, while patients who have to pay a lot out of pocket may be less likely to seek such expensive care [5]. Both physicians and patients are asked to behave responsibly [9,10], but this is not easy when interests of each individual party diverge. In times of financial and overall societal uncertainty, all stakeholders are struggling to exploit healthcare systems to serve their own interests best.

Some health care interactions are Prisoners' Dilemmas

So, the perfect storm has been created, the one that will inevitably pitch doctors against patients [11,12]. When there is an interaction between common and conflicting interest between two 'players' – a doctor and a patient – the situation can be described using game theory [13,14]. Game theory models situations

fraught with conflict and cooperation [13,14]. It assumes that everyone has 'skin in the game' and that people act strategically to advance their interests [14]. The best known example of strategic games is the Prisoners' Dilemma game [14].

The Box describes a paradigmatic situation: a patient seeking opioids for pain may have real pain or may be faking. If he has real pain, the rational choice for the doctor is to treat him. If he has fake pain, it is still in the doctor's best interest to treat the patient. Otherwise, the patient will give him a low satisfaction score – resulting in loss of reputation and reduced income. Thus, a doctor will prescribe opioids regardless of whether the patient needs them, and the patient addicted to opioids will demand these opioids for short-term satisfaction notwithstanding that their long-term use may eventually harm his health and society at large. Such a strategy will lead to the wasting of resources and poor outcomes, that is a 'tragedy of commons' [15] – seemingly, rational decisions according to self-interest is contrary to the societal long-term best interests leading to depletion of common resources. The most important aspect of the Prisoners' Dilemma is that when both 'players' play their best strategy, together they are worse off. Fundamentally, when different values are involved, there is inevitable trade-offs in the consequences experienced by different 'players' (i.e. patients vs. physicians in our case).

Emotions are inevitable in any human interaction: adding trust, regret, guilt and frustration to the game

Awareness of these situations is the first step in considering how to change these games in directions that may satisfy both individual and societal expectation [14]. Although informed by a real case, the pain example that we discussed is a simplification of a typical clinical encounter, because it neglects the professionalism and ethical obligations of the doctors to their individual patients' well-being [8]. Importantly, the prisoners' dilemma in its original form does not take into account *trust*, which is important in a physician–patient relationship [16,17]. Without trust, clinical medicine might well cease to exist [17].

Box

Prisoners' Dilemma for prescribing opioids to potentially drug-seeking patients (after ref# [14])

Relieving pain and suffering is one of the most venerable roles of medical profession; that is what doctors are trained to do – the physicians take a great pride when they are able to help their patients. Society too expect them to successfully manage pain; in fact, the appropriate management of pain is one of the accreditation criteria by the organization such as the Joint Commission, which accredits and certifies more than 20 000 healthcare organizations and programmes in the United States [38]. In addition, starting in January of 2015, 30% of physicians' compensation may depend on patients' satisfaction scores [39,40]. So, doctors are both intrinsically and extrinsically motivated to help alleviate patients' suffering. However, some patients may fake the pain, may request narcotics for other reasons, including nonmedical ones to obtain narcotics for illegal purposes, or because of addiction habits. While physicians may suspect that the patients are not in pain, there is no objective test to prove that the patient who states that he is in pain is actually not experiencing it. Prescribing narcoanalgesics to these patients is inappropriate as may continue to feed addiction and/or illegal behaviour and represents squandering resources. However, refusing to prescribe pain medications may leave the patient dissatisfied, which in turn may result in low satisfaction scores and eventual penalty for doctors. In addition, not prescribing pain medications to those who are not in pain will not improve doctors' satisfaction scores. Should the physicians always prescribe narcotics to the patients requesting the pain medications, even if they suspect they may not be in pain?

This is a classic Prisoners' Dilemma situation: what is the best strategic move for individual is not best for society (see table below).

		Doctor	
		Prescribe narcotics (Pay-off)	Do not prescribe narcotics (Pay-off)
Patient	Real pain	(the patient satisfied; high satisfaction score for the doctor, professionally rewarding)*	(the patient dissatisfied; low satisfaction for the doctor)
	Fake pain	(patient satisfied; high satisfaction for the doctor even if it is professionally less rewarding)	(the patient dissatisfied; low satisfaction for the doctor even if it is professionally most rewarding)

*Dominant (best) strategy for both 'players' (a doctor and a patient).

Loss of trust accentuates the Prisoners' Dilemma while its preservation may help avoid it.

The situation between the physician and the patient is asymmetrical: the patients by necessity have to place themselves in a position of vulnerability, where their trust can be abused [13]. Their interests can diverge from their physicians' interests and utilities. Moreover, the physician cannot guarantee absolutely correct recommendations and successful outcomes [18]. Consequently, both patients and physicians may *regret* [19,20] the treatment choices they made [13], for example when the physician fails to treat someone who has disease, or gives unnecessary treatment to someone without disease. *Guilt* affects a physician abusing the trust of the patient, for example when he prescribes treatment which he should not have prescribed to the patient who trusted him [21,22]. The clinical encounter is also frequently characterized by *frustration*, which is a feeling of anger or annoyance caused by being unable to do something, resistance to fulfilment of individual's will. It occurs, for example, when due to lack of trust, the patient refuses the treatment and causes the doctor to

have lower satisfaction or smaller utilities, or when the doctor's refusal to offer treatment causes the patient to be less satisfied. Feelings of regret, guilt or frustration can relate to any of diverse clinical outcomes such as life expectancy, morbidity or mortality rates, absence of pain, satisfaction with offered care and cost.

Generic game theory model for healthcare decisions

These concepts can be formally modelled. Figure 1 describes a generic game theory model depicting the situations when the physician has to decide whether to recommend certain healthcare intervention in the circumstance when obtaining further information is not feasible (e.g. to give a treatment when all diagnostic testing is exhausted). We also consider the possibility that the patient may demand treatment, which the doctor does not recommend. We then analyse two situations: (i) the patient does not get a treatment he wanted, and (ii) the patient gets the therapy he demanded. The model is both

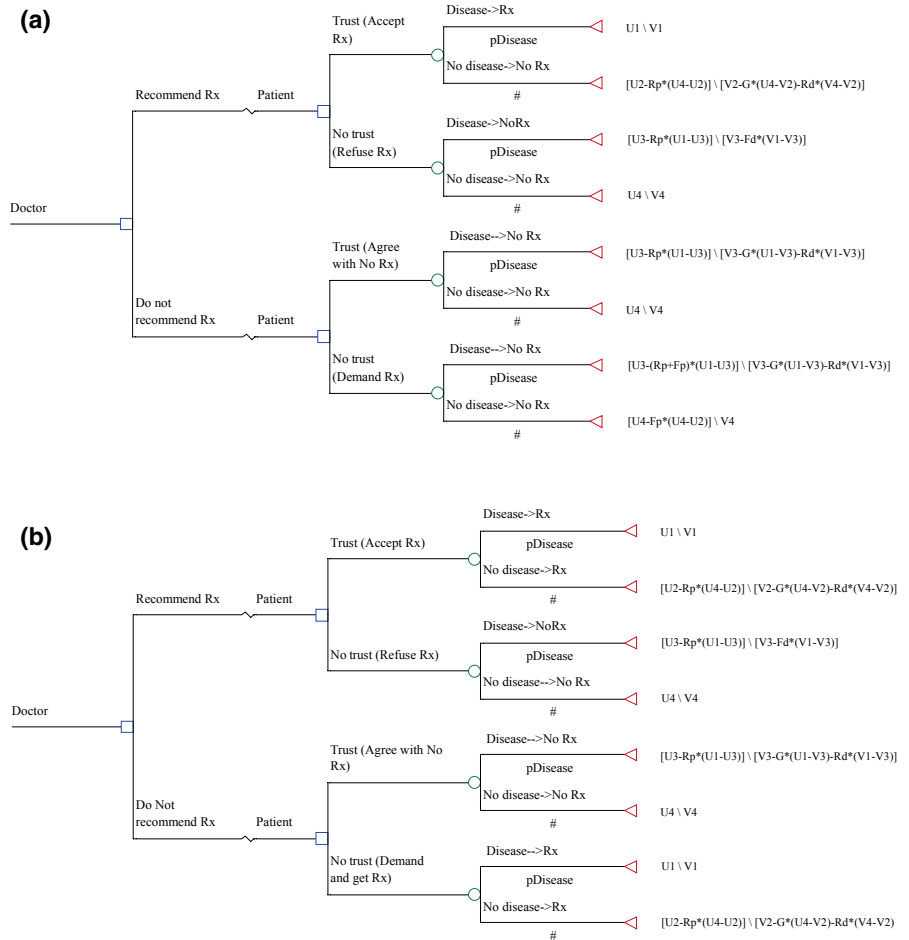


Figure 1 (a) A game theory model related to decision whether a physician should give treatment when no further diagnostic testing is available, and whether a patient should accept the recommendation (The patient demands treatment but does not get it). (b) A game theory model related to decision whether a physician should give treatment when no further diagnostic testing is available, and whether a patient should accept the recommendation (The patient demands treatment and gets it). The utilities of patients (U) and doctors (V); Rx: treatment; NoRx: no treatment; G: guilt; R: regret; the subscripts p and d refer to the values for a patient and a doctor, respectively (see text for definitions and details).

simple to allow easier exposition of the conceptual model that we are proposing, but also realistic enough to allow us to draw some conclusions important for health policy. It satisfies two key assumptions of game theory [23,24]: common knowledge and rationality. *Common knowledge* assumes both players can deduce what the other will do contingent on each player's move, that is each player knows the consequences of each action, knows that both know it, knows that both know that both know it, etc. This assumption is particularly evident in trust version of game, which insists on its maximum transparency. *Rationality* assumes that the players are instrumentally rational in the sense that they will always choose strategies that maximize their own individual pay-offs, relative to their knowledge and beliefs about benefits and harms of each chosen strategy.

When faced with the situation depicted in Fig. 1, a physician has to decide whether to recommend the treatment, and the patient then decides whether to accept it and trust the physician (doctor). What is the most rational strategy for each 'player'? Mathematically, this will amount to solving for the

case when the expected utilities (pay-offs) for a patient and a physician are maximal. In particular, we are interested in finding out: (i) under what circumstances, there is an obvious superior ('dominant') strategy from both 'player's' points of view, and (ii) under what circumstances the best strategy for each player is represented by choosing a **mixed strategy** (where a player chooses one strategy with probability P and the other with probability $1-P$), resulting in the so called Nash's equilibrium. We first simplify the problem by presenting this 'game' in the form of a pay-off matrix (see Table 1).

The pay-off matrix can be visualized as 2×2 table with two rows (row 1: patient decides to trust his doctor; row 2: the patient decides not to trust his doctor) and two columns [column 1: doctor decides to administer treatment (Rx); column 2: the doctor decides not to give Rx]. Thus, the pay-offs denoted as P_{11} relate to the utilities of outcomes for the patient who decided to trust his doctor, and who in turn chooses to administer treatment. On other hand, the pay-offs labelled as D_{12} relate to the utilities of outcomes for the doctor who chose not to give treatment to the patient who decided to trust him.

Table 1 Generic game theory model for healthcare decisions

'Player'		Doctor	
	Strategy	Rx	NoRx
Patient	Trust	$(E[\text{Trust}, \text{Rx}], E[\text{Rx}, \text{Trust}])$	$(E[\text{Trust}, \text{NoRx}], E[\text{NoRx}, \text{Trust}])$
	No Trust	$(E[\text{NoTrust}, \text{Rx}], E[\text{NoRx}, \text{Trust}])$	$(E[\text{NoTrust}, \text{NoRx}], E[\text{NoRx}, \text{NoTrust}])$
= Patient		$\begin{pmatrix} \text{Doctor} \\ \text{Rx} & \text{NoRx} \\ \text{Trust} & (P_{11}, D_{11}) & (P_{12}, D_{12}) \\ \text{No Trust} & (P_{21}, D_{21}) & (P_{22}, D_{22}) \end{pmatrix}$	

It is then obvious that if $P_{11} > P_{21}$ and $P_{12} > P_{22}$, the patient has a dominant strategy and should choose to trust; analogously, if the doctor pay-offs $D_{11} > D_{12}$ and $D_{21} > D_{22}$, the doctor should rationally choose treatment (Rx) over no treatment (NoRx), etc.

The pay-offs shown in the Table 1 relate to the utilities that refer to various clinical outcomes such as life expectancy, morbidity or mortality rates, absence of pain, satisfaction with care and cost. We denote the physician's utilities as V , and the patient's utilities as U . Each of the alternative courses of actions shown in Fig. 1a and 1b is associated with the pay-offs (utilities). The utilities are likely different between the patients (U) and doctors (V) (see below).

We assume that a physician will value more outcomes associated with treatment of the patient with disease (V_1) than outcomes associated with no action, that is administration of no treatment in someone without disease (V_4). We think this is a reasonable assumption to make in the contemporary medicine, which is dominated by expectations to act rather than do nothing. For example, the doctors who fail to prescribe treatment or order a diagnostic test may be sued more often than those who ordered an unnecessary test or treatment [25]. Similarly, a recent estimate indicated that overuse of low-value services in Medicare affects about 42% of beneficiaries [26]. V_4 , however, will be valued more than V_2 (outcomes of treating someone without disease); this is because 'first do no harm' remains a time-honoured ingredient in the practice of medicine, despite the fact that it is being widely violated by administration of unnecessary, or harmful health interventions. The outcomes of V_2 , in turn, are assumed to be valued more than outcomes associated with failing to administer treatment to someone who should have received it (V_3). The rationale for this assumption is also based on the current default-action-oriented medical practice. We also assume that the patient's utility of being treated when he has a disease (U_1) is higher than the physician's value of failing to administer treatment to someone who should have received it (V_3). Similarly, we assume that U_4 (the patient's utility of not being treated if he

has no disease) will be greater than V_2 (the physician's utilities related to outcomes when treating someone without disease).

The models described in this study represent an extension of our previously published model, which is based on incorporation of trust, regret and guilt [13]. Regret (R) is defined as a fraction of the difference between the utility of the action taken and the utility of the best outcome we should have taken, in retrospect [19,20,27]. In this model, we expressed it as a fraction of loss of potential utilities [28]. Although regret under scenarios 'Trust' and 'No Trust' is likely different, in our model, for simplification purposes, we kept it as identical. Similarly, a physician may feel guilt (G) because he abused the patient's trust [21], which, however, can also occur due to an honest mistake. Guilt expresses the psychological reaction of a physician abusing the trust of the patient resulting in diminished doctor's utility by a fraction of the difference between his and his patient's utilities, when he prescribes treatment when he should not have, as shown in Fig. 1a and 1b [28]. Frustration (F) is a feeling of anger or annoyance caused by being unable to do something, resistance to fulfilment of individual will and occurs when due to lack of trust, the patient refuses the treatment and causes the doctor to realize smaller utilities by being forced to do what is less than optimal management course, or when the doctor's refusal to offer treatment causes the patient to lose some of his utilities. Note that frustration represents the difference in utilities across the patient and doctor [$U.-V.$ or $V.-U.$], while regret denotes the difference in utilities for doctor ($V.-V.$), or a difference for the patient ($U.-U.$) (see Fig. 1a and 1b). Finally, we assumed that the 'game' can be played only once such as in a clinical encounter in the emergency room, surgical decisions, etc. [The repeated interactions between the patient and his doctor may or may not generate the same outcomes and may require more complex modelling].

Consider now Model A (Fig. 1a): the patient demands treatment but does not get it.

As explained above, we define utilities so that we have the following inequalities:

$$0 \leq V_3 < V_2 < V_4 < V_1 \leq 1$$

$$V_2 \leq U_4 \text{ and } V_3 \leq U_1$$

$$0 \leq U_3 < U_2 < U_4 < U_1 \leq 1$$

The expected pay-offs for each situation shown in Table 1 are then equal to the probability of outcome times utilities associated with each outcome. Thus, the expected values are equal to:

$$P_{11} = E[\text{Trust, Rx}] = p \cdot U_1 + (1 - p) \cdot (U_2 - R_p \cdot (U_4 - U_2))$$

$$P_{21} = E[\text{No Trust, Rx}] = p \cdot (U_3 - R_p \cdot (U_1 - U_3)) + (1 - p) \cdot U_4$$

$$P_{12} = E[\text{Trust, NoRx}] = p \cdot (U_3 - R_p \cdot (U_1 - U_3)) + (1 - p) \cdot U_4$$

$$P_{22} = E[\text{No Trust, NoRx}] = p \cdot (U_3 - (R_p + F_p) \cdot (U_1 - U_3)) + (1 - p) \cdot (U_4 - F_p \cdot (U_4 - U_2))$$

$$D_{11} = E[\text{Rx, Trust}] = p \cdot V_1 + (1 - p) \cdot (V_2 - G \cdot (U_4 - V_2) - R_d \cdot (V_4 - V_2))$$

$$D_{21} = E[\text{Rx, NoTrust}] = p \cdot (V_3 - F_d \cdot (V_1 - V_3)) + (1 - p) \cdot V_4$$

$$D_{12} = E[\text{NoRx, Trust}] = p \cdot (V_3 - G \cdot (U_1 - V_3) - R_d \cdot (V_1 - V_3)) + (1 - p) \cdot V_4$$

$$D_{22} = E[\text{NoRx, No Trust}] = p \cdot (V_3 - G \cdot (U_1 - V_3) - R_d \cdot (V_1 - V_3)) + (1 - p) \cdot V_4$$

STRATEGIES:

Let's now analyse the **optimal strategies** both for the patient and the doctor. For example, if from the patient's view, the expected pay-offs satisfy the inequalities $P_{11} > P_{21}$ and $P_{12} > P_{22}$, then strategy 'Trust' is considered superior, and if $P_{11} < P_{21}$ and $P_{12} > P_{22}$, the strategy 'No Trust' is clearly better. Similarly, if the expected doctor's pay-offs $D_{11} > D_{12}$ and $D_{21} > D_{22}$, the doctor should rationally choose treatment ('Rx'), and if $D_{11} < D_{12}$ and $D_{21} < D_{22}$, the doctor should choose no treatment ('NoRx'). These are so called **pure strategies**.

However, when the inequalities are mixed (for example, if $P_{11} > P_{21}$ but $P_{12} < P_{22}$), then neither of the pure strategies is

always better. In this situation, the player's choice yielding the highest expected pay-off involves using **mixed strategies**, where a player chooses one strategy with probability p and the other with probability $1 - p$.

Exploring these situations in a little more detail, we have the following

1 If $P_{11} > P_{21}$ and $P_{12} > P_{22}$, then the Patient has a dominant strategy 'Trust'. The Doctor now knows that the patient will play the first row in Table 1, so she/he should play Rx or NoRx depending on whether D_{11} or D_{12} is larger. In other words:

$$\text{If } P_{11} > P_{21} \text{ and } P_{12} > P_{22} \Rightarrow \text{Patient} = \text{'Trust'},$$

and

$$\begin{cases} \text{if } D_{11} > D_{12} \text{ then Doctor} = \text{'Rx'} \\ \text{if } D_{11} < D_{12} \text{ then Doctor} = \text{'NoRx'} \end{cases}$$

If $P_{11} < P_{21}$ and $P_{12} < P_{22}$, then the Patient has a dominant strategy 'No Trust'. The Doctor knows the patient will play the second row and therefore should play Rx or NoRx depending whether D_{21} or D_{22} is larger. In other words:

$$\text{If } P_{11} < P_{21} \text{ and } P_{12} < P_{22} \Rightarrow \text{Patient} = \text{'No Trust'},$$

and

$$\begin{cases} \text{if } D_{21} > D_{22} \text{ then Doctor} = \text{'Rx'} \\ \text{if } D_{21} < D_{22} \text{ then Doctor} = \text{'NoRx'} \end{cases}$$

The first two situations describe the set of pure strategies available to the patient.

In all other situations, the patient does not have a clear pure strategy, that is, we have $P_{11} < P_{21}$ and $P_{12} > P_{22}$ or $P_{11} > P_{21}$ and $P_{12} < P_{22}$. In other words, we have either $P_{11} - P_{21} < 0$ and $P_{22} - P_{12} < 0$ or $P_{11} - P_{21} > 0$ and $P_{22} - P_{12} > 0$. In either case, the ratio $\frac{P_{11} - P_{21}}{P_{22} - P_{12}} > 0$. Under this circumstance, we need a mixed strategy for the patient.

This leads to the following question: under which circumstances the patient will be indifferent (has the same pay-offs) regardless of what the doctor does?

If the doctor chooses Rx x per cent of time and NoRx $(1 - x)$ per cent of the time, then the patient will be indifferent to the doctor's 'move' if:

SOLVING FOR MIXED STRATEGY

$$E[\text{Trust}] = x \cdot P_{11} + (1 - x) \cdot P_{12} = x \cdot (P_{11} - P_{12}) + P_{12}$$

$$E[\text{No Trust}] = x \cdot P_{21} + (1 - x) \cdot P_{22} = x \cdot (P_{21} - P_{22}) + P_{22}$$

$$x \cdot (P_{11} - P_{12}) + P_{12} = x \cdot (P_{21} - P_{22}) + P_{22}$$

$$x \cdot [(P_{11} - P_{12}) - (P_{21} - P_{22})] = P_{22} - P_{12}$$

$$x = \frac{P_{22} - P_{12}}{(P_{11} - P_{21}) + (P_{22} - P_{12})} = \frac{1}{1 + \frac{P_{11} - P_{21}}{P_{22} - P_{12}}}$$

So if the doctor plays Rx x per cent of the time and NoRx $(1-x)$ per cent of the time, the patient will have the same pay-off no matter which strategy he chooses.

[Note: As we only consider mixed strategy if $\frac{P_{11}-P_{21}}{P_{22}-P_{12}} > 0$, we have $0 < x < 1$].

Applying this formula for x to the actual values of the utilities, we obtain:

$$P_{11} = p \cdot U_1 + (1-p) \cdot (U_2 - R_p \cdot (U_4 - U_2))$$

$$P_{21} = p \cdot (U_3 - R_p \cdot (U_1 - U_3)) + (1-p) \cdot U_4$$

$$P_{12} = p \cdot (U_3 - R_p \cdot (U_1 - U_3)) + (1-p) \cdot U_4$$

$$P_{22} = p \cdot (U_3 - (R_p + F_p)(U_1 - U_3)) + (1-p) \cdot (U_4 - F_p \cdot (U_4 - U_2))$$

$$\begin{aligned} P_{11} - P_{21} &= p \cdot U_1 + (1-p) \cdot (U_2 - R_p \cdot (U_4 - U_2)) \\ &\quad - p \cdot (U_3 - R_p \cdot (U_1 - U_3)) - (1-p) \cdot U_4 \\ &= p \cdot U_1 + (1-p) \cdot U_2 - R_p \cdot (1-p) \cdot (U_4 - U_2) \\ &\quad - p \cdot U_3 + R_p \cdot p \cdot (U_1 - U_3) - (1-p) \cdot U_4 \\ &= p \cdot (U_1 - U_3) + R_p \cdot p \cdot (U_1 - U_3) \\ &\quad - R_p \cdot (1-p) \cdot (U_4 - U_2) - (1-p) \cdot (U_4 - U_2) \\ &= p \cdot (1 + R_p) \cdot (U_1 - U_3) \\ &\quad - (1 + R_p) \cdot (1-p) \cdot (U_4 - U_2) \\ &= (1 + R_p)[p(U_1 - U_3) - (1-p)(U_4 - U_2)] \\ &= -(1 + R_p)(1-p)(U_4 - U_2) \left[1 - \frac{p}{1-p} \frac{U_1 - U_3}{U_4 - U_2} \right] \end{aligned}$$

$$\begin{aligned} P_{22} - P_{12} &= p \cdot (U_3 - (R_p + F_p)(U_1 - U_3)) \\ &\quad + (1-p) \cdot (U_4 - F_p \cdot (U_4 - U_2)) \\ &\quad - p \cdot (U_3 - R_p \cdot (U_1 - U_3)) - (1-p) \cdot U_4 \\ &= p \cdot U_3 - p \cdot (R_p + F_p)(U_1 - U_3) + (1-p) \cdot U_4 \\ &\quad - F_p \cdot (1-p) \cdot (U_4 - U_2) - p \cdot U_3 + p \cdot R_p \cdot (U_1 - U_3) \\ &\quad - (1-p) \cdot U_4 \\ &= -p \cdot F_p \cdot (U_1 - U_3) - F_p \cdot (1-p) \cdot (U_4 - U_2) \\ &= -F_p[p(U_1 - U_3) + (1-p)(U_4 - U_2)] \\ &= -F_p \cdot (1-p)(U_4 - U_2) \left[1 + \frac{p}{1-p} \frac{U_1 - U_3}{U_4 - U_2} \right] \end{aligned}$$

Then, using the standard (benefits/harms) notation for patient's utilities [29,30]:

$B_p = U_1 - U_3$ and $H_p = U_4 - U_2$, the expression for x becomes:

$$x = \frac{1}{1 + \frac{-(1+R_p)(1-p)(U_4 - U_2) \left[1 - \frac{p}{1-p} \frac{U_1 - U_3}{U_4 - U_2} \right]}{-F_p \cdot (1-p)(U_4 - U_2) \left[1 + \frac{p}{1-p} \frac{U_1 - U_3}{U_4 - U_2} \right]}} = \frac{1}{1 + \frac{(1+R_p) \left[1 - \frac{p}{1-p} \frac{B_p}{H_p} \right]}{F_p \cdot \left[1 + \frac{p}{1-p} \frac{B_p}{H_p} \right]}}$$

Note that the sign of $P_{11} - P_{21}$ is then the same as the sign of $- \left[1 - \frac{p}{1-p} \frac{B_p}{H_p} \right]$, as we are assuming that $1-p \geq 0$ and $U_4 > U_2$.

Similarly, the sign of $P_{22} - P_{12}$ is always negative, as, according to our assumptions, all of F_p , $1-p$, $U_4 - U_2$ are non-negative.

STRATEGIES:

In a completely analogous way, we can now analyse the doctor's choice of strategies:

- 1 If $D_{11} > D_{12}$ and $D_{21} > D_{22}$, then the Doctor has a dominant strategy to treat [Doctor = 'Rx']. Therefore, the Patient should choose 'Trust' if $P_{11} > P_{21}$ and choose 'No Trust' if $P_{11} < P_{21}$
- 2 If $D_{11} < D_{12}$ and $D_{21} < D_{22}$, then the Doctor has a dominant strategy not to treat [Doctor = 'NoRx']. Therefore, the Patient should choose Trust if $P_{12} > P_{22}$ and choose No Trust if $P_{12} < P_{22}$.

As above, the first two situations describe the set of pure strategies available to the doctor or the patient.

- 3 Otherwise, we have $D_{11} > D_{12}$ and $D_{21} < D_{22}$ or $D_{11} < D_{12}$ and $D_{21} > D_{22}$. In other words, we have either $D_{11} - D_{12} > 0$ and $D_{22} - D_{21} > 0$ or $D_{11} - D_{12} < 0$ and $D_{22} - D_{21} < 0$. In either case, the ratio $\frac{D_{11}-D_{12}}{D_{22}-D_{21}} > 0$. As above, under this circumstance, the optimal strategy for the doctor cannot be pure one; rather, we need a mixed strategy.

As in the case of the patient, this leads to the following question: under which circumstances the doctor will be indifferent (has the same pay-offs) regardless of what the patient does?

If the patient trusts [Patient = 'Trust'] doctor y per cent of time and does not trust [Patient = 'No Trust'] $(1-y)$ per cent of time, then the doctor will be indifferent to the patient's 'move' if:

SOLVING FOR MIXED STRATEGY

$$y \cdot D_{11} + (1-y) \cdot D_{21} = y \cdot D_{12} + (1-y) \cdot D_{22}$$

$$y \cdot D_{11} + D_{21} - y \cdot D_{21} = y \cdot D_{12} + D_{22} - y \cdot D_{22}$$

$$y = \frac{D_{22} - D_{21}}{D_{11} - D_{12} - D_{21} + D_{22}} = \frac{1}{1 + \frac{D_{11} - D_{12}}{D_{22} - D_{21}}}$$

Note that since $\frac{D_{11} - D_{12}}{D_{22} - D_{21}} > 0$, we have: $0 < y < 1$, so the Patient should choose 'Trust' y per cent of the time

The Nash equilibrium for (Patient, Doctor) = (y, x) .

Just as with x , for our particular values of the utilities, we have our version of the formula for the y (using the notations for Doctor's utilities: $B_D = V_1 - V_3$ and $H_D = V_4 - V_2$):

$$D_{11} = E[Rx | Trust] \\ = p \cdot V_1 \cdot (1 - p) \cdot (V_2 - G \cdot (U_4 - V_2) - R_d \cdot (V_4 - V_2))$$

$$D_{21} = E[Rx | No Trust] = p \cdot (V_3 - F_d \cdot (V_1 - V_3)) \\ + (1 - p) \cdot V_4$$

$$D_{12} = E[NoRx | Trust] \\ = p \cdot (V_3 - G \cdot (U_1 - V_3) - R_d \cdot (V_1 - V_3)) + (1 - p) \cdot V_4$$

$$D_{22} = E[NoRx | No Trust] \\ = p \cdot (V_3 - G \cdot (U_1 - V_3) - R_d \cdot (V_1 - V_3)) + (1 - p) \cdot V_4$$

$$D_{11} - D_{12} = p \cdot V_1 + (1 - p) \cdot (V_2 - G \cdot (U_4 - V_2) - R_d \cdot (V_4 - V_2)) \\ - p \cdot (V_3 - G \cdot (U_1 - V_3) - R_d \cdot (V_1 - V_3)) - (1 - p) \cdot V_4 \\ = p \cdot V_1 + (1 - p) \cdot V_2 - G \cdot (1 - p) \cdot (U_4 - V_2) \\ - R_d \cdot (1 - p) \cdot (V_4 - V_2) - p \cdot V_3 + G \cdot p \cdot (U_1 - V_3) \\ + R_d \cdot p \cdot (V_1 - V_3) - (1 - p) \cdot V_4 \\ = p \cdot (1 + R_d) \cdot (V_1 - V_3) - (1 - p) \cdot (1 + R_d) \cdot (V_4 - V_2) \\ - G \cdot (1 - p) \cdot (U_4 - V_2) + G \cdot p \cdot (U_1 - V_3) \\ = p \cdot (1 + R_d) \cdot B_D - (1 - p) \cdot (1 + R_d) \cdot H_D \\ + G \cdot p \cdot (U_1 - V_3) - G \cdot (1 - p) \cdot (U_4 - V_2) \\ = -(1 - p) \cdot H_D \left[(1 + R_d) \cdot \left(1 - \frac{p}{1 - p} \cdot \frac{B_D}{H_D} \right) \right. \\ \left. + G \cdot \left(\frac{U_4 - V_2}{H_D} - \frac{p}{1 - p} \cdot \frac{U_1 - V_3}{H_D} \right) \right]$$

$$D_{22} - D_{21} = p \cdot (V_3 - G \cdot (U_1 - V_3) - R_d \cdot (V_1 - V_3)) + (1 - p) \cdot V_4 \\ - p \cdot (V_3 - F_d \cdot (V_1 - V_3)) - (1 - p) \cdot V_4 \\ = p \cdot V_3 - G \cdot p \cdot (U_1 - V_3) - R_d \cdot p \cdot (V_1 - V_3) + (1 - p) \cdot V_4 \\ - p \cdot V_3 + F_d \cdot p \cdot (V_1 - V_3) - (1 - p) \cdot V_4 \\ = -G \cdot p \cdot (U_1 - V_3) - R_d \cdot p \cdot (V_1 - V_3) + F_d \cdot p \cdot (V_1 - V_3) \\ = -(R_d - F_d) \cdot p \cdot (V_1 - V_3) - G \cdot p \cdot (U_1 - V_3) \\ = -(1 - p) \cdot H_D \cdot \frac{p}{1 - p} \left[(R_d - F_d) \cdot \frac{B_D}{H_D} + G \cdot \frac{U_1 - V_3}{H_D} \right]$$

Hence

$$y = \frac{1}{1 + \frac{D_{11} - D_{12}}{D_{22} - D_{21}}} \\ = \frac{1}{(1 + R_d) \left(1 - \frac{p}{1 - p} \cdot \frac{B_D}{H_D} \right) + G \cdot \left(\frac{U_4 - V_2}{H_D} - \frac{p}{1 - p} \cdot \frac{U_1 - V_3}{H_D} \right) \\ + \frac{\frac{p}{1 - p} \cdot \left[(R_d - F_d) \cdot \frac{B_D}{H_D} + G \cdot \frac{U_1 - V_3}{H_D} \right]}{1 + \frac{D_{11} - D_{12}}{D_{22} - D_{21}}}$$

Note that the sign of $D_{11} - D_{12}$ is then the same as the sign of $-\left[(1 + R_d) \cdot \left(1 - \frac{p}{1 - p} \cdot \frac{B_D}{H_D} \right) + G \cdot \left(\frac{U_4 - V_2}{H_D} - \frac{p}{1 - p} \cdot \frac{U_1 - V_3}{H_D} \right) \right]$, as we are assuming that $1 - p \geq 0$ and

$H_D \geq 0$. Similarly, the sign of $D_{22} - D_{21}$ same as the sign of $-\left[(R_d - F_d) \cdot \frac{B_D}{H_D} + G \cdot \frac{U_1 - V_3}{H_D} \right]$.

SUMMARY of best possible strategies:

Let's now summarize all possible 'best' strategies we considered so far:

1 If $P_{11} - P_{21} > 0$ or $\frac{p}{1 - p} \cdot \frac{B_D}{H_D} > 1$, then the Patient has a dominant strategy to 'Trust', and the Doctor knows that the patient will play the first row of the pay-off matrix (Table 1). So, she/he should choose 'Rx' or 'NoRx' depending whether D_{11} or D_{12} is larger.

In other words, if $\frac{p}{1 - p} \cdot \frac{B_D}{H_D} > 1 \Rightarrow$ Patient = 'Trust', and the doctor should choose 'Rx' if

$$-\left[\left(1 - \frac{p}{1 - p} \cdot \frac{B_D}{H_D} \right) + \frac{G}{1 + R_d} \cdot \left(\frac{U_4 - V_2}{H_D} - \frac{p}{1 - p} \cdot \frac{U_1 - V_3}{H_D} \right) \right] > 0 \text{ and 'NoRx' if } \\ -\left[\left(1 - \frac{p}{1 - p} \cdot \frac{B_D}{H_D} \right) + \frac{G}{1 + R_d} \cdot \left(\frac{U_4 - V_2}{H_D} - \frac{p}{1 - p} \cdot \frac{U_1 - V_3}{H_D} \right) \right] < 0.$$

Note that the relationship $\frac{p}{1 - p} \cdot \frac{B_D}{H_D} > 1$ is equivalent to the classic expected utility threshold [30,31], $p > \frac{1}{1 + \frac{B_D}{H_D}}$, that is, this

means that **the most rational strategy for the patient is to trust whenever** the probability of disease is larger than the expected utility threshold, i.e. **when doctor assesses that expected net benefit (B_D) of the treatment is larger than its expected net harms (H_D)**.

2 If $D_{11} - D_{12} > 0$ and $D_{22} - D_{21} < 0$, or in other words, if $-\left[(1 + R_d) \cdot \left(1 - \frac{p}{1 - p} \cdot \frac{B_D}{H_D} \right) + G \cdot \left(\frac{U_4 - V_2}{H_D} - \frac{p}{1 - p} \cdot \frac{U_1 - V_3}{H_D} \right) \right] > 0$ and $-\left[(R_d - F_d) \cdot \frac{B_D}{H_D} + G \cdot \frac{U_1 - V_3}{H_D} \right] < 0$, then the Doctor has a dominant strategy to treat [Doctor = 'Rx']. Therefore, the Patient should choose 'Trust' if $-\left[1 - \frac{p}{1 - p} \cdot \frac{B_D}{H_D} \right] > 0$ and choose 'No Trust' otherwise.

3 If $D_{11} - D_{12} < 0$ and $D_{22} - D_{21} > 0$, or in other words, if $-\left[(1 + R_d) \cdot \left(1 - \frac{p}{1 - p} \cdot \frac{B_D}{H_D} \right) + G \cdot \left(\frac{U_4 - V_2}{H_D} - \frac{p}{1 - p} \cdot \frac{U_1 - V_3}{H_D} \right) \right] < 0$ and $-\left[(R_d - F_d) \cdot \frac{B_D}{H_D} + G \cdot \frac{U_1 - V_3}{H_D} \right] > 0$ then the Doctor has a

dominant strategy not to treat [Doctor = 'NoRx']. Under this circumstances, the Patient should choose Trust as we have already noticed that we always have $P_{22} - P_{12} < 0$.

That is, when the doctor recommends no treatment, it is rational for the patient to accept it.

- 4 Otherwise, we have both: the ratio $\frac{P_{11}-P_{21}}{P_{22}-P_{12}} > 0$ and the ratio $\frac{D_{11}-D_{12}}{D_{22}-D_{21}} > 0$, resulting in the mixed strategies: the rational strategy for the patient is to choose 'Trust' y per cent of the time and 'No Trust' $(1-y)$ per cent of the time, and the rational strategy for the Doctor is to choose 'Rx' x - per cent of the time and 'NoRx' $(1-x)$ per cent of the time, where

$$x = \frac{1}{1 + \frac{(1+R_p) \left[1 - \frac{p}{1-p} \frac{B_p}{H_p} \right]}{F_p \cdot \left[1 + \frac{p}{1-p} \frac{B_p}{H_p} \right]}}$$

$$y = \frac{1}{1 + \frac{(1+R_d) \left(1 - \frac{p}{1-p} \cdot \frac{B_D}{H_D} \right) + G \cdot \left(\frac{U_4-V_2}{H_D} - \frac{p}{1-p} \cdot \frac{U_1-V_3}{H_D} \right)}{\frac{p}{1-p} \cdot \left[(R_d - F_d) \cdot \frac{B_D}{H_D} + G \cdot \frac{U_1-V_3}{H_D} \right]}}$$

Let us now consider Model B (Fig. 1b): the patient demands treatment and gets it!

Following the same approach as above, we get:

$$P_{11} = E[\text{Trust, Rx}] = p \cdot U_1 + (1-p) \cdot (U_2 - R_p(U_4 - U_2)).$$

$$P_{21} = E[\text{No Trust, Rx}] = p \cdot (U_3 - R_p(U_1 - U_3)) + (1-p) \cdot U_4.$$

$$P_{12} = E[\text{Trust, NoRx}] = p \cdot (U_3 - R_p(U_1 - U_3)) + (1-p) \cdot U_4.$$

$$P_{22} = E[\text{No Trust, NoRx}] = p \cdot U_1 + (1-p) \cdot (U_2 - R_p(U_4 - U_2))$$

$$D_{11} = E[\text{Rx, Trust}] = p \cdot V_1 + (1-p) \cdot (V_2 - G \cdot (U_4 - V_2) - R_d \cdot (V_4 - V_2))$$

$$D_{21} = E[\text{Rx, No Trust}] = p \cdot (V_3 - F_d \cdot (V_1 - V_3)) + (1-p) \cdot V_4$$

$$D_{12} = E[\text{NoRx, Trust}] = p \cdot (V_3 - G \cdot (U_1 - V_3) - R_d \cdot (V_1 - V_3)) + (1-p) \cdot V_4$$

$$D_{22} = E[\text{NoRx, No Trust}] = p \cdot V_1 + (1-p) \cdot (V_2 - G \cdot (U_4 - V_2) - R_d \cdot (V_4 - V_2))$$

In this case, $P_{11}-P_{21}$ and $D_{11}-D_{21}$ are the same as before, however, the other two differences will change slightly:

$$P_{11} - P_{21} = -(1+R_p)(1-p)H_p \left[1 - \frac{p}{1-p} \frac{B_p}{H_p} \right]$$

$$D_{11} - D_{12} = -(1-p) \cdot H_D \left[(1+R_d) \cdot \left(1 - \frac{p}{1-p} \cdot \frac{B_D}{H_D} \right) + G \cdot \left(\frac{U_4-V_2}{H_D} - \frac{p}{1-p} \cdot \frac{U_1-V_3}{H_D} \right) \right]$$

$$\begin{aligned} P_{22} - P_{12} &= p \cdot U_1 + (1-p) \cdot (U_2 - R_p \cdot (U_4 - U_2)) \\ &\quad - p \cdot (U_3 - R_p \cdot (U_1 - U_3)) - (1-p) \cdot U_4 \\ &= p \cdot U_1 + (1-p) \cdot U_2 - R_p \cdot (1-p) \cdot (U_4 - U_2) - p \cdot U_3 \\ &\quad + R_p \cdot p \cdot (U_1 - U_3) - (1-p) \cdot U_4 \\ &= p \cdot (U_1 - U_3) + R_p \cdot p \cdot (U_1 - U_3) - (1-p) \cdot (U_4 - U_2) \\ &\quad - R_p \cdot (1-p) \cdot (U_4 - U_2) \\ &= p \cdot (1+R_p) \cdot B_p - (1-p) \cdot (1+R_p) \cdot H_p \\ &= -(1+R_p)(1-p)H_p \left[1 - \frac{p}{1-p} \frac{B_p}{H_p} \right] \end{aligned}$$

So – in this case – the ratio $\frac{P_{11}-P_{21}}{P_{22}-P_{12}} = 1$, so the 'mixed strategy' is $x = \frac{1}{2}$, that is the Doctor should simply flip a coin to determine which strategy to choose akin to what he would be if the patient would participating in a randomized trial.

$$\begin{aligned} D_{22} - D_{12} &= p \cdot V_1 + (1-p) \cdot (V_2 - G \cdot (U_4 - V_2) - R_d \cdot (V_4 - V_2)) \\ &\quad - p \cdot (V_3 - G \cdot (U_1 - V_3) - R_d \cdot (V_1 - V_3)) - (1-p) \cdot V_4 \\ &= p \cdot V_1 + (1-p) \cdot V_2 - G \cdot (1-p) \cdot (U_4 - V_2) \\ &\quad - R_d \cdot (1-p) \cdot (V_4 - V_2) - p \cdot V_3 + G \cdot p \cdot (U_1 - V_3) \\ &\quad + R_d \cdot p \cdot (V_1 - V_3) - (1-p) \cdot V_4 \\ &= p \cdot (1+R_d) \cdot (U_1 - V_3) - (1-p) \cdot (1+R_d) \cdot (V_4 - V_2) \\ &\quad - G \cdot (1-p) \cdot (U_4 - V_2) + G \cdot p \cdot (U_1 - V_3) \\ &= p \cdot (1+R_d) \cdot B_D - (1-p) \cdot (1+R_d) \cdot H_D \\ &\quad - G \cdot (1-p) \cdot (U_4 - V_2) + G \cdot p \cdot (U_1 - V_3) \\ &= -(1-p) \cdot H_D \cdot \left[(1+R_d) \cdot \left(1 - \frac{p}{1-p} \frac{B_D}{H_D} \right) \right. \\ &\quad \left. + G \cdot \left(\frac{U_4-V_2}{H_D} - \frac{p}{1-p} \frac{U_1-V_3}{H_D} \right) \right] \end{aligned}$$

So – in this case – the ratio $\frac{D_{11}-D_{12}}{D_{22}-D_{21}} = 1$, so the 'mixed strategy' is $y = \frac{1}{2}$, the patient should also simply flip a coin, or to choose

to participate in randomized trial to determine which strategy to choose.

Liability model

Another possible parameter consideration for this particular problem is when the physician fears of law suit if he refuses to prescribe treatment to the patient who demands it. DeKay and Asch defined liabilities as Lrx_t = Liability of (Rx and D-) with Trust; Lrx_{nt} = Liability of (Rx and D-) with NoTrust; Lnr_{xt} = Liability of (NoRx and D+) with Trust; Lnr_{xt} = Liability of (NoRx and D+) with NoTrust [32]. However, in our set-up, a natural way to introduce liabilities is by controlling their magnitude by considering them as proportion of loss of patient's utilities, which makes this definition of liability not substantively different from regret in our model. So, conceptually regret incorporates liabilities although the units may differ.

Effect of probability of disease on the choice of strategy

Our model assumes that we are not certain that the patient has a disease or not. It is natural to ask whether the choice of strategy depends on the probability of disease. Figure 2 shows that that the situation is fairly confusing for low values of $P < 0.25$; however, when we are fairly certain in the presence of the disease ($P > 0.5$), the prevailing strategy becomes 'Doctor recommends treatment (Rx)' and 'Patient Trusts (T)'. If we further split the occurrences of all strategy combinations into two categories: Rx-T-D+ (treatment in the setting of trust when

the disease is really present) and Rx-T-D- (treatment in the setting of trust when the disease is not present), we can see that as P approaches certainty the choice of strategy Rx-T-D+ becomes inevitable.

Simulating clinical situations of the Prisoners' Dilemma

We complemented this analysis by employing Monte Carlo modelling technique by varying all variables. We assumed similar values for the utilities as those in our original model [13]. We run the analysis for 100 000 trials (the results are shown in Table 2). The latter analyses were performed using the Microsoft EXCEL software (available from the authors upon the request). The concerning results emerged: attempts to advance individual strategic interests led to inappropriate management (under- or overtreatment) in 42% of simulations. The results were different if the different utilities we assumed in the model. However, regardless of the initial values of the utilities we assumed in the model, a sizeable proportion of the simulations resulted in inappropriate under or over-treatment. Obviously, the precise answer remains an open empirical question, stressing the importance of obtaining empirical data related to the model parameters.

In general, we were able to derive the following generic findings (see Fig. 2 and Table 2):

- 1 When the patient's utilities clearly indicate that the dominant strategy for the patient is to trust the physician, the physician should choose whatever she/he thinks is best for the patient;
- 2 When the doctor's utilities clearly indicate that the dominant strategy is to recommend treatment, the patient's best strategy is to choose to trust the physician provided that he is assured that expected benefits outweigh the expected harms for the given probability of disease;
- 3 Interestingly, when the doctor's utilities indicate that the strategy of recommending against treatment is dominant, the patient should trust the doctor regardless of his own utilities;
- 4 When neither strategy is dominant, a rational approach would be to randomize the strategy of choice. That is, each 'player' is better off if he/she is to choose a **mixed strategy**, i.e. select one strategy with probability P and the alternative strategy with probability $(1-P)$. The value of this probability depends on the expected utilities in the pay-off matrix, which depend on a collection of assumptions on utilities, the patient and doctor's regret, guilt and frustration between recommending/not recommending and accepting/not accepting treatment, respectively. Sometimes, this may mean that the best option for both the patient and the physician is to participate in a randomized controlled trial [13].

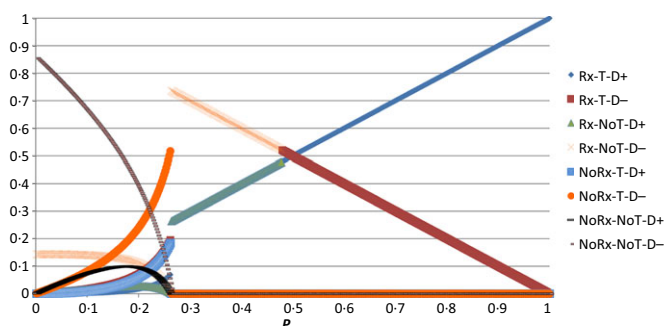


Figure 2 Sensitivity analysis. Effect of probability of disease on the choice of strategy. Abbreviations: Rx-T-D+: treat-trust-disease positive; Rx-T-D-: treat-trust-no disease; Rx-NoT-D+: treat-no trust-disease positive; Rx-NoT-D-: treat-no trust-no disease; NoRx-T-D+: no treatment-trust-disease positive; NoRx-T-D-: no treatment-trust-no disease; NoRx-NoT-D+: no treatment-no trust-disease positive; NoRx-NoT-D-: no treatment-no trust-no disease.

Table 2 Choosing the best strategy*

Correct Treatment with Trust (Administering Rx to the patient who has disease within a setting of mutually trustful relationship between the physician and the patient)	33.19% [32.62, 33.76]
Overtreatment with Trust (Administering unnecessary Rx to the patient who may not have disease in mutual trustful relationship between the physician and the patient)	24.59% [24.19, 24.99]
Correct Treatment with Mistrust (Administering Rx to the patient who has disease but within a setting of mutually distrustful relationship between the physician and the patient)	10.29% [9.92, 10.66]
Overtreatment with Mistrust (Administering unnecessary Rx to the patient who may not have disease but within the setting of mutually distrustful relationship between the physician and the patient)	10.24% [9.93, 10.56]
Undertreatment with Trust (Failing to administer Rx to the patient who has disease within a setting of mutually trustful relationship between the physician and the patient)	3.99% [3.78, 4.2]
Correct nontreatment with Trust (Correctly not administering Rx to the patient who does not have a disease within a setting of mutually trustful relationship between the physician and the patient)	8.13% [7.78, 8.48]
Undertreatment with Mistrust (Failing to administer Rx to the patient who has disease but within a setting of mutually distrustful relationship between the physician and the patient)	2.51% [2.4, 2.63]
Correct nontreatment with Mistrust (Correctly not administering Rx to the patient who does not have a disease within a setting of mutually distrustful relationship between the physician and the patient)	7.05% [6.74, 7.36]
Total	Of total 100%, only 58.66% recommendations are correct

*Based on Monte Carlo simulation (100 000 runs).

5 When the probability of a clinical event (e.g. the probability of disease and response to therapy) is high (> 50%), the best strategy for the doctor is to recommend treatment and for the patient to trust the doctor and accept his recommendation.

Escaping the Prisoner's Dilemma

The decision whether to commit to one management strategy or another heavily depends on our ability to know accurately enough the probability of health outcomes of interest. This means that we need unbiased evidence both on the prevalence of outcomes and on the effects of available interventions on them, that is, we need better-informed, evidence-based practice [33,34]. In addition, specific solutions of health care 'games' depend on our knowledge of the physician and patient-specific characteristics such as understanding the stakes (pay-offs) in the 'game' as well as other key variables related patient-reported outcomes including emotions such as regret of both patient and physicians, guilt of the doctor, and the level of frustration the patient may feel. This situation highlights the importance of having reliable data on these aspects to determine the most optimal strategy. Regret, guilt

and frustration can be quantified using psychometric measurement approaches.

The fundamental way out of the Prisoners' Dilemma is to enable clinical interactions within a framework of trust in the healthcare system. Unfortunately, the medical profession does not currently enjoy much trust as it has historically [35–37]. Current trends in health care may further incentivize self-interests of all parties involved in health care and may likely further undermine the patients' trust in physicians. When trust is eroded, the Prisoners' Dilemma creeps in the relationship and may dominate human interactions. The only way out is to change the structure of the game [14]. Society should incentivize the alignment of interests of doctors and patients. When the pay-offs of different players are similar, the game theory conflict does not apply any more. The alignment can be improved by having more transparency in health care including clarifying expectations on part of both physicians and patients. When the utilities of the patient are such that the trust is high, the Prisoners' Dilemma is avoidable [14]. It is building trust that historically has kept a patient–physician encounter outside of the confines of the game theory [17].

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