The Cochrane case: an epistemic analysis on decision-making and trust in science in the age of information

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Abstract

In this study we analyze a recent controversy within the biomedical world, concerning the evaluation of safety of certain vaccines. This specific struggle took place among experts: the Danish epidemiologist Peter Gøtzsche on one side and a respected scientific institution, the Cochrane, on the other. However, given its relevance, the consequences of such a conflict invest a much larger spectrum of actors, last but not least the public itself. Our work is aimed at dissecting a specific aspect happening in this complex scenario: strategy. In other words, we want to highlight the value and the impact of strategic decisions when complex issues, as those analyzed, are at stake. In order to address this we have decided to adopt a game-theoretic approach. Our work will be structured as it follows. First, we will introduce the controversy and the two main actors: Peter Gøtzsche and the Cochrane. Second we will explain why this controversy is important and its value beyond its academic relevance. Third, we will frame the controversy as a game and will provide several models representing different situations, also furnishing an analysis of these distinct scenarios. In the end we will argue why such game-theoretic approach can be useful in dissecting this type of issues.

Keywords: Cochrane, HPV vaccine, decisions, public health policies, experts disagreement.

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1 Introduction

Taking decisions, in general, is not an easy task. When science is involved, this is, obviously, even more complicated. Indeed, scientific research is a cornerstone of contemporary societies. Virtually any sector of everyday life is shaped by scientific research. Science is not just a pure epistemic enterprise whose unique aim is the search for truth. Rather, scientific activities mirror the type of society that express them. In turn, as in dialectical relation, the outcomes of scientific endeavor frame and modify the constitution of society itself. To put it roughly: science is not neutral (to this respect, see for instance [16, 14]). For this reason, decisions concerning science are not only deeply intertwined with other factors (such as economical and political) but they often reveal different accounts on what science is or should be, thus different images of science itself. Of course, many levels of analysis and approaches have been elaborated in order to investigate how decisions are taken when science and its value are at stake. One may ask whether a particular way of doing (i.e. a given choice) is *reasonable*, in the sense that it is in compliance with the methodological standards and the well established practices and procedures of contemporary scientific research. Differently, one may want to investigate whether certain actions are in line with specific images of science or whether a decision matches with a given *ethics of science*. Last, but not least, it is possible to examine if a certain course of action concerning science is convenient given the socio-political and economic context in which a particular scientific effort takes place. All these aspects are important and a lot of work has already be done (see for instance [14]). Indeed, it is certainly true that a question of this complexity, such as decisions concerning evidence and its consequences on policies and public dimension of science, is definitely influenced and shaped by various factors. In the present work we certainly do not intend to forget this fact. However, we believe that a "game-theoretic" approach should not be considered, *per se*, "external". Rather, its adoption reflects not just an ontological commitment but rather a methodological choice, consisting in decomposing a problem into more manageable ones, in order to be studied and explained. Therefore, we are perfectly aware that our proposal deals with just one aspect of the entire issue. Indeed, it simply represents the effects of only one of these factors. As previously mentioned, it is obvious that this situation represents a simplification and present an unavoidable degree of idealization. Nevertheless, we believe this is an intrinsic limitation occurring whenever mathematics and formal methods are used to model complex phenomena such as human behavior.

Bearing this in mind, in our analysis we want to focus on another aspect, also crucial: rationality of decisions in a more technical sense.

Our work is aimed at dissecting a specific aspect happening in complex decisions: strategy. In other words, we want to highlight the value and the impact of strategic decisions when complex issues, as those analyzed, are at stake. In order to address this we have decided to adopt a game-theoretic approach. *Game theory*

refers to a particular way to analyze situations in which actions and decisions can be labelled as rational. Accordingly, a conflict (i.e. a game) is defined by at least two players, a bundle of pure strategic options for each player and the players' payoffs derived by combinations of actions. The advantage of this approach is that it allows to emphasize the rational components of a choice, often hidden by other layers of investigation, in order to provide new insights in the the epistemic analysis of a complex phenomenon.

In this study we analyze a recent controversy within the biomedical world, concerning the evaluation of safety of certain vaccines. This specific struggle took place among experts: the Danish epidemiologist Peter Gøtzsche on one side and a respected scientific institution, the Cochrane, on the other. However, given its relevance, the consequences of such a conflict invest a much larger spectrum of actors, last but not least the public itself.

Therefore, we plan to structure our work as follows. First, we will introduce the controversy and the two main actors: Peter Gøtzsche and the Cochrane. Second, we will explain why this controversy is important and why its value goes beyond its academic importance. Third, we will frame the controversy as a game and will provide several models representing different situations, also furnishing an analysis of these distinct scenarios. In the end we will argue why such game-theoretic approach can be useful in dissecting this type of issues. Accordingly, the paper is organized into seven sections. We begin by setting context of the dispute, in Section 2. Next, we present the aim of the present paper, in Section 3, while dedicate Section 4 to focus on the philosophical and social issues that are at stake in the Cochrane case. Section 5 is devoted to the introduction of the some basic games: the aim is modelling the possible the strategic interactions that might have occurred between Gøtzsche and the Cochrane, in the whole case. Section 6 focuses on the public relevance of the case, while the conclusion to be drawn from our model (and the relative discussion) is left to Section 7.

2 Framing the context: Peter Gøtzsche vs Cochrane

Recently, the Cochrane[1] (formerly known as "Cochrane Collaboration"), one of the most important independent scientific institutions concerning the review of clinical and health practices, has been invested by a heated controversy which can have important repercussions on both the world of clinical research and the perception of it by the general public.

[1]The name comes from Archie Cochrane, a Scottish epidemiologist, who first proposed the idea of a medicine based on evidence of effectiveness and efficiency, the so-called "evidence-based medicine" (EBM).

Last September, during the twenty-fifth Cochrane Colloquium, a meeting of Cochrane representatives dedicated to the discussion of the soundness and solidity of the tools and evidence (*i.e.* the criteria of Evidence Based Medicine or EBM, according to which decisions, concerning the efficacy and potential harm of drugs and other medical devices, are taken in the biomedical world), one of the members of the Nordic Cochrane Center and co-founder of Cochrane itself, the Danish scientist Peter Gøtzsche (since 2010, professor of Clinical Research Design and Analysis at the University of Copenhagen), was accused, by the leadership of the Cochrane, of misconduct and subsequently expelled from the Cochrane itself. The event actually concludes a long fight between Gøtzsche and the new leaders of the organization. Gøtzsche accused Cochrane board of being increasingly prone to the economic interests related to the business produced by biomedical research and progressively less concerned with the robustness and solidity of scientific work[2]. Roughly speaking, Gøtzsche claims that Cochrane seeks money rather than "truth". As a matter of fact, his expulsion is a direct reaction to his critical move.

Peter Gøtzsche is not completely new to this type of critique. Throughout his entire career, Gøtzsche has often raised doubts about methodological and ethical issues concerning biomedical research. He particularly focused on meta-analysis, suggesting ongoing issues in data-extraction [5] and advocating for a broader and more solid perspective in this field [8]. Moreover, he also called attention towards scientific misconduct[3] [6]. Gøtzsche has a long history of clashing with the pharmaceutical world (*e.g.* publicly criticizing the way psychiatric drugs are prescribed and used[4]). He is also famous for having harshly criticized public health policies, such as mammography screenings [7], generating an intense public debate. More recently, in 2013, he published a book entitled "*Deadly Medicines and Organized Crime: How Big Pharma has Corrupted Healthcare*" [4], in which he denounces the pharmaceutical industry, both from the scientific stance and in its financial dimension, blaming it for immoral (even illegal) behavior and supporting the need for a radical reform of the entire sector.

In July 2018, Gøtzsche and two other colleagues published an article [12] criticizing one of Cochrane meta-analysis [1] (produced by another group), questioning the results concerning the safety of *papilloma virus*(HPV) vaccines. According to Gøtzsche and his colleagues, that review was unreliable and compromised by different bias (including cherry picking, reporting bias and biased trial designs). Gøtzsche article was also, and above all, a clear accusation of superficiality (or even worse, of misconduct), for the perpetration of several methodological errors

[2]See for instance https://blogs.bmj.com/bmj/2018/11/08/peter-c-gotzsche-cochrane-no-longer-a-collaboration/.

[3]See also https://www.madinamerica.com/2017/02/editorial-misconduct-finnish-medical-journal-rejects-paper-suicide-risk/.

[4]See https://www.theguardian.com/commentisfree/2014/apr/30/psychiatric-drugs-harm-than-good-ssri-antidepressants-benzodiazepines

and for ignoring almost half of the studies on the HPV vaccines. Moreover, and probably more seriously, it has been also claimed that those studies had already been pointed out to the authors of the review, thus suggesting a deliberate exclusion of them. Lastly, Gøtzsche and colleagues also insinuated that the review presented serious issues concerning conflicts of interest, implying that such aspects were uncritically presented to the public.

The fact that Gøtzsche had advanced these objections on the official Cochrane letterhead (an element that, some argued, could be taken as evidence of authority by anti-vaccine movements) has been severely condemned by the Cochrane leaders. Gøtzsche was thus accused of "bad behavior", responsible of discrediting the Cochrane and potentially contributing to public distrust towards science. Therefore, according to the internal regulations[5], he was considered subject to expulsion, which promptly took place. In disagreement with this decision, four other members of the councilor resigned, followed (for technical reasons that allowed the board to remain in office) by two others.

3 Aim

The aim of our contribution is to show that Peter Gøtzsche's decisions constitute the best response (i.e. the most rational one) given his convictions and the attitude of Cochrane. Of course, this result must be intended within the specific conceptual paradigm that sees science as an ethical and collective enterprise, fully transparent and less conditioned as possible by the interests of the industry. We are fully aware that this is a form of idealization. However, the fact that actual scientific research is not pure or isolated as desired, does not mean that models of improving the current situations are futile or doomed to fail. On the contrary, we believe that not all scientific agendas are good to be pursued as such nor all scientific debates are equally important. Analyzing and criticizing them is precisely part of the work of philosophers of science. For instance, the work of Philip Kitcher [14], in its attempt to construct a social and political framework to scrutinize, discuss and evaluate scientific research, goes precisely in this direction. Of course our goal here is not to build an alternative framework. However, we want to show that, in this case, given that specific, widely shared and desired, image of science, Gøtzsche's decisions are not only justified and motivated by strong ethical and political considerations. They are also the most rational ones. In doing so, we opt for the specific way in which rationality is usually addressed in *game theory*, where players' actions are usually (but not always) selected according to the principle of maximization of expected utility. We are perfectly aware that the chosen approach is not the only way to deal with "rationality" in a broad sense. Moreover, we recognize that this kind of approach has limitations [13]. However, for our purposes, we believe game theory is the most adequate one, because it allows to focus on the strategic

[5]See https://www.cochrane.org/news/statement-cochranes-governing-board.

dimension of decision making, which is the aspect we want to analyze. Of course, we are also aware that decision making is not fully represented by just strategies. Nevertheless, since the controversy has a public impact, it needs to be judged also in terms of gain and losses that have to be measurable or quantifiable. This is somehow necessary when decisions are likely to be turned into policies, guidelines or recommendations (such as the outcomes of Cochrane reports).

We believe that our approach can be useful in, at least, two ways. First, it can contribute to foster a particular approach to deal with this kind of issues, just from a methodological point of view. Second, more importantly, the insights and details provided by this kind of analysis could provide a more solid ground for dealing with serious and complex problems concerning scientific/academic struggles with a strong impact on society. The complexity and the relevance of this scenario is due to the fact that the Cochrane is not just a simple organization. It is quite unique and precious, considering the difficulties of scientific research and its public perception. In an age of crisis of scientific publishing (a sector often infested by "predatory magazines", where, by paying, almost anything can be published) current scientific investigation is facing the so called *reproducibility crisis* [9]. Although misleading, according to some scholars [2], the expression describes a situation of trouble for both scientific enterprise as and its justification in the public sphere. The scenario is also worsened by the fact that an immense amount of results, especially negative or unfavorable [17], are likely to remain unknown[6]. These problems, combined with a lack of transparency, have the potential of threatening both the efficacy of science itself and the necessary trust science needs to be pursued at the public level. Moreover, the increasing lack of independent funds bends many scientific research to external interests (not always for the sake of knowledge) which makes this quarrel more than just an academic one. Finally, biomedical sciences are intrinsically value-laden due to their impact on public life. A more accurate and careful representation of biomedicine is crucial to both determine its internal efficacy and its societal support. Because of that, even if EBM definitely provides an improvement, it must be integrated with other elements, such as feasibility and economic sustainability, patients' preferences and needs, in order to furnish clinical recommendations useful to physicians and patients.

Therefore, a correct evaluation of research, the soundness of the methodologies adopted, and the range of possible implications, is not an easy task. Even for professional scientists there are too many studies, too many data, too many specializations, too many different areas of investigations, tools, approaches. Bearing this in mind, the Cochrane activity has begun and has been pursued following the idea that science is a collective, collaborative enterprise. The purpose was to combine experts able to collect, select and analyze the data emerged from the different

[6]Hence one of the most pressing demands of researchers close to Gøtzsche is the possibility to access the original data, despite their size and type, in order to reach even more reliable conclusions.

studies published on a given topic, in order to respond to a clinical question with a clear, precise and solid review. Because of that, it is easy to recognize the public value of Cochrane, besides its scientific one.

Moreover, the case of Cochrane clearly exhibits a tension between two fundamental values of contemporary technological society: the right to inform and research freedom. On one hand, science rests on critical thinking. In other words, it is at core of scientific practice the possibility to question its own methods and organization. On the other hand, scientific disagreement and debate, always legitimate, can cause troubles in the way science is effectively pursued and perceived, first by scientific community itself, and by the public. A crisis of this kind concerning the Cochrane can be a serious threat for the world of science itself[7].

4 What is at stake?

The Cochrane issue concerns the epistemic possibility of establishing reliable criteria for the assessment of clinical and scientific evidence. The ways according to which "science works" and is effective are still a philosophical puzzle in many details. From a practical perspective, there are several aspects that might help to determine a "good scientific work". Data must be solid as much as the collection strategies adopted to obtain and to organize them (let's call this "scientific methodologies") are rigorous. In the age of information, the need to gather and integrate distinct pieces of different types knowledge (obtained by various approaches, via different procedures and certified by different journals) is particularly demanding and yet necessary. Since it is not something that a single scientist or group can do, the chance to delegate to these capable people these very complicated analyzes, is crucial for several reasons:

1. First, there is the recognition that contemporary science (at least in biomedicine) requires a competence which has to be based on multiple forms of expertise, thus shared and discussed with different kinds of experts and checked against non-experts priorities, needs, expectations.

2. Second, researchers need to be free to discuss their results, to question their methods, practices and conclusions at any time, using reliable, reproducible, controlled criteria (see, for instance [11]).

3. Third, the unavoidable delegation of knowledge should rely on trust. The type of trust that experts' judgment will be based on solid, reproducible, controlled research. Without trust, information as such, something we all need to make informed choices, is not enough (this is somehow related to the questions discussed by Philip Kitcher [14].

[7] See https://blogs.bmj.com/bmj/2018/09/17/ray-moynihan-lets-stop-the-burning-and-the-bleeding-at-cochrane-theres-too-much-at-stake/.

Information and freedom are two key aspects of scientific research. Yet, one may ask, also in scientific disputes, whether there will be ways to analyze and model those situations in which different viewpoints are in conflict and, accordingly, specific actions/decisions are taken, bearing in mind the aim of scientific research and its intrinsic social value.

Given this context, our epistemic analysis aims at providing an operational frame that might serve as an indication or a potential guideline, in cases of scientific conflicts. In this respect we plan to work on different levels in the following manner:

a) First, we will provide a variety of simple models, through a game-theoretic approach that can represent the situation of Cochrane vs. Gøtzsche as a game between two players.

b) Second, we will discuss and interpret the results of our analysis as a morale to briefly discuss the issue of struggles in science where there is an impact onto the public sphere, (in the sense suggested by Kitcher [14])

5 A game theoretical analysis

It is our conviction that the case of Peter Gøtzsche vs Cochrane goes beyond the mere academic quarrel and cannot be fully reduced to a struggle over the soundness of methodology within biomedical and clinical science. Epistemic issues do not live in a rarefied space detached from actual world. On the contrary, very often, "epistemic fights" of this kind are deeply intertwined with, and will eventually have an impact on, social and political dimensions concerning the relationship between science, society and public policies. Therefore, we believe that a first move to dissect this issue, being out of the quarrel and aiming to a clarification that can benefit both scientific research and the public, could be to determine whether the conflict at stake can be somehow formally modelled and, if this is the case, how the information provided by the model can improve a better understanding of the affair[8]. In particular, we firmly think that both the actors involved in the clash (Gøtzsche and Cochrane) took their decisions taking into account the strategic implications of their acts, meaning that they have weighed the consequences of their choices and actions. Given this as granted, we will use *game theory* and see how some very basic models can provide a picture of how the situation has evolved to provoke Gøtzsche's expulsion as a *reaction* of the Cochrane to the criticism he

[8]We are perfectly aware that a formal model has limitations in representing the complexity of a situation like the one at stake. However, the purpose of a model is precisely to abstract and distort certain relevant features in order to highlight precise dynamics which will be invisible to the simple observation. Thus, the purpose of the model(s) we will propose is not that of "solving" a complex issue by neglecting its complexity but rather to point out certain relevant features that might contribute to a better understanding of that complex scenario.

moved. In particular, we aim at individuating possible strategic interactions taking place in the Cochrane case, as outlined above. First, we will briefly recall the basic notions of game theory[9].

A *game* is a model of interaction between decision-makers. Decision-makers are interpreted as *players*, and each of them has a set of (possible) *actions*. A *preference* relation allows each player to order actions dependently on the opponents' actions.

In the case under analysis, the strategic interaction took place between two main actors: Peter Gøtzsche, on the one side, and the Cochrane (entire) board, on the other. For our purpose, we may think as the latter player as a unique agent representing the interest of Cochrane itself, as a unitary institution. This assumption may sound as a simplification; however, we are concerned with the *effect* of a decision of the Cochrane with respect to (the misconduct of) one of its members, Peter Gøtzsche, and not with the internal dynamics of interactions of the the Cochrane.

Games can be *simultaneous*, i.e. players can be assumed to take action at the same time[10], or *sequential*, namely that players act one after another. In other words, if we consider a two-players game, one player acts first, and, only afterwards, the opponent reacts.

Gøtzsche's actions can be schematized as follows: either to fully disclose his opinions, namely to publish a paper which strongly criticizes the Cochrane's review or to discuss his objections privately within the Cochrane itself. On the other hand, the board of Cochrane, in quality of Gøtzsche's opponent (in this abstract game) may either opt for *approving* of *disapproving* his behaviour. Given the structure of the actions, the game is clearly sequential, as the Cochrane's action comes necessarily after Gøtzsche's choice to either share his criticism publicly or only privately, within the Cochrane's board. The tree structure of the game is drawn in Figure 1.

Preferences of the players are ordered according to the payoffs depicted on the leaves of the tree. We use numbers as numerals providing the set of actions with a preference relation: an action getting a higher payoff (depending on the opponent's move) is preferred over one getting a lower payoff. We will describe different strategic situations by changing players' payoffs[11]. Table 1 summarizes the payoffs of the game (Gøtzsche is the row player). Recall that his actions are: "Public" (he chooses to share his ideas publicly, for instance submitting a

[9]For a comprehensive book in the discipline, we refer to the classic [18].

[10]This does not mean that actions *actually* takes places simultaneously: players fix the choice of actions simultaneously.

[11]We could describe the same situations, in a more abstract way, by setting, for example, g_1 and g_2 as the payoffs of G when goes public, g_3 and g_4 when goes Private, and similarly for the Cochrane. However, we believe that opting for numbers increase clarity of exposition and comprehension also for the reader who is not familiar with game theory.

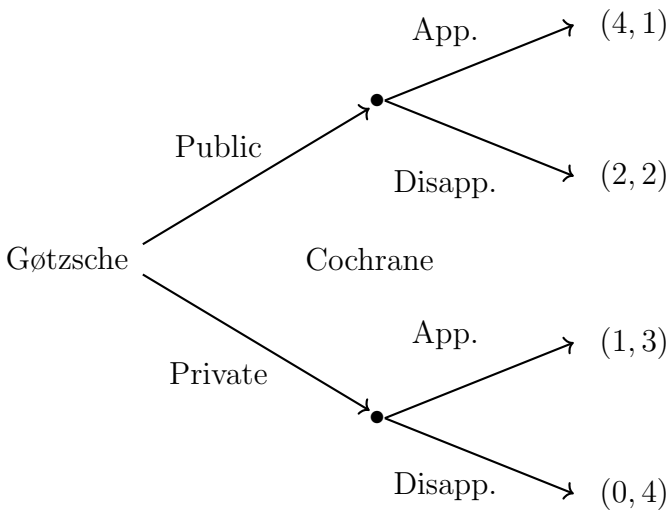

Figure 1: Representation of the sequential structure of the game: Gøtzsche firstly chooses whether to go "Public" (upper part) or to stay "Private" (lower part), afterwards the Cochrane decides whether to "approve" or "disapprove" his conduct. Payoffs are displayed on the leaves (the first number of the pair corresponds to Gøtzsche's payoff) and correspond to each possible combination of choices.

paper for publication), "Private" (he privately exposes his criticism within the Cochrane organization). The choice of payoffs reflects the assumption that he has well founded reasons for criticizing Cochrane's review in any case. Cochrane (the column player) can either "approve" or "disapprove" Gøtzsche's conduct.

	Approve	Disapprove
Public	4,1	2,2
Private	1,3	0,4

Table 1: The payoff matrix for a game-theoretical account of the quarrel between Gøtzsche and the Cochrane.

It follows a more detailed description for the choice of the payoff. The entire case has started from Gøtzsche having motivated scientific reasons to disagree with the opinion reported in Cochrane's HPV vaccine review. Being a scientist and considering the public relevance and implications the review actually has, he has a preference in making his criticism public, as public debates are desirable for the practice of science as well as for the reputation of Cochrane. In his own

words[12] :

> The Board and the CEO believe that public debates undermine Cochrane's reputation. I disagree. Scientific debates further science, to everyone's benefit.

Accordingly, his preferred situation (he gets a payoff of 4) is the one where he makes his opinion public and the Cochrane approves his conduct, appreciating the criticism as the honest position taken by a free scientist, even when this goes against the work and convictions of honorable colleagues from the same organization. This conviction is also supported by Ioannidis words [10], who advocated for a different behaviour, upon agreeing that a highly probable consequence of Cochrane's disapproval is Gøtzsche expulsion.

> Expelling an elected member of the Board who expresses a different viewpoint with some vague excuse that cannot even be disclosed does not befit a scientific organization.

Gøtzsche preference on Cochrane's approval (instead of disapproval) can be supported by several motivations, reflecting a particular image of science: the organism involved is a respected scientific institution and shall accept freedom of (its members') research. Moreover science itself should be transparent in order to increase its trust by society. On the other hand, disapproval could be a motivation of personal harm (as it has actually happened to be the case[13]). The payoff matrix clearly shows that the choice of keeping his opinion private is less preferred. Moreover, he receives lower payoffs in case disapproval is the action of Cochrane (2 and 0, accordingly to whether he has gone public or not).

On the other hand, we assume the board of Cochrane to be a single agent, faithfully representative for the organization itself (at least in its operative decisions in this respect). Cochrane, as an organization, aims at protecting the work of the team in charge of the HPV vaccine review as well as its reputation of leading institute in the EBM community. Moreover, we can think of the organization as being confidently sure both of the honesty and the competence of the team appointed for the specific task[14]. Cochrane's payoffs depend on Gøtzsche's initial action: if he goes public then disapproval gives payoff 2, while approval gets 1; differently, approval gives 3 and disapproval 4. This reflects a preference (for Cochrane) for the

[12]https://blogs.bmj.com/bmj/2018/11/08/peter-c-gotzsche-cochrane-no-longer-a-collaboration/.

[13]Not only Gøtzsche has been expelled by Cochrane but he has also been suspended from his role at "Rigshospitalet" in Copenhagen. See for instance https://www.sciencemag.org/news/2018/11/hospital-s-suspension-evidence-based-medicine-expert-sparks-new-controversy.

[14]As also stated by Cochrane itself in a response to criticism. See https://www.cochrane.org/news/scientific-expert-reaction-new-cochrane-review-hpv-vaccine-cervical-cancer-prevention-girls-and.

question to remain a private and internal affair (payoffs are higher in this branch of the tree). The motivation is that this option may better preserve organization's reputation and might also mitigate the relationship with a non-aligned member. It has been argued that Gøtzsche's conduct can fuel anti-science movements, thus obtaining the opposite effect Gøtzsche himself would have aimed for[15].

The main aim of game theory consists in finding *steady situations* in games, namely action profiles (a vector such that each component is an action of one player) where no player has an incentive to change his/her strategy, namely he/she cannot gain more for changing his/her action. These combinations of actions are called *equilibria*.

In the game depicted above, the equilibrium is easy to be identified. Indeed, Peter Gøtzsche chooses his action first. Given the assumption of the players aim at maximizing their payoff (a standard criterion in game theory), Gøtzsche knows how Cochrane will reply to his action, namely if he opts for "Public" then Cochrane disapproves (it gets a higher payoff in such case), similarly if he opts for "Private" (Cochrane would get 4 instead of 3). Therefore, given that Cochrane's action will be "disapproval" in any case, Gøtzsche chooses to publicly share his opinion (getting 2 instead of 0). Therefore, the game gets to the unique equilibrium situation in which Gøtzsche publishes his criticism and the Cochrane disapproves his conduct.

It shall be noticed that, according to the payoff matrix in Table 1, the strategy of choosing the action "Public" is (strictly) *dominant* for Gøtzsche, i.e. it grants him higher payoffs with respect to the action "Private", independently on the opponent's reply.

Changing the payoff of the players make our approach capable of describing other scenarios (or other relevant features) that may have occurred in the quarrel. In the next part of the section, we aim at showing how different interests of the players may lead to different strategic interactions. For instance, one may want to consider what could have happened if the actual Cochrane were more similar to what Gøtzsche had in mind about the nature of Cochrane itself. As he directly states[16] (italic is ours):

> When Iain Chalmers started the [Cochrane] Collaboration 25 years ago, he wrote in the invitational letter to 50 people, including me, that the collaboration is "committed to opposing any tendency for it to become dominated by any nation, institution, or individual." Unfortunately, Cochrane has gone in that direction. *Academic freedom*

[15]In this respect, Ioannidis [10] went for the opposite conclusion and stated that "One may also argue that the extremely critical positions of PG fuel anti-science, for example, anti-vaccine movements. This argument is unfounded. In fact, anti-science nonsense may be fuelled more by his expulsion when quacks like MMR vaccine deniers (who actually PG has fought against) can weaponize that a scientific critic with such strong credentials was dismissed with petty machinations."

[16]https://blogs.bmj.com/bmj/2018/11/08/peter-c-gotzsche-cochrane-no-longer-a-collaboration/.

has gone, scientific debates are unwelcome, and transparency is a thing of the past. Cochrane's public statements deny this, but I am a witness on the inside and Cochrane's show trial against me is illustrative.

If Cochrane had been closer to what Gøtzsche thinks it should be, we may then model its attitude through the preferences expressed in the payoff matrix in Table 2, where Gøtzsche's payoffs are the same as in Table 1, while Cochrane's are changed.

	Approve	Disapprove
Public	4,2	2,0
Private	1,4	0,1

Table 2: The payoff matrix where Cochrane reacts as an "idealized" Institution.

The "idealized" version of Cochrane is very open to criticism with little fear or concern about its reputation, in face of genuine doubts cast by researchers or by agents of public concern (as scientific institutions should be according to Gøtzsche himself but also to the common/perceived standards of scientific community, see for instance [10]). Accordingly, Cochrane strictly prefers approving the conduct of one of his mostly honorable scientists and members (payoffs in the left-most column are higher than the right-most column). However, the Institution has also a clear preference in keeping the criticism private, as this would not affect both its integrity and reputation (it gets 2 if Gøtzsche opts for public sharing and 4 otherwise).

In this game, Cochrane's preferred action is "Approve". On the other hand, "Public" is still a dominant strategy for Gøtzsche, who indeed would play it. Also in this case, the equilibrium (which differs from the previous game) is reached when Gøtzsche publicly reveals his doubts. It is relevant to stress that Table 2 displays an "idealized", or "hypothetical", situation which indeed does not render how facts have happened in the actual world.

Another possible scenario is one where the Cochrane welcomes private discussion of the doubts raised by Gøtzsche, and the Institution would eventually approve (some) of them. This is exemplified by the payoff matrix in Table 3.

In this version, the game models a situation where Cochrane welcomes criticism unless this remains a private fact. Public sharing is perceived as a threat for the credibility of the integrity of the whole Institution. This is rendered by fixing a higher payoff to disapproval in case the news are publicly shared (2 versus 0), while the payoff for approving is (much) higher in case the whole affair is kept private (4 versus 0).

	Approve	Disapprove
Public	4,0	2,2
Private	1,4	0,0

Table 3: The payoff matrix where Cochrane welcomes Gøtzsche's opinion only if this remains private.

Since Gøtzsche's payoff are the same, he has a dominant strategy, then it is not difficult to check that the game has a unique equilibrium, where Gøtzsche goes public and Cochrane disproves his critical conduct.

In all the games introduced until here, the strategy of publicly sharing his criticism is dominant for Gøtzsche. The choice of this preference's relation on the set of actions is supported by his own words when he claimed that public debates benefit both science and society (see note 9) and somehow reinforces the idea that Gøtzsche would have opted for making his criticism public anyway, even if we assume that he could have raised doubts about the attitude of Cochrane with respect to internal criticism (which does not seem to be the case).

Although Gøtzsche's attitude towards a criticism (which he finds pretty well grounded) is clear from his statements[17], we cannot state the same for the Cochrane collaboration and for this reason, we have tried to analyze three situations which differ only for Cochrane's preferences.

We are interested in proposing a last variant of the game (according to the payoffs given in Table 4), where we have also modified Peter Gøtzsche's payoff: this focuses on a hypothetical situation where preferences (and thus, interests) of the two players are more aligned. The table indeed shows that Peter has a clear preference for the issue to be publicly exposed (even if this implies disapproval). However, he prefers private discussion to Cochrane unconditional disapproval.

	Approve	Disapprove
Public	2,0	0,2
Private	1,4	0,1

Table 4: The payoff matrix where both Gøtzsche and Cochrane have partially aligned preferences.

In this game, Gøtzsche does not have a dominant strategy anymore. Indeed, he knows that his action of publicly sharing his opinion would imply disagreement of Cochrane (that would get 2 instead of 0) getting him a payoff of 0. On the other hand, choosing to keep the discussion private would let Cochrane approve

[17]See for instance https://blogs.bmj.com/bmj/2018/11/08/peter-c-gotzsche-cochrane-no-longer-a-collaboration/.

his conduct (getting 4 instead of 1), and since he would get 1, this last situation represents the equilibrium of the game. Surprisingly enough, this is another hypothetical situation which reveals an equilibrium which is different from how facts has happened.

The four different games picture different, plausible, strategic interactions that may have occurred. In two of them, the equilibrium coincide on how facts actually happened: Gøtzsche publicly criticized and was then expelled from the Cochrane. Different equilibria are found by modeling Cochrane as an "idealized" institution (second game) or letting Gøtzsche have a preference on private discussion over Cochrane's unconditional disapproval (last game). We have argued in favor of the first game, as it seems to us the most plausible picture of the strategic interaction that has taken places. The more accurate description of the situation shall not be judged however by the resulting equilibrium, but given the manifest attitudes of both players (which guided us in the choice of the payoffs). In other words, the game theoretical analysis clearly shows that those situations which end into different equilibria (second and last game) are characterized by attitudes which are far from the reality of facts: as Cochrane is not an ideal institution and (it is clear that) Gøtzsche does not have a real interest into resolving the question in a private discussion.

6 The public relevance

As already mentioned, the case of Gøtzsche vs Cochrane goes beyond how to take decisions within scientific world. As said, science is never neutral. It has always an impact on society and, conversely, it is shaped by societal pressure [14], [16]. Thus, the public dimension of science is not something that can be ignored when analyzing scientific decisions. In this case, given the topic of public relevance (i.e vaccination) and the deep ties of this kind of biomedical research with pharmaceutical industry, all of this is even more obvious. The case we have analyzed is also particularly interesting because it regards experts disagreement[18] when public concern is at stake. By considering the media impact of the controversy, one may want to argue whether Gøtzsche's decision to go public would benefit scientific enterprise. As already mentioned, some researchers seem to envisage that public discussions on delicate problems (often complicated by technical details) is something that should be avoided, and scientific community should rely on its own capacity to judge and rule itself. On the contrary, as already mentioned, Peter Gøtzsche believes that public discussion is definitely a good way to promote a better science, by fostering those virtues, such as transparency and independence, that make scientific research also ethical and orientated towards public good. Beyond his strategy and reasons, Gøtzsche's decision to go public incarnates a particular

[18]which is a growing field of research, involving the contribution of scholars of different fields of research, see for instance http://whenexpertsdisagree.ucd.ie.

image of scientific enterprise. Namely, the idea that science on its own is not sufficient in taking decisions concerning science itself. The public can be a careful and useful watchdog, against distortions of scientific research. As recently argued by Germain and colleagues [3] for another scientific struggle of public relevance (i.e. the legitimacy of animal experimentation) the question of public accountability of science seems to be a priority that cannot be neglected by contemporary research world. As Germain and colleagues write:

> Science is no more abnormal because of the hideous nature of some of its members, but rather hijacked by economic and political interests unaccountable for, when not positively in conflict with the common good. [...] [S]cience cannot regain public legitimacy from its elite and bureaucrats, or by knowledge dissemination: it instead requires a direct encounter with the citizenry, starting with the protests voiced by its representatives.

We believe that Gøtzsche would not negatively consider such a perspective. Indeed, as evidence of this, we suggest to evaluate accordingly the publication, by Gøtzsche himself, of a book dedicated to the general public (*Death of a whistleblower and Cochrane's moral collapse*, People's Press, 30 January 2019 [**?**])on this precise affair. Of course, one may argue whether this is the right and adequate *space* to deal with this kind of issues. In other words, even if we want to accept that public discussion is not just unavoidable but also necessary for a new model of scientific research, it is also easy to recognize that current methods, infrastructures and institutions seem not ready to fully assess and deal with these issues without provoking collateral damages (such as the possible rise of a suspicious attitude towards science from the public). The need of a *well ordered science*, as advocated by Philip Kitcher [14], (or, at least, alternatives that might fulfill the same public functions) is still far from being satisfied. The case of Peter Gøtzsche vs. Cochrane, precisely in its strategic modeling, can be seen also as a symptom of this unsolved tension concerning the public image of science, but also as a perfect example of the need of a call to action for scholars of different fields.

7 Discussion and conclusions

Right after the expulsion of Peter Gøtzsche, 4 members of the board resigned against the decision[19]. The Board members who disagreed and resigned seem to believe that the expulsion can discredit Cochrane way more than the actions of Gøtzsche himself. On this basis, one may argue that our model has the limit of considering the Cochrane Board as a single player, while, in fact, deep disagreement emerged in its internal composition. This is certainly true. However, we believe

[19]See for instance: https://blogs.plos.org/absolutely-maybe/2018/09/18/boilover-the-cochrane-hpv-vaccine-fire-isnt-really-about-the-evidence-but-its-critical-to-science/.

that our choice is still justified since the entire controversy, till the explusion of Gøtzsche, has been articulated between Gøtzsche himself and the Cochrane (as a single agent). As a matter of fact, the CEO has played as a truthful representative of the entire institution and the disagreement took place only after the expulsion of Gøtzsche, meaning that the situation has already changed or that the "game was over". We are perfectly aware that this does not mean that the actual controversy has come to an end. On the contrary, we believe that the original "struggle" was just the tip of the iceberg. As a matter of fact, the issue, in a broader sense, is far from being solved, involving other actors and further levels of discussion. For instance, in January 2019, two Australian scholars highlighted, on *BMJ Evidence-Based Medicine*, that the inadequacy of quadrivalent HPV vaccine safety studies is still ongoing[15], arguing that, concerning the entire sequence of events,

> Conclusions permitted by the study's reviewers are not adequately supported by its data, power or premise. Evidence-based medicine is not served.

Bearing this in mind, we believe that our approach can be useful in providing reasons for the kind of choices in this types of context. Moreover our results offer a more solid ground in the understanding decisions that affect specific representation models of scientific research (e.g. participatory models vs solely expert based models).

In conclusion, the approach adopted in the paper has consisted in providing several games (see Section 5) in order to show how strategic aspects might have triggered the dynamics of happenings in the Cochrane case. Games are formal models and, as such, move necessarily from certain basic assumption. In particular, in all the games proposed we kept the players (agents) fixed (Peter Gøtzsche and the Cochrane), as well as their possible strategic moves, while we differentiate the games by changing players' utility functions. Each choice of payoffs provides a different picture or reality. We will briefly recap all of them in Figure 2.

Different payoff matrices (defining different games) model differences in the players' *attitudes*. While the aim of (our application of) games is finding equilibrium situations, aim of the philosopher of science is showing adequacy of such models with reality of facts. In Section 5, we have discussed plausible motivations behind the choice of one or another payoff matrix. Our preference to provide a coherent picture of reality is Game 1 (in Table 1).

The game theoretical analysis shows that, in two games, equilibrium coincides with the actual situation, i.e. Gøtzsche going for public and the Cochrane for disapproval of his conduct, when there is *disalignment* of preferences between the two players. We believe that this has triggered the actual state affair, creating the case leading to Gøtzsche's expulsion.

On the other hand, in the two games resulting in equilibria that differ from the actual situation, players have more alligned preferences. In one case (Game 2), Cochrane is inclined to discussion; in the other (Game 4) Gøtzsche fears an

Game 1	Approve	Disapprove
Public	4,1	2,2
Private	1,3	0,4

Game 2	Approve	Disapprove
Public	4,2	2,0
Private	1,4	0,1

Game 3	Approve	Disapprove
Public	4,0	2,2
Private	1,4	0,0

Game 4	Approve	Disapprove
Public	2,0	0,2
Private	1,4	0,1

Figure 2: The payoff tables of all the games introduced in Section 5.

expulsion and thus welcomes also private discussion. We have diffusely discussed the reason why such attitude are far from the actual situation.

Finally, the formal dissection of Gøtzsche's and Cochrane's combined choices is potentially revealing of a deeper struggle, investing different views concerning the image of scientific enterprise (and consequently different ideas on the nature of scientific research itself). A strife between those who see science as purely autonomous, self-regulating field of pure researchers and those who believe[20] that, given its scope and nature, science and its achievements constitute a heritage for all humankind, that needs to be always related to it and sometimes even questioned by it.

Conflict of interest
On behalf of all authors, the corresponding author states that there is no conflict of interest.

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[20]See for instance: https://issues.org/crispr-democracy-gene-editing-and-the-need-for-inclusive-deliberation/.

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