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talking point

The precautionary principle should not be used as a basis for decision-making

Talking Point on the precautionary principle

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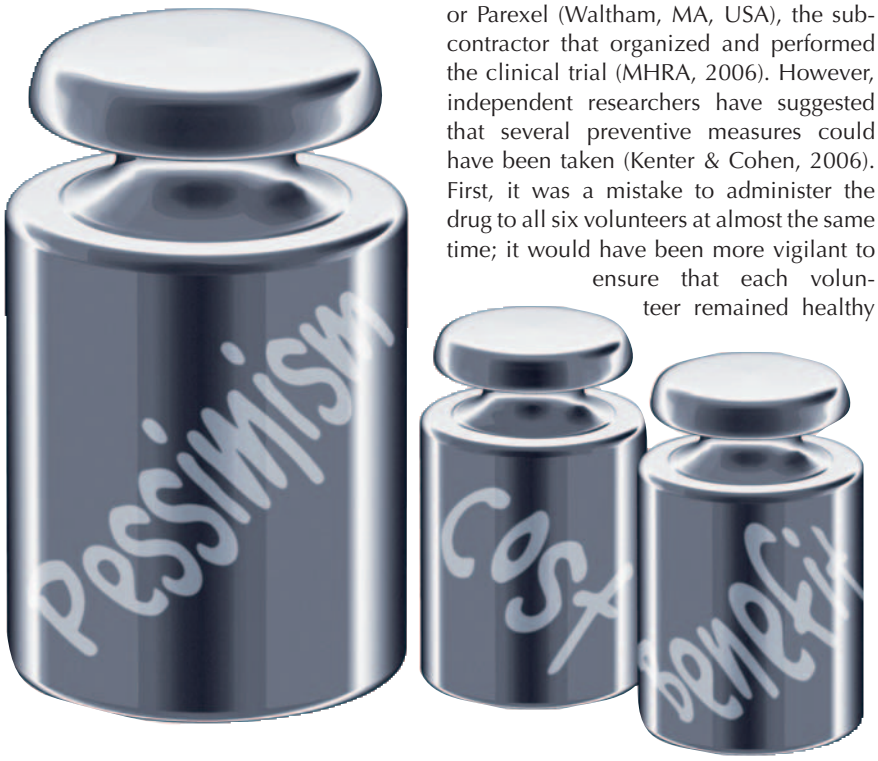
In March 2006, a phase I clinical trial turned into tragedy when six healthy volunteers became critically ill in response to a new humanized monoclonal antibody, TGN1412. Soon after receiving the anti-inflammatory substance intravenously at Northwick Park Hospital in London, UK, the participants complained of headaches, fever and pain, and then began vomiting. All six were transferred to the hospital's intensive care unit, where they were treated in response to a severe allergic reaction. Within one month of the incident, five of the volunteers had returned home, but the sixth remained in hospital for a further two months. Despite their recovery, there have been suggestions that the drug could have caused long-term damage to the volunteers' immune systems.



An investigation by the UK Medicines and Healthcare Products Regulatory Agency (MHRA; London, UK) concluded that the adverse effects were caused by an unprecedented biological action of the drug and not by errors made by either TeGenero AG (Würzburg, Germany), the company that developed the antibody, or Parexel (Waltham, MA, USA), the subcontractor that organized and performed the clinical trial (MHRA, 2006). However, independent researchers have suggested that several preventive measures could have been taken (Kenter & Cohen, 2006). First, it was a mistake to administer the drug to all six volunteers at almost the same time; it would have been more vigilant to ensure that each volunteer remained healthy before proceeding onto the next. Second, from an ethical point of view, it would have made more sense to test the drug in a patient suffering from the disease that the substance was designed to treat, because it might have had some beneficial effects.

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That said, it is worth remembering—and accepting—that such situations are likely to occur again. It is impossible to foresee all possible adverse reactions that a new drug might cause without actually testing it on humans. Even if a trial ends in tragedy, we must nevertheless continue with clinical trials simply because the benefits outweigh the risks; knowledge about safety and efficacy cannot be obtained in any other way, and it is important that tragic accidents should be accepted, depending on the expected benefit of the new drug.

The example of TGN1412 underlines the main argument of this article: we should resist any temptation to use the precautionary principle as a basis for decision-making. When applied, the precautionary principle would prohibit the majority of clinical trials, because it holds that when decision-makers lack sufficient knowledge about the effects of a potentially dangerous activity, one should not proceed. Of course, numerous authors and

organizations have formulated the precautionary principle in slightly different ways, but the basic message is the same: it is better to be safe than sorry.

Arguably, there is no fundamental difference between using the precautionary principle to abolish clinical trials, mobile phones or genetically modified food. In all three examples, there is scientific uncertainty about possible long-term effects on public or environmental health. In my opinion, this shows that the precautionary principle is incoherent, and the example of clinical trials is possibly the best illustration of why. There is no doubt that a clinical trial might be dangerous and that precautionary measures should be taken to avoid unnecessary risks; however, the precautionary principle makes a much stronger claim about decision-making. It tells us to replace traditional cost–benefit analyses with a more imprecise reasoning that focuses on possible negative effects. The precautionary principle therefore replaces the balancing of risks and benefits with what might best be described as pure pessimism.

This criticism is admittedly rather blunt. To be more precise, my view of the precautionary principle is based on two arguments. First, it should not be used by itself as a basis for decision-making. As I will explain in more detail, there are strong reasons for doubting its usefulness as a rule for making decisions, either because it contradicts other more fundamental principles of rationality or is normatively empty—that is, has no implications for what ought to be done. The second argument is more positive, however. Although I doubt that the precautionary principle can be used as an independent basis for decision-making, it can nevertheless modify the epistemic basis on which a decision is made. For example, in the case of TGN1412, it would certainly have made sense to expect the new drug to cause an inflammatory overreaction, which would have prompted the decision not to give the drug to all volunteers at the same time.

Before presenting my argument, I must say a few words about decision theory—that is, the theory of rational decision-making. The most widely accepted rule in decision theory is the principle of maximizing expected utility. According to this principle, rational individuals should choose an act so that the sum of the utilities of all the possible outcomes of the act, weighted by the probability of each outcome, is maximized. For example, suppose that I offer to sell you a lottery ticket. The probability is 50% that you will win US$100 and 50% that you will win nothing. How much should you pay for the ticket? Given that the utility for money is linear, the expected utility of the game is $0.5 \times 100 + 0.5 \times 0 = 50$. Therefore, it would be rational to pay US$50 at most for the ticket.

Seen from a theoretical perspective, the precautionary principle is very different from the principle of maximizing expected utility because it is applied only when decision-makers are unwilling to assign numerical probabilities and utilities to the outcomes. Instead, most formulations of the precautionary principle favour qualitative evaluations of utility and probability, as well as non-arithmetic aggregation mechanisms. When discussing the precautionary approach, the Rio Declaration on Environment and Development—presented at the 1992 United Nations Conference on Environment and Development—speaks of "serious or irreversible damage", which one might plausibly interpret as a qualitative evaluation of utility (UN, 1992). Furthermore, the Rio Declaration speaks of a "lack of full scientific certainty". This is a qualitative expression of uncertainty on a par with the probability calculus used in quantitative decision theory; accordingly, the branch of decision theory concerned with decisions based on qualitative information is called qualitative decision theory.

THE FUNDAMENTAL PRINCIPLES OF RATIONAL DECISION-MAKING

Dominance: If one act yields outcomes that are at least as good as another under all possible states and strictly better under a specific state, then the former act is preferred to the latter.

Archimedes: If the relative likelihood of a non-fatal outcome is increased in relation to a strictly better non-fatal outcome, then some decrease of the relative likelihood of a fatal outcome would counterbalance this precisely.

Total Order: Preferences between acts are complete, anti-symmetric and transitive.

Precaution: If one act is more likely to give rise to a fatal outcome than another, then the latter should be preferred to the former, given that both fatal outcomes are equally undesirable.

The fact that the precautionary principle is a qualitative, rather than a quantitative, decision rule does not mean that there is something wrong with it. Qualitative decision theory is a small but fully respectable sub-discipline of decision theory. However, the problem with basing the precautionary principle on qualitative decisions is that it is either normatively empty or an unreasonable qualitative decision rule. I shall defend this claim by considering each point separately.

My argument for the first hypothesis is based on the observation that nearly all formulations of the precautionary principle in the literature tend to be vague. In fact, there is no single formulation that everyone can agree on, because every scholar and organization cherishes its own version. Furthermore, the enormous and ever-expanding literature on the principle also indicates that no generally accepted formulation will ever emerge, no matter how much effort is put into discussing the advantages and disadvatages of each one. In essence, the precautionary principle is not a well-defined, single idea. It makes more sense to describe it as a cluster of vaguely related intuitions about risk aversion, burdens of proof, irreversible damage and normative obligations.

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Of course, this does not in itself pose a problem, as long as each formulation can be discussed and critically assessed. However, in my experience, advocates of the precautionary principle seldom commit themselves to a single, precise formulation. Instead, the standard manoeuvre is to speak loosely about a core idea or basic insight and leave the task of formulating a fully operational version of the precautionary principle to a later occasion. From an intellectual point of view, this is not good enough. The respectable way to discuss decision-making based on qualitative information is to use qualitative decision theory, which requires that we have one or more precise formulations of the decision rule. Essentially, we need a principle that tells us what to do and what not to do for each possible input of qualitative information. Until such a formulation of the

precautionary principle is agreed on, it is normatively empty.

I shall now defend the second hypothesis of my argument by showing that the precautionary principle is an unreasonable qualitative decision rule. My main point is that the principle expresses a value judgement that few of us would be prepared to accept once we realize that it conflicts with other, more important value judgements. Of course, all decision rules express value judgements, so that alone is not a problem. A decision rule simply tells decision-makers what to do, given what they believe about a particular problem and what they seek to achieve. Different decision-makers might, of course, hold different beliefs and seek to achieve different aims.

However, any reasonable formulation of the precautionary principle will imply a value judgement that no rational decision-maker would be prepared to accept. To prove this point, I briefly recapitulate a recent analysis (Peterson, 2006), which shows that no formulation of the precautionary principle can be consistent with three fundamental principles of rational decision-making: dominance, Archimedes and total order (see sidebar). A fourth condition—termed 'precaution'—is a partial and very weak formulation of the precautionary principle that all its advocates could agree on. Or, put in slightly different words, precaution is a minimal condition that should be implied by every plausible formulation of the precautionary principle.

The term 'fatal outcome' in the definition of the precaution condition is qualitative; however, for the theorem to hold true, we do not have to assume that the boundary between fatal and non-fatal outcomes is sharp but can accept an area of vagueness. The dominance principle is a widely accepted condition for rational decision-making: suppose that your doctor tells you to take a particular pill if you start to feel ill. When you start to feel ill, you know that taking the pill will not lead to any adverse drug reactions; furthermore, since you have already bought the pill and it cannot be stored for future illnesses, it would not cost you anything to take it. Given this information, should you take the pill or not? The point is that regardless of whether the pill cures your disease, you will fare at least as well if you take the pill as if you do not. Therefore, according to the dominance principle, you should take the pill as you have nothing to lose.

The Archimedean condition is more difficult to explain, but the underlying idea seems to be equally plausible. All else being equal, if the relative likelihood of a non-fatal outcome, such as a fever, is increased in relation to a strictly better non-fatal outcome, such as headache, the situation becomes slightly worse because the better outcome is more unlikely. However, according to the Archimedean principle, this negative effect can be counterbalanced by decreasing the relative likelihood of a fatal outcome, such as death, thereby making the modified act just as attractive as the original one. This is, of course, a theoretical abstraction. To perform such a trade-off between different values in practice might well turn out to be impossible, but this does not invalidate the ideal of rationality to which it appeals.

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Total order is merely a technical condition in which preferences between acts are complete, anti-symmetric and transitive. An ordering of preference is complete if—and only if—for every pair of acts x and y, act x is at least as preferred as y, or y is at least as preferred as x. Anti-symmetry means that if x is at least as preferred as y, and y is at least as preferred as x, then x and y are equally preferred. Finally, transitive means that if x is preferred to y, and y is preferred to z, then x is preferred to z.

In Peterson (2006), I show in detail that these four conditions—precaution, dominance, Archimedes and total order—are logically inconsistent. Together, they express value judgements that cannot be accepted for reasons of consistency and intellectual honesty. Therefore, the point is not that the value judgements expressed by the precautionary principle are strange or implausible from a normative point of view. The claim I make is much stronger: at least one of the four conditions must be given up in order to preserve logical consistency. Of course, as the three general principles of rationality—dominance, Archimedes and total order—are fundamental, it makes sense to give up the precautionary principle. This completes my argument in favour of the claim that the precautionary principle is either normatively empty or an unreasonable qualitative decision rule.

However, many people feel strongly that there must be some truth in the precautionary principle. Therefore, rejecting the very idea behind it on the basis of decision theory alone might be futile if academics and politicians are likely to continue promoting it, no matter what arguments are raised against it. The best strategy for the sceptic is thus to show that there is indeed some element of truth in the precautionary principle, even though it cannot be used as a decision rule.

Personally, I believe that the only legitimate interpretation of the precautionary principle is as an epistemic principle. The difference between decision rules and epistemic principles is subtle, but important. If the precautionary principle is interpreted as a decision rule, then the problem outlined above cannot be avoided. However, by interpreting the precautionary principle as an epistemic principle, it can be used to influence decisions more indirectly (John, 2007). For example, an epistemic interpretation of the precautionary principle would imply that it is rational to believe that a new substance—such as TGN1412—is dangerous until sound scientific knowledge shows that it is safe. Arguably, this belief would then have motivated those involved in the TGN1412 clinical trial to make even more risk-averse decisions, without adopting the incoherent decision rules discussed above. That is, by modifying the beliefs of the decision-maker, the decisions can be indirectly modified without violating any principle of rationality.

… the burden of proof rests with anyone who makes a claim, regardless of what is being claimed

Briefly, an epistemic principle tells people what to believe and what not to believe. For example, statisticians believe that two or more parameters are correlated only if there is at least a 95% probability that the correlation is not due to random effects. As argued in Peterson (2007), the precautionary principle can be interpreted as an analogous epistemic principle that prescribes that it is always more desirable to avoid

false negatives than false positives when it comes to assessing risks.

Of course, this argument is far from uncontroversial. As every scientist knows, it is generally more important to avoid false positives than false negatives in research. If offered a choice between failing to reject a false hypothesis or failing to adopt a true hypothesis, scientists would generally prefer not to discover an additional truth than to believe in something that is in fact false. There is a simple and sound explanation for this epistemic preference: new scientific beliefs are often instrumental when making further discoveries, so any mistake in the corpus of scientific knowledge is likely to give rise to more mistakes further down the road.

There is nothing wrong with the precautionary principle—as long as it is not used for decision-making

Still, the aim of science differs from that of a risk assessment. Scientists aim to acquire as many true beliefs as possible, while minimizing false ones. A risk assessment, however, aims to protect people or the environment from potential hazards. When assessing the risk of a new substance, the consequences of mistakenly believing that it is hazardous are seldom disastrous. The consequence of falsely believing it to be safe might, however, be catastrophic.

The principle of preferring false positives is frequently combined with the claim that the burden of proof should be reversed when the risks are high. According to this view, it is not the person who claims that something is hazardous who has the burden of proof, but rather the person who claims that the substance is safe who should support this claim with arguments.

I wish to make two points related to this idea. First, the idea of a reversed burden of proof is less plausible than many of its advocates believe. Arguably, the burden of proof rests with anyone who makes a claim, regardless of what is being claimed. Consider, for example, the case of genetically modified (GM) food. If the idea of a reversed burden of proof is taken literally, one should believe that GM food is hazardous until it has been proven safe. The problem is, however, that many people already believe that GM food is safe. Should they really change their view without being given any reason for doing so? Second, the preference for false positives can be accepted without simultaneously adopting the idea of a reversed burden of proof. The two epistemic principles are distinct: the former is a methodological rule derived from statistics; the latter is a more general meta-epistemological principle about how one should decide what to believe. I find the first principle acceptable, but not the second.

There is nothing wrong with the precautionary principle—as long as it is not used for decision-making. The problem is by no means the precautionary principle itself; however, when used as a basis for decision-making, it comes into conflict with other, more fundamental principles of rational decision-making. That said, there are other legitimate interpretations of the precautionary principle. In particular, it seems that an epistemic interpretation makes sense, according to which it is more desirable that risk assessments avoid making false-negative rather than false-positive errors.

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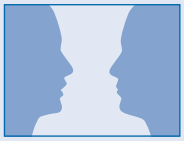

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Stirling A (2007) Risk, precaution and science: towards a more constructive policy debate. This issue p309.