

Implications of the Precautionary Principle for research and policy making *Implicazioni del Principio di Precauzione sulla ricerca e sull'azione politica*

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Summary

The Precautionary Principle has recently been formally introduced into national and international law. The key element is the justification for acting in the face of uncertainty. The Precautionary Principle is thereby a tool for avoiding possible future harm associated with suspected, but not conclusive, environmental risks. Accordingly, the burden of proof is shifted from demonstrating the presence of risk to demonstrating the absence of risk. Past experience shows the costly consequences of disregarding early warnings about environmental hazards. Today, the need for applying the Precautionary Principle is even greater. New research is needed to expand current insight into disease causation, to elucidate the full scope of potential adverse implications resulting from environmental pollutants, and to identify opportunities for prevention. Research approaches should be developed and strengthened to counteract innate ideological biases and to support our confidence in applying the Precautionary Principle for decision-making in the public policy arena. *Eur. J. Oncol.*, 9 (1), 9-12, 2004

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Introduction

The Precautionary Principle has recently been formally introduced into national and international law, including the European Union¹. The key element is the justification for acting in the face

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Riassunto

Il Principio di Precauzione è stato recentemente introdotto ufficialmente nelle legislazioni nazionali ed internazionali. L'elemento chiave è la giustificazione ad agire in situazioni di incertezza. Il Principio di Precauzione è quindi un mezzo per evitare possibili danni futuri dovuti a rischi ambientali possibili ma non ancora definiti. L'onere della prova passa quindi dal dimostrare la presenza di un rischio al dimostrare l'assenza di un rischio. Le esperienze del passato hanno dimostrato le spiacevoli conseguenze di trascurare i primi allarmi sui rischi ambientali. La necessità di applicare il Principio di Precauzione è oggi ancora maggiore. Sono necessarie nuove ricerche per ampliare le attuali conoscenze sulle cause delle malattie, per chiarire completamente le potenziali implicazioni negative per la salute, conseguenza dell'inquinamento ambientale, e per identificare le possibilità di prevenzione. Gli orientamenti della ricerca dovrebbero essere sviluppati e rafforzati per contrastare pregiudizi innati e sostenere la nostra fiducia nell'applicare il Principio di Precauzione nell'ambito della sanità pubblica. *Eur. J. Oncol.*, 9 (1), 9-12, 2004

Parole chiave: salute ambientale, sostanze pericolose, prevenzione primaria, sanità pubblica, determinazione dei rischi

of uncertain knowledge about risks from environmental exposures. Appropriate public health action should be taken in response to limited, but plausible and credible, evidence of likely and substantial harm. The Precautionary Principle is thereby aimed at avoiding possible future harm associated with suspected, but not conclusive, environmental risks. The burden of proof is shifted from demonstrating the presence of risk to demonstrating the absence of risk.

Precautionary action is as old as medicine, and prudence has always been advised in regard to decisions affecting human health. The lack of precautionary or preventive action despite early warnings has resulted in severe harm to health and damage to ecosystems². Too often, unreasonable delays in preventive responses have resulted from demands for detailed proof of causation, including detailed knowledge of mechanistic actions. The adverse effects on human health and ecosystem sustainability have in some cases been catastrophic.

Asbestos is perhaps the best known example of a preventable health hazard for which there was credible evidence of harm long before the causal link was generally accepted. However, asbestos is still being used in many developing countries, with attendant increases in cancer and pulmonary disease. The same sequence of events occurred with other toxic materials, such as benzene. The toxic properties of these well-known hazards have now been clearly documented, and prevention efforts are justified without any need to employ the Precautionary Principle. Had appropriate action been taken when the first evidence of adverse effects emerged, then a truly precautionary intervention could have ensued, preventing much illness and many premature deaths.

Similarly, when tetraethyllead was synthesized in the 1920s, a strong precautionary argument was made by Professor Yandell Henderson of Yale University. A medical physiologist and chemical warfare expert, Henderson warned, based on best available evidence, that adding lead to gasoline would poison the entire planet. His warning was ignored, and the large-scale production of lead additives began. At its peak, 250,000 tons of lead were released into the atmosphere each year in the US alone. The cessation of this practice began in the 1970s and was completed in the US, most of Europe and Japan 20 years later. The US average blood-lead concentration dropped from 155 µg/L (0.77 µmol/L) in 1970 to 21 µg/L (0.10 µmol/L) in 1999. For the US birth cohort of children born in 1998 alone, the monetized benefit from this lowering of their blood-lead concentration was estimated by the US Centers for Disease Control and Prevention to range in the hundreds of billions of dollars. Still, while this primary prevention effort was highly successful, it was not precautionary, because it was initiated only after a preponderance of evidence had become available.

Many new and potentially hazardous chemicals are released to the environment, and the magnitude of exposures and their effects, singly and in combination, are only partially understood. The need for precautionary action has therefore increased. In recognizing this imperative, the European Commission Communication (2000) on the Precautionary Principle states that precautionary decisions are indicated when preliminary objective scientific evaluation suggests reasonable grounds for concern. Limited precautionary action has been taken so far in relation to more proximate exposures. In regard to global change, precaution needs to be exercised in relation to the more complex mix of determinants that act to degrade environmental carrying capacities and endanger sustainable development. Maintaining the integrity of the global environment, and its various life-supporting ecosystems, is essential to human survival. The greater the potential for disastrous, large-scale, or catastrophic impacts on health related to environmental degradation, the greater the need for precaution. Because the consequences for human health and well-being from changes of global scale are orders of magnitude greater than those from more proximate hazards, precautionary strategies and actions are even more critical for minimizing harm.

Lessons from applying precaution

In public health, removing one risk may produce others. Removing one risk may incur other unanticipated hazards. When the evidence on leaded gasoline was finally considered to be convincing, other additives were sought to raise octane levels. From a precautionary viewpoint, enough was known about benzene to impose limits on the content of this carcinogen in gasoline: instead, methyl-*tert*-butylether (MTBE), a less studied octane booster, was employed. This substance has now produced health risks from severe water contamination, which was not easily anticipated despite the highly persistent nature of MTBE. Another example relates to the microbiological safety of drinking water in developing countries, where precaution suggested that well water from underground aquifers would be less likely to be contaminated with infectious agents than surface water. However, the release of arsenic and fluoride from naturally occurring subterranean sources have now caused mass intoxication in Bangladesh and India.

In these examples, the preventive approach failed to anticipate the risk from the substitutes. Especially when the uncertainty about risks is high, the likelihood of a false positive will invariably increase, and the need to assess alternatives and evaluate the intervention becomes even more important.

Current risk assessment and standard-setting are generally based on limited information about single hazards. Uncertainty has been taken into account when hypothesized safety factors or uncertainty factors were invoked to calculate legal limits. However, the history of declining exposure limits for many substances testifies to the failures of this approach. Early warnings were often misinterpreted or ignored².

Science for precaution

The tools and principles of science, when applied to public policy, have often implicitly worked against precaution. In particular, the absence of universally accepted evidence demonstrating damage or harm has often been misinterpreted as evidence of safety.

Implementing a precautionary approach in decision-making must be linked to established scientific principles. The Precautionary Principle therefore has important implications for scientific strategies, methods, interfaces with policy-making, and risk communication. These considerations present science with opportunities and challenges and relate to the way scientific studies are conducted and how the results are communicated. The interrelationships, for instance between science and policy, should reflect the needs for new knowledge generated from using precaution in public-health decisions. Although most attention has been paid to specific applications of the Precautionary Principle, this prevention strategy should stimulate the development and strengthening of research approaches that aim to increase public confidence in applying the Precautionary Principle for decision-making.

Science has traditionally placed emphasis on replication of results or observations. Still, by insisting on confirmatory evidence, science may penalize false positives more than false negatives. A probability value of 5% is usually required to reject a hypothesis of no effect, but this tradition places an unreasonable preference on the absence of an effect. Under the Precautionary Princi-

ple, incomplete, but credible, scientific documentation may be deemed sufficient for decision-making.

A mere replication or simple extension of the scientific knowledge base beyond a minimal requirement may no longer constitute a priority. While current research has often focussed on simplified model systems and the effects of single hazards, one by one, an expanded and refocussed research agenda should rather emphasize the sources of variability and uncertainty, including individual susceptibility, impacts of mixed and variable exposures, susceptible life-stages, and vulnerable communities.

Statistical analysis of research data has aimed at testing whether an effect could be considered a possible result of natural variability. This strategy has been considered a necessary part of scientific rigour, although it is often coupled with demands for the demonstration of causality. It is also necessary to consider both the severity of potential adverse outcomes and their likelihood. Although a prerequisite for implementing the Precautionary Principle, such information has not usually been considered a standard product of the scientific endeavour.

In general, statistical analysis of research data tends to bias the conclusions toward the null hypothesis. For example, the standard application of a limit of 5% for ‘statistical significance’ will rule out many findings of causal associations, simply because the study was too small and thus lacked statistical power, or because some imprecision or limited sensitivity of the parameters precluded a more definitive observation. Table 1 shows examples that current research practices are biased by producing many more instances of false negatives than false positives.

Decisions should not be based on an assumed certainty of scientific information, but rather on an estimate of the uncertainty. Science should therefore provide the necessary information to facilitate consideration of the risk of both false negatives and false positives. Type II errors, i.e., overlooking a true hazard, become an essential issue in the decision-making process.

Uncertainty has always been recognized as a key component of our incomplete understanding of human disease and the environment. An important goal now is to achieve a better character-

ization of these uncertainties and their implications. Appropriate statistical methods should therefore be developed and applied to determine the likelihood of adverse or extreme outcomes and how they may be affected by precautionary actions.

Science should continue to update existing knowledge and to improve communication of risks as well as their associated uncertainties. In analyzing and communicating such information, science should help frame the debate and facilitate the dialogue among stakeholders on where and how to apply the Precautionary Principle.

Research should emphasize studies to determine the societal impacts and benefits of preventive interventions. Such research is required to determine if precautionary action was successful and to modify actions that may have resulted in new risks.

Conclusions

Scientific uncertainty has too often been the excuse for limiting and postponing preventive efforts. In addition, debates over details in risk assessments have resulted in delayed action to protect the public health and the environment. New research is needed to expand current insight into disease causation, to elucidate the full scope of potential implications for health and the biosphere resulting from pollutants and other hazards, and to identify opportunities for the prevention of risks at the source. Recognizing the nature of cumulative, complex and synergistic effects on whole ecosystems, essential to the support of life, is foundational to precautionary action, and necessary to avert the serious consequences of ecological disintegrity.

Current scientific research agendas, funding priorities, science education, risk communication, and science policy need to be re-examined in light of the Precautionary Principle. The need for better links between science and public policy in the spirit of the Precautionary Principle are clearly warranted as reflected in the Statement from the Collegium Ramazzini published in the present issue of the Journal.

Table 1 - Potential sources of bias in environmental research using standard methodological approaches in experimental and observational studies.

Type of scientific study	Methodological feature	Main direction of error
Experimental study	High doses	False positive
	Limited number of dose levels	False negative
	Low genetic variability	False negative
	Exposure to single substances only	False negative
	Chronic rather than foetal-lifetime exposure	False negative
	Standard effect measures	False negative
Observational studies	Inappropriate controls	False negative
	Exposure misclassification	False negative
	Concomitant exposures	False positive
	Residual confounding	False positive
	Inadequate follow-up	False negative
	Lost cases	False negative
Both types of studies	Low statistical power (e.g., small studies)	False negative
	Use of 5% probability level to minimize chances of false positives	False negative
	Use of 20% probability level to minimize chances of false negatives	False negative
	<i>Post hoc</i> hypothesis	False positive
	Scientific and social pressure against false alarm	False negative
	Publication bias toward positive findings	False positive

We recommend that researchers, in collaboration with research funding agencies, regulatory bodies and stakeholders, revise current scientific paradigms and traditions to ensure that scientific information is used in decision-making within a framework that facilitates the application of precaution to supplement prevention.

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References

1. European Commission. Communication from the Commission on the Precautionary Principle (COM(2000) 1). Brussels, 2000. URL: http://europa.eu.int/comm/dgs/health_consumer/library/pub/pub07_en.pdf (accessed, 30 November, 2003).
2. European Environment Agency. Late lessons from early warnings: the precautionary principle 1896-2000. Environmental Issue Report No. 22. Luxembourg: Office for Official Publications of the European Communities, 2001.
3. Grandjean P, Soffritti M, Minardi F, Brazier J, eds. The Precautionary Principle. Implications for research and prevention in environmental and occupational health. Eur J Oncol Library 2: 1-245. URL: <http://www.collegiumramazzini.org> (accessed, 30 November, 2003).