Problems with precaution: the transfusion medicine experience

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Abstract

The precautionary principle is a dominant paradigm governing risk-based decision-making. Today, there are increasing pressures to re-examine aggressive precautionary approaches, and to assess how the principle should be applied in the modern system. In this paper, we examined three key applications of precautionary approaches in the field of transfusion medicine to provide insight into the risks and benefits of these approaches. The three case studies examined were the donor deferral policies to safeguard against transfusion transmission of human immunodeficiency virus, variant Creutzfeldt–Jacob disease, and, lastly, xenotropic murine leukemia virus-related virus. Characterization of precautionary applications was conducted using an embedded case study design. Our findings indicate that transfusion transmission mitigation strategies have become increasingly aggressive in the face of theoretical risks. In contrast, the review processes for implementation and reversal of precautionary policies have been slow, and historical donor deferral policies are still in place today. Application of precautionary approaches has proved challenging with both benefits and pitfalls. In light of emerging threats to the blood system, policy-makers should consider the implementation of frameworks to guide the appropriate application of precaution in transfusion medicine in the future.

Keywords

Blood transfusion; precautionary principle; donor exclusion; risk–benefit assessment

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Introduction

The precautionary principle has emerged as a dominant paradigm governing risk-based decision-making (Steingraber 1998; Wynia 2005). The principle initially emerged out of the European environmental movement of the 1970s, and stems from the German concept of 'vorsorge' or 'foresight' (Morris 2000; Alban 2005). While it has been articulated in various ways, the precautionary principle essentially states that complete evidence of risk is not required to justify taking measures to protect the public against the risk in question. Transfusion medicine has arguably pioneered the use of the precautionary principle in the public health sector for issues that do not have an environmental dimension (Wilson and Ricketts 2004a). As a result of previous scientific uncertainty around the transfusion transmission potential of Hepatitis C and Human Immunodeficiency Virus (HIV) and a perceived failure in existing risk management strategies, national blood systems have moved toward applying precautionary decision-making standards for matters pertaining to the safety of the blood supply (Stein et al. 2011; Kramer, Verweij, and Zaijjer 2015). Canada's 'Tainted Blood Tragedy' in the latter part of the 1970s to 1990s saw a critical turning point for the use of precaution in public health matters in this country (Wilson 2007). Consequently, the use of precaution has emerged as a driver in transfusion policy decision-making, setting a standard for authorities to act even if there is only a theoretical risk of harm (Wilson et al. 2003).

As time distances blood systems from such public health tragedies, there is increasing pressure to revisit aggressive precautionary approaches. In this study, we examine the use of precautionary approaches across three case studies.

In this paper, we refer to precautionary approaches as opposed to the principle itself, given the ambiguity of the precautionary principle's definition and application in transfusion medicine – although we do acknowledge there is controversy over whether such a distinction should be made. The use of the term 'precautionary principle' may imply a legal connotation while the term 'precautionary approach' reflects the lens through which decisions are made. The latter more accurately describes how precaution has been implemented in blood safety decisions. Our analysis therefore serves to provide insight into the application of the precautionary approach and to speculate on how it may be applied in the future to guide transfusion safety policies.

Materials and methods

Objective

The overarching objective of this study was to characterize how precautionary approaches have been used to guide risk-based policy decision-making in transfusion safety within Canada, across three separate case studies. The following three cases were identified for analysis: (1) the men who have sex with men (MSM) donor deferral policy implemented at the discovery of transfusion transmission potential of HIV; (2) the U.K. donor deferral decision designed to protect against transfusion transmission of variant Creutzfeldt Jacob Disease (vCJD) and; (3) the introduction of a donor deferral policy for individuals suffering from fatigue to protect against the theoretical transfusion transmission of the xenotropic

murine leukemia virus-related virus (XMRV) as the postulated cause of Chronic Fatigue Syndrome (CFS). These cases were selected based on literature scan, consultation with subject matter experts, and a theoretically grounded categorization of both 'typical' and 'atypical' applications of precautionary approaches in the Canadian context ('Frequently Asked Questions about Variant Creutzfeldt-Jakob Disease [Variant CJD]' 2011; 'Five-year Blood Donor Deferral Period for MSM' 2013; Taylor 2010). Specifically, for each case we looked to identify notable cases in transfusion medicine that spanned different time periods, ranging from the re-organization of the Canadian blood system to present. We sought to determine the characteristics of application of precautionary approaches and whether international guidelines for its use were applied. Lastly, we attempted to identify themes characterizing the policy-making process.

Data collection

Characterization of the use of precautionary approaches was conducted using an embedded case study design as described elsewhere (Wilson et al. 2001). Data were collected through a combination of document review and semi-structured interviews with subject matter experts. Publicly available literature was obtained first through targeted PubMed and Internet queries, and a review of their reference lists. Additional records were gathered following recollection of case studies from subject matter experts. Subject matter experts were identified through a review of the relevant literature and were contacted to participate. Informed consent was obtained from all subject matter experts interviewed. In total, two authors interviewed 21 subject matter experts in relevant decision-making and advocacy organizations. The lead interviewer had extensive experience in expert interviews and policy analysis.

Analysis

Interviews were audio-taped, transcribed by an individual external to the study and thematically coded using the NVIVO program ('NVIVO Quality Data Analysis Software' 2012). Expert interviews were all conducted in English and lasted 30 min to 2 h in duration. Coded data were grouped into categories, based on the properties of the public health risk being managed, and the guidelines for applying precaution, which served as the unit of analysis. Interviewing, transcription, and analysis proceeded concurrently to permit exploration of ideas that emerged from early data (Strauss 1987; Wilson et al. 2001). From the coded data, we identified major themes characterizing decision-making processes. We specifically sought to determine the characteristics of the risk or perceived risk being addressed by precautionary policies and of the application of the precautionary approach itself. This included identifying: the proportion of the population exposed to risk, the severity of harm caused by the exposure, the health benefits of precautionary actions, potential health harms of precautionary actions, potential economic consequences of precautionary actions, and the level of scientific evidence required to trigger action. Adherence of precautionary approaches to the European Union's guidelines on the use of the precautionary principle was examined. The European Union's recommendations were chosen because the precautionary principle is a core concept of the Maastricht Treaty. The EU's guidance represents one of the first formal incorporations of the principle into international law, and thus reflects the guidance of a jurisdiction with the most experience

with the principle (UNEP 1992a). The Canadian guidelines mirror the concepts in the European guidelines, but are more focused on issues related to trade that are not relevant to this analysis ('A framework for the application of precaution in science-based decision-making about risk' 2003).

Results

Description of case studies

Donor deferral of MSM—The decision to consider precautionary approaches to blood safety risk management in Canada was largely motivated by the high rate of transfusion transmission of HIV and Hepatitis C in the late 1970s through the 1990s, later referred to as the 'Tainted Blood Scandal' (Picard 1995). This was arguably Canada's largest public health crisis, with an estimated 1000 Canadians contracting HIV from tainted blood products (Krever 1997b; Wilson 2007). An additional 30 000 Hepatitis C transfusion-transmitted infections occurred during this time (Krever 1997a), devastating entire families of hemophiliacs who regularly received therapeutic blood products.

Cases of an illness that would later become known as Acquired Immunodeficiency Syndrome (AIDS) were first characterized in MSM in 1981 (CDC 1983b). Initially, affected members of the MSM community began experiencing rare pneumocystis infections and Kaposi sarcoma. Within the remaining months of the year, a cumulative total of 270 reported cases of severe immune deficiency in the MSM community had been described. By early 1982, concern was building about whether the unidentified condition was transfusion-transmissible, despite an absence of clinical evidence or viral etiology (Wilson, Atkinson, and Keelan 2014b).

In response, a suite of temporary and permanent global deferral policies followed, varying from lifetime exclusions to shorter 1 to 10 year deferral periods. The Canadian Red Cross Society's Blood Transfusion Service's donor deferral policy included an indefinite ban for MSM who had sex with men any single time after 1977. In the 1983 March, 4th Edition of its Morbidity and Mortality Weekly Report, the Centers for Disease Control suggested that in addition to sexual transmission, AIDS may be transmitted through exposure to blood or blood products. The report further acknowledged that most cases of AIDS had been reported in MSM, injection drug users, Haitians, and hemophiliacs (CDC 1983a). In 1984, researchers from the Pasteur Institute in Paris, France held a press conference to announce their identification of the virus causing AIDS (Gallo et al. 1984; Barre-Sinoussi et al. 2004).

Since the initial implementation of MSM deferral policies, the scientific climate surrounding HIV and AIDS has changed dramatically. Laboratory testing for the virus was developed and substantially improved with nucleic acid testing (NAT) which permitted identification of individuals in the early stages of infection (Busch et al. 2000). NAT allowed blood operators to screen blood products, safely disposing of infected blood prior to distribution. Importantly, use of NAT facilitated the calculation of disease prevalence within donor populations.

As new measures for risk management against HIV/AIDS transmission in the blood supply became available and public pressure mounted, citing scientifically unjustified discrimination, some jurisdictions began to revisit their deferral policies. Today, global variation remains – ranging from the maintenance of highly restrictive lifetime deferrals in some jurisdictions, to others where deferral policies for high-risk sexual behavior are harmonized, regardless of sexual orientation (Wilson, Atkinson, and Keelan 2014b). Indefinite MSM deferrals in Canada were abolished in 2013 in favor of an intermediary five-year deferral policy (Pillonel et al. 2012; Davison, Conti, and Brailsford 2013; Slowther, Watkins, and Kelly 2013; Wilson, Atkinson, and Keelan 2014b; FDA 2015; ‘CHS Position on Donor Deferrals’ 2017) and were more recently further reduced to a one-year deferral (CBS 2016b). Other jurisdictions, such as the U.K. (2011) and the United States (2015), moved lifetime deferrals directly to a one-year deferral, with no intermediary step. Some jurisdictions are still navigating the transition, such as Northern Ireland whose one-year policy took effect in September 2016 (BBC 2016).

During the ‘Tainted Blood Tragedy’ in Canada, the role of MSM as an incubator population of HIV and Hepatitis C served as the central argument for application of aggressive lifetime donor deferrals. While blood-product testing is now available, and an evidence base collected, components of MSM deferral policies linger. While arguments contend that MSM tend to have higher rates of sexually transmitted infections compared to the general donor population (‘Specific Populations: Men who have Sex with Men (MSM)/Women who have sex with Women [WSW]’ 2013), no new threats to the blood supply have stemmed from this population. Rather, emerging blood borne pathogens observed since HIV/AIDs have relied on other reservoirs for incubation such as food (vCJD) and mosquitoes (West Nile Virus).

Donor deferral of individuals with vCJD risk factors—The 1996 discovery of variant Creutzfeldt–Jakob disease (vCJD) was the first major infectious threat to the blood system to arise after HIV/AIDS (Will et al. 1996; Wilson and Ricketts 2004b; Wilson et al. 2007a). Following the outbreak of bovine spongiform encephalopathy (BSE), or mad cow disease, in the U.K. during the 1990s, there was heightened surveillance for human transmissible spongiform encephalopathies (TSE). Identification of a new human prion disease strongly linked to consumption of contaminated bovine meat piqued international attention (Will et al. 1996; Lee et al. 2013). vCJD, as the condition later became called, typically afflicted individuals in their 20s and 30s with early psychiatric or sensory symptoms, progressing into neurological deficits and often death within a 14-month period (Will et al. 1996). Precautionary measures were instigated in response to biological evidence demonstrating the existence of prions within the lymphoreticular system and the potential for animal to animal transmission of prions via transfusion. (Foster et al. 1996; Manuelidis, Gorgacz, and Manuelidis 1978; Brown 1995; Brown et al. 1998; Hill et al. 1999). Blood operators in the U.K. responded swiftly to the threat of vCJD by instituting requirements for leukodepletion of blood products and halting citizen blood collection, switching to imported plasma products from other countries (Wilson and Ricketts 2004a; Wilson et al. 2007b). Other countries also sought to determine how they might handle donations from potentially infected individuals who had traveled to the U.K. during the peak of the BSE epidemic. Risk assessment analyses on vCJD (Wilson et al. 2001) prompted blood agencies in Canada and

the United States to implement deferral policies that targeted individuals who had spent 6 months in the U.K. between 1980 and 1996 (D99-02 1999; Wilson et al. 2001). These policies are notable because they were enacted prior to any documented cases of transfusion transmission of vCJD and took into account the impact of such deferrals on public blood supplies (Wilson and Ricketts 2004a). In 2003, the first case of transfusion transmitted vCJD was reported. Only three confirmed cases of vCJD related to blood transfusion have been documented to date (Wilson and Ricketts 2006b; WHO 2012).

Canadian policy maintains a deferral period for individuals who have spent three or more cumulative months in the U.K. or France between 1980 and 1996, and/or 6 months or more in Saudi Arabia between 1980 and 1996, and/or five years or more in countries of Western Europe between 1980 and 2007 (CBS 2016c). Thus, vCJD continues to remain a policy of interest due to an inability to completely rule out ongoing risk to the blood supply despite a comparative absence of any new symptomatic cases (Peden et al. 2004, 2010; NCJDRSU 2016). The primary driver for the maintenance of the vCJD policies is a theoretical concern for a genetically at-risk population who may develop the condition at a later time, harboring infectious prions in lymphatic tissues (Wilson and Ricketts 2006a). There is no blood or urine test for the identification of vCJD, although this remains an area of active research interest (Edgeworth et al. 2011; Moda et al. 2014; Douet et al. 2016).

Donor deferral for individuals with chronic fatigue syndrome—The most recently publicized application of precautionary approaches in transfusion safety was the 2010 decision to defer donations from individuals with a history of chronic fatigue syndrome (CFS). This policy was triggered by a 2009 article published in the academic journal, *Science* (Lombardi et al. 2009). The article implicated xenotropic murine leukemia virus-related virus (XMRV), a human retrovirus, in the development of CFS and generated wide interest and a series of subsequent studies that ultimately produced conflicting results (Wilson, Atkinson, and Keelan 2014a).

Internationally, there was little consistency in the approach to management of the potential threat of XMRV and CFS to national blood supplies (Lombardi et al. 2009). Many jurisdictions, including Canada, Australia, and the U.K., evaluated the available evidence, applied precautionary approaches, and implemented additional measures (from temporary to indefinite or permanent deferrals for any history of CFS diagnosis) to safeguard blood supplies (JPAC 2015; ARCBS 2016; CBS 2016a). Other jurisdictions, with the same available evidence, chose not to take any action against XMRV, citing reasons such as seriousness of the threat (not deadly), a lack of confirmatory evidence after the *Science* paper, or any evidence to support transfusion transmission (ECDC 2011).

Ultimately, it was determined that the original findings reported in the *Science* publication were a result of laboratory artifacts, and that XMRV posed no risk to blood donors or recipients (Dodd 2011a, 2011b; Dodd et al. 2012; van Kuppeveld and Van der Meer 2012; Kakisi et al. 2013). The original and related papers suggesting a link between XMRV and CFS have all since been retracted, with or without author permission (Silverman et al. 2009; Alberts 2011; Lo et al. 2010). Nevertheless, the policies created in their wake continue to exist in many instances (Wilson, Atkinson, and Keelan 2014a).

Evaluation of case studies

Characteristics of the risks and precautionary measures—The properties of the transfusion risk managed, and the precautionary measures instituted for the above-described case studies are summarized in Table 1. While in all cases the size of the exposed group (transfusion recipients) was small, if one assumes that transfusion propagates risk then the potential for disease spread increases as exposed individuals subsequently become donors. The severity of the threat being managed varied across all cases. On one hand, vCJD was a rare yet invariably fatal condition. Meanwhile, HIV while initially fatal, has become a chronic, medically manageable condition. CFS sufferers are not at risk of death, but many experience serious, if not debilitating symptoms in quality of life and ability to work or contribute economically to society.

The health benefits of precautionary actions also varied across case studies. MSM deferral policies removed only one potential source of risk for transmitting HIV and theoretically protected against other transfusion transmissible sexually transmitted infections potentially emerging from this population. The vCJD donor deferral policy only partially eliminated affected donors, as a full ban on donations from individuals who had spent any time in the U.K. between 1980 and 1996 was not implemented. The CFS policies were highly theoretical in identifying an at-risk population and as such their ability to reduce risk was also highly theoretical and subsequently disproven.

The health harms identified in the case studies examined here include implications to the blood supply, stigmatization of exposed populations, and economic consequences. In most instances, the risk of reduction in the donor pool was considered manageable. This was particularly true for the situation arising from CFS donor deferral, although the degree of donor loss that the blood supply system was expected to sustain was not ascertained. Stigmatization of the MSM community as a result of MSM deferral policies has had lasting implications, and has contributed to the recent review of these policies globally. Economic consequences of the precautionary actions outlined in our three cases were minimal and mainly centered around increasing screening procedures and donor recruitment. The evidence upon which these policies were enacted was minimal in all cases with no firm epidemiological evidence of risk. On a continuum, the MSM policies were most supported by available scientific evidence at the time of institution, followed by vCJD and CFS donor deferral policies.

Consistency with international guidance—The precautionary principle is detailed in Article 191 in the *Treaty on the Functioning of the European Union* (EURLex 2012). This original articulation of the principle focused on the environment, stating:

Union policy on the environment shall aim at a high level of protection taking into account the diversity of situations in the various regions of the Union. It shall be based on the precautionary principle and on the principles that preventive action should be taken, that environmental damage should as a priority be rectified at source and that the polluter should pay.

(EURLex 2012; ‘Risk-based decision-making framework for blood safety’ 2014)

Use of the principle is guided by a communication from the European Commission in 2000 (CEC 2000). These guidelines indicate that the precautionary principle shall be informed by three specific principles: (1) the fullest possible scientific evaluation, the determination, as far as possible, of the degree of scientific uncertainty, (2) a risk evaluation and an evaluation of the potential consequences of inaction, and (3) the participation of all interested parties in the study of precautionary measures, once the results of the scientific evaluation and/or the risk evaluation are available. In addition, the following five general principles of risk management are to be utilized when the principle is invoked; (1) proportionality between the measures taken and the chosen level of protection, (2) non-discrimination in application of the measures, (3) consistency of the measures with similar measures already taken in similar situations or using similar approaches, (4) examination of the benefits and costs of action or lack of action, and (5) review of the measures in light of scientific developments. These European guidelines on the principle are also consistent with those provided by Canadian frameworks (Wilson et al. 2006; Weir et al. 2010).

In examining our three cases of donor deferral policies with respect to their consistency with European Union guidelines, we contend that precautionary responses have become increasingly disproportionate to perceived risk over time. Furthermore, despite known difficulties in repealing or changing donor policies, policies have become more rapidly implemented and more aggressive (Table 2). Early application of precautionary approaches in the case of MSM deferral policies, was an application in response to the risk posed by the rapid spread of HIV/AIDS in the mid-1980s. With vCJD in Canada, sustainability of the Canadian blood system was considered, and a six-month deferral policy was introduced to maintain an estimated 3% reduction of blood supply (Wilson et al. 2003). In contrast, deferral decisions regarding XMRV introduced an indefinite ban for individuals with a medical history of CFS. Here however, the overall impact to the blood supply system was expected to be minimal given that most ‘fatigued’ individuals were unlikely donors. The review process for each of the described donor deferrals policies was particularly slow due to political, regulatory, and theoretical challenges posed by removing precautionary policies.

Major themes emerging from case studies—Four major themes emerged from a review of the case studies: (1) the distinction between precautionary approaches and risk management needs to be clarified; (2) the removal of legacy precautionary policies can be problematic even when evidence supporting their removal exists; (3) there are harms associated with precautionary policies; and (4) intermediate applications of precautionary approaches that balance health risks are well-suited to transfusion medicine.

Precaution and risk management—Of the case studies examined, the area of greatest confusion was the distinction between precautionary approaches and risk management, likely derived from the diverse range of interpretations of the precautionary principle. The Wingspread Statement argues that, ‘When an activity raises threats of harm to human health or the environment, precautionary measures should be taken even if some cause and effect relationships are not fully established scientifically.’ (Steingraber 1998; CEC 2000). In contrast, the Rio Declaration states, ‘Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-

effective measures to prevent environmental degradation.’ (UNEP 1992b). The Maastricht Treaty states that the precautionary principle:

relates to an approach to risk management whereby if there is the possibility that a given policy or action might cause harm to the public or the environment and if there is still no scientific consensus on the issue, the policy or action in question should not be pursued.

(UNEP 1992a)

Thus, ambiguity of definition likely contributes to variable application and interpretation of the precautionary principle. One might argue that the precautionary principle should only be applied to truly theoretical risks. Under such an understanding, once a risk is quantified the decision-making process would then transition into a classic risk management approach, where risks and benefits of any decision are compared. In complex cases however, even when some aspects of risk are quantified, others may remain in the theoretical realm, thus blurring the distinction between precautionary approaches and risk management. For example, MSM donor deferral policies have been largely maintained even after the risk was quantified, with one of the arguments being that the MSM community remains a potential incubator population for other transfusion-transmitted conditions. Similarly, despite the comparative absence of new vCJD cases, there remains a theoretical risk for development of disease in individuals with a susceptible genotype, and thus donor deferral policies are still common place for individuals who have traveled to high-risk jurisdictions.

Removal of precautionary policies can be problematic—Review of the case studies identified a common issue associated with removal of precautionary policies even when evidence supporting their removal existed. Ideally, precautionary policies would be applied when an uncertainty of risk exists, and its application modified or removed as new evidence is brought to light. Such an approach is rarely taken, however. In transfusion medicine, it has proven politically challenging to reverse a decision that was introduced for the purposes of protecting the public. Second, the regulatory process is slow and consequently policy changes often lag behind the accumulation of new scientific evidence. Third, as discussed previously, theoretical risks may be ongoing, thus favoring the preservation of the existing policies. When a highly risk-averse approach is applied to policy-making, it can be challenging to rescind policies – a form of anchoring bias (Kahneman et al. 2006). The issue of changing legacy policies is particularly salient for the ongoing application of the precautionary principle and precautionary approaches. Difficulties encountered in changing CFS donor deferral policies highlight these challenges, where scientific evidence has ruled out the causal relationship between XMRV and CFS, and yet the deferral policy continues.

There are harms associated with applying precautionary approaches—One of the challenges of applying precautionary approaches to guide public health policy is avoiding harm caused by mitigating the theoretical risk itself (Attaran and Maharaj 2000; Miller and Conko 2001). In cases of transfusion medicine, the obvious consequence of introducing donor deferral policies is the loss of potential blood donors. The impact of donor loss on public health is difficult to quantify. However, reducing the donor supply limits the ability to introduce policies to address future risks to the blood supply. Public sensitivity to

donor deferral policies must be accounted for as well. As illustrated by the MSM donor deferral case study, members of the MSM community often view continuation of the policy as discriminatory.

A second potential harm of applying precautionary approaches includes economic consequences. In precautionary decision-making, traditional cost-effectiveness ratios cannot be calculated but can only be estimated as potential risks, since the benefit of any measure is uncertain. Risk-averse policy-making processes impact on cost in areas of risk management is more quantifiable, however. Other areas of blood safety such as nucleic acid amplification testing for Hepatitis B have cost-effectiveness ratios in the millions per QALY (Menitove et al. 2014); considerably out of proportion to standard ratios for health care, approximately \$100 000/QALY (Laupacis et al. 1992; AuBuchon, Petz, and Fink 2001; Custer and Janssen 2015).

Intermediate approaches that balance health risks are well suited to public health—The dual nature of many precautionary decisions in public health (whereby measures taken to mitigate risk can actually induce risk itself) favors weaker application of the principle. However, instead of the trade-off being between cost and benefit, the attempt is to balance two risks (risk–risk analysis; Goklany 2002). The vCJD donor deferral policy is an example of an effective application of a policy that attempts to balance both the risk of donor loss and the risk vCJD transfusion transmission (Wilson and Ricketts 2004a).

Discussion

Application of precautionary approaches to transfusion medicine has been both transformative and problematic. On one hand, failure to use precautionary approaches has arguably resulted in one of the worst public health crises in Canada, while on the other hand, application of the principle has created challenges for blood agencies. Through case study analysis, we have examined the decision-making properties and the extent to which external guidelines on precautionary approaches were adhered. Two trends were observed – precautionary responses have become more aggressive over time, and the review process for reassessing precautionary policies is slow. Furthermore, our review of applications of precautionary approaches in this field has indicated that there is a need for clarification between precautionary approaches and risk management strategies; the removal of precautionary policies can be problematic; there are harms associated with the implementation of the principle; and intermediate precautionary approaches appear to be best for managing risk in transfusion medicine.

The overarching issue encountered with application of the precautionary principle in other policy domains has been one of clearly defining the principle itself (Vanderzwaag 1999). The issue of definition has also proven problematic in applying precautionary approaches in areas of public health, including blood safety. Additionally, while provision of guidelines on using the precautionary principle has been of value to policy-makers, issues of when to transition from precautionary to risk management policies when new scientific evidence becomes available remain challenging.

Developing policy on the foundation of an aggressive precautionary approach creates a form of anchoring bias toward highly risk-averse policies. Such an anchoring bias creates obstacles to policy change even when new evidence arises, and hinders the application of risk management approaches. As a consequence, in transfusion medicine we see significant challenges to removing precautionary policies despite strong scientific evidence supporting their reversal. Aggressive deferral policies can also have a negative impact on public health – an issue that is in direct conflict with the very nature of the principle. We see this as the double-edged sword of precautionary health applications.

How then can the benefits of enacting precautionary approaches be accrued while concurrently mitigating all potential harms? Frameworks for the application of the precautionary principle and risk management strategies have been developed to address the unique issues of blood safety (Wilson 2011; ‘Risk-based decision-making framework for blood safety’ 2014). The Alliance of Blood Operators’ *Risk-based Decision-Making Framework for Blood Safety* specifically alludes to the use of precaution in scenarios where uncertainty is high, although in general favors proportional responses. This framework is guided by the concept that safety of the blood supply must be optimized, while acknowledging that zero-risk is not attainable. The Alliance of Blood Operators’ framework, which was not available at the time of the decisions examined in our analysis, is reflective of the adaptive management design utilized in the environmental sector (Holling 1978). Based on our review of the application of the precautionary principle to blood safety in Canada we believe these following principles should be incorporated in any risk-based decision-making framework:

1. Upon identification of risk, determine the strength of evidence supporting the risk, its magnitude, and the potential harms imposed by precautionary policies. For theoretical risks with potentially high magnitudes of harm introduce precautionary policies. Here, consider a weaker articulation of the principle where the harms of applying precautionary approaches can be balanced against the benefits.
2. When further evidence on the nature of risk emerges, migrate the policy-making process toward traditional risk management approaches. This will require regular assessment of available scientific evidence, flexibility in the policy-making process to enable policy changes, and insulation of the risk management process from bias toward risk aversion created by the initial institution of the policy. The latter may require independent evaluators not involved in the original risk assessment and policy development.

Our recommendations are consistent with adaptive management strategies employed in environmental frameworks that seek to deal with decision-making in the presence of scientific uncertainty. We do believe however, that the issue of anchoring bias will remain a fundamental challenge. The aforementioned Alliance of Blood Operators’ guidance on risk-based decision-making has sought to address these challenges (‘Risk-based decision-making framework for blood safety’ 2014). Ultimately, an optimized comprehensive framework that integrates both precautionary approaches and traditional risk management approaches will be beneficial not only to blood safety but also to other public health sectors.

Conclusion

Transfusion medicine has arguably pioneered the use of the precautionary approach in the public health sector. However, application of the approach has proven challenging. As we move forward and policy-makers are confronted with cases with potential precautionary applications, implementation of reference guidelines will improve the policy-making process. Such frameworks should provide guidance on when to introduce the precautionary principle, how to balance the risk and benefits of precautionary policies, how to transition from precaution to risk management when evidence of risk emerges, and when to remove precautionary policies.

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Table 1

Properties of decision.

Properties of decision	Deferral policy		
	MSM	vCJD	CFS
Proportion of population exposed to risk	Small Transfusion recipients of potentially infected products High proportion of high-risk populations (e.g. hemophiliacs)	Small Transfusion recipients of potentially infected products High proportion of high-risk populations (e.g. hemophiliacs)	Small Transfusion recipients of potentially infected products High proportion of high-risk populations (e.g. hemophiliacs)
Severity of harm caused by exposure	Initially high Low quality of life, illness, and death Now lower as HIV is manageable with medical treatment	High Rapid decline and death. No of treatment available	Not fatal but potentially disabling
Reversibility harm caused by exposure	Irreversible but HIV now treatable.	Irreversible	Irreversible Severity of symptoms waxes and wanes
Health benefits	Protection of blood supply from a potentially transmittable infection	Protection of blood supply from a potentially transmittable infection	Protection of blood supply from a potentially transmittable infection
Health harms	Blood supply shortage Stigmatization of MSM population	Blood supply shortage. Potential inappropriate self-deferral	Blood supply shortage but very unlikely to have a significant effect on its own as these individuals would likely not be donors
Economic consequences	Cost of screening procedures and recruitment of new donors	Cost of screening procedures and recruitment of new donors	No large economic impact
Level of evidence that triggered policy	Pattern of transmission initially appeared limited to homosexual community	Initially purely theoretical based on a biological model	Evidence of risk reported in one academic study which was subsequently retracted

Table 2

Adherence to external guides.

European union guidelines	Deferral policy		
	MSM	vCJD	CFS
Proportionality of initial response.	Initially strong precautionary response Complete ban on MSM population Has been subsequently reduced in scope	Intermediate precautionary response Risk management approach; deferral policy of 6 months on a corresponding blood supply reduction of 3%	Strong precautionary response Complete ban on individuals with medical history of CFS
Non-discrimination	Policy focused on MSM population. Considered to be discriminatory as other populations also at risk of transmitting	Ban focused on those that met residency requirements in the United Kingdom but within this population was non-discriminatory	Policy focused on individuals with CFS, but embraced by community because it legitimized the illness with a biological cause
Consistency	First major threat to blood supply so new policies were implemented	First major threat to blood supply so new policies were implemented Consistent with MSM approaches but more disproportional because risk not as established Decision influenced by previous experience in Canadian blood system that indicated that a 3% reduction in the blood supply was sustainable	More disproportional than other approaches, with limited evidence
Examining costs and benefits	Unclear	Donor impact analysis performed	Impact on donor pool was expected to be small
Subject to review	Policies have evolved as subsequent HIV tests became available. Deferral period progressively reduced	Was reviewed with changes made to donor deferral period influenced by impact of policies on donor population	Policies are still in place despite evidence supporting their introduction identified to be inaccurate