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Chapter 3:

Arguments for tolerance or intolerance towards risks of blood transfusion: views of stakeholders in the Dutch blood supply

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ABSTRACT

Introduction: The perception of transfusion-transmitted infections (TTIs) is sensitive to various concerns besides the probability of infection. These factors may reflect legitimate ethical considerations. Understanding stakeholders' reasons to consider TTI risks tolerable or intolerable is imperative to advance thinking on reasonable blood safety.

Methods: We held 25 interviews and 2 focus group discussions with policy-makers, hematologists, blood donors, and blood product recipients. Respondents discussed the tolerability of TTI risks by comparing TTIs to other hazards, and by commenting on the costs of blood safety. Arguments for tolerance or intolerance towards TTI risks were identified and categorized by qualitative analysis.

Results: 414 relevant quotes were extracted from the interviews and group discussions. These quotes could be clustered into 7 categories: the clinical impact, probability, and avoidability of infection; cost and health benefits and other consequences of safety measures; non-consequentialist ethical arguments; and stakeholders' interests.

Discussion: Remarkable findings included contrasting views on whether TTI risks are tolerable because the a priori probability of becoming infected is low; and the controversial idea that lower safety standards may be applied for patients with a poor prognosis. On the assumption that resources spent on inefficient blood safety measures could be applied more beneficially elsewhere, several responders expressed tolerance towards TTI risks. Others argued that the value of life cannot be translated into monetary costs, or that saving money on blood safety would not make a difference elsewhere, suggesting that initiatives to increase efficiency in blood safety should be matched by similar initiatives in other domains of health care.

INTRODUCTION

According to health economic research, certain tests to detect transfusion transmissible infections (TTIs) in donated blood rank among the least efficient health care interventions. Incremental cost-effectiveness ratios exceeding €1.000.000 per quality-adjusted life-year (QALY) have been reported, for example for serologic testing on human t-cell lymphotropic virus (HTLV) and nucleic acid testing (NAT) on hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) [1-4]. These costs per QALY reflect how few infections these safety measures prevent, given the presence of further safety measures. For example, if effective donor selection and sensitive serological screening for HBV, HCV, and HIV are in place, adding NAT screening will have limited value for safety. While cost-sensitive decision-making approaches have recently been proposed [5], initiatives to downscale inefficient safety measures have been scarce [6], and blood services continue to introduce safety measures of questionable efficiency (e.g. Zika virus NAT in the United States and hepatitis E NAT in Ireland, the United Kingdom and the Netherlands).

The continuation and introduction of inefficient safety policies presumably reflects a low public tolerance for TTI risks. A number of studies have applied risk perception theory to chart public attitudes towards the risks of blood transfusion (see [7] for an overview). These studies found that blood transfusion was considered more risky than many activities with a comparable or a higher mortality rate. The perception of blood transfusion risks, which focused strongly on TTI risks, was dependent on test subjects' demographic variables, worldviews, and cognitive heuristics. The perception of these risks was also sensitive to the three 'risk dimensions' from psychometric theory: the extent to which risks are dreaded and considered severe; the extent to which they are considered controllable and well-understood; and the extent to which the activity that generates these risks is considered beneficial. Compared to other hazardous activities, blood transfusion was perceived as very beneficial, and its risks as moderately severe and uncontrollable [7-10].

One might conclude that the perception of TTI risks is distorted by irrational biases. For example, whereas Ngo et al. [7, p.120] call a probabilistic approach to risk 'rational', 'systematic', and 'reliable', they call the public's perception of risk 'intuitive' and 'subjective'. On this appraisal, decision-makers face a dilemma: they must either prioritise rationality in their choices but ignore public perception, or take public perception into account even if this implies that some policies are less rational [cf. 11,12].

Public estimates of the probability that hazards will strike, e.g. of the chance of contracting a TTI, may indeed be unreliable. However, risk perception may not (only) concern probability. Risk perception appears sensitive to ethically relevant characteristics of risks, including the extent to which being at risk is voluntary; the distribution of risks and benefits; and the existence of alternatives to hazardous activities [11-14]. Furthermore, risk perception may be based upon emotions but such emotions may well point to valid ethical concerns. Anger might for example be a reasonable response to injustice, and fear to a significant threat to one's well-being [12]. Dismissing public risk perception as subjective and irrational may thus be too hasty: rather than being a distorted appraisal of probability, public risk perception may be responsive to a complex set of ethical issues [12, 14]. This does not mean that public perceptions should be accepted at face value. Analysing views towards risks may yield relevant ethical perspectives, but further reflection may reveal mistaken empirical assumptions or problematic ethical implications [12, 13].

Previous studies considered whether insights from established theories on risk perception, notably Slovic and others' psychometric theory, applied to TTI risks [cf. 7]. Therefore, these studies could not identify influences on TTI risk perception that risk perception theory did not already recognize. Furthermore, these quantitative studies used closed answer formats and did not attempt to understand the reasons behind respondents' answers. In what ways were risks of blood transfusion considered controllable or uncontrollable, for example, and why were they dreaded? On what assumptions and emotions were such perceptions based? This paper offers an overview of arguments for tolerance or intolerance towards TTI risks, based on qualitative empirical research among stakeholders in the Dutch blood supply. It clusters and categorizes these arguments, highlights remarkable and controversial arguments, and offers explanatory stakeholder citations. This reveals whether previous research has overlooked or undertheorized perspectives on the tolerability of TTI risks.

(Note on terminology: we hold that 'tolerating' a risk means having a negative attitude towards a risk but choosing, for certain overriding reasons, not to reduce it. The term risk 'acceptance' may be more applicable when a risks is not regarded negatively at all or cannot be reduced. In what follows, though, we do not distinguish arguments for risk tolerance from arguments for risks acceptance.)

METHODS

Selection of respondents

Aiming for a broadly constituted set of respondents, we planned to interview 5 blood product recipients, 5 donors, 5 haematologists, 5 policy-makers (members of the Dutch Ministery of Health, Welfare and Sport [VWS], members of the Dutch Parliament with blood safety in their portfolios, and members of Sanquin's Board of Directors), and 5 policy-advisors (members of Sanquin's Medical Advisory Board). In addition, we planned to have one focus group discussion with 5 donors and one focus group discussion with 5 blood product recipients. The dynamics between participants in group discussions was expected to yield perspectives that could not be attained in interviews. Recruiting haematologists, policy-makers and policy-advisors for group discussions was judged unfeasible.

Blood product recipients were recruited via the Dutch haemophilia society (NVHP), an advocacy group for patients with haematological malignancies (Hematon), and an advocacy group for patients with rare blood disorders (SZB). Donors were approached through donor societies (DVNL and DAR). Blood product recipients and donors were preferably recruited by means of open calls, but when open calls yielded insufficient response, our contacts at patient and donor societies approached candidates personally. Haematologists, policy-advisors, and policy-makers (members of the Dutch Parliament with blood safety in their portfolio, representatives of the Dutch Ministry of Health, and members of Sanquin's Board of Directors) were approached directly. Diversity among respondents was a key consideration in these recruitment efforts.

Potential respondents were informed that the interviews and focus group discussions would be recorded, that their personal data would be stored locally, that all published data would be anonymized, and that they could opt out of the research at any time.

Because few policy-makers external to Sanquin proved willing to partake in our research, we set up a combined category for policy-makers and policy-advisors, which consisted of 1 member of Parliament, 2 members of Sanquin's Board of Directors, and 5 members of Sanquin's Medical Advisory Board. Also, we decided to expand the number of interviews with blood product recipients, as the group discussion included fewer participants than planned, owing to last-minute cancellations. Respondent data is listed in table 1.

Table 1: Data of participants in interviews and focus group discussions

Code	*Age*	*Sex*	*Education*
Blood product recipients, interviews			
R01	70-79	M	Mid-level professional
R02	40-49	M	Mid-level professional
R03	50-59	F	Mid-level professional
R07	50-59	F	High-level professional
R09	50-59	M	Mid-level professional
R10	50-59	M	Mid-level professional
R12	50-59	M	Academic
Blood product recipients, group discussion			
R11	20-29	M	Academic
R13	70-79	M	High-level professional
Blood & plasma donors, interviews			
D01	40-49	M	Academic
D02	60-69	F	Academic
D03	30-39	M	Academic
D04	60-69	M	High-level professional
D08	40-49	F	High-level professional
Blood & plasma donors, group discussion			
D05	50-59	M	High-level professional
D06	60-69	M	Academic
D11	60-69	M	High-level professional
D15	20-29	F	High-level professional
D16	40-49	M	Academic
Haematologists			
H01	40-49	M	Academic
H02	40-49	F	Academic
H03	30-39	F	Academic
H04	50-59	M	Academic
H05	50-59	F	Academic
Policy-makers & policy-advisors			
P01	60-69	M	Academic
P02	60-69	M	Academic
P03	60-69	M	Academic
P04	40-49	M	Academic
P05	70-79	M	Academic
P06	50-59	M	Academic
P07	60-69	M	Academic
P08	60-69	M	Academic

Design and execution of interviews and focus group discussions

Interviews and group discussions were scheduled for an hour. Some interviews took more than an hour to complete, especially interviews with blood product recipients who had intricate medical and personal histories, some of which lasted 2 hours. The interviews were performed by the first author, the focus group discussions were led by a professional moderator. Oral permission was acquired before recording each session.

The interviews and group discussions had four main parts and were semi-structured, meaning that a list of questions was followed in a flexible order and that respondent input that was unrelated to preconceived questions was stimulated. In the first part, which was meant to break the ice, we asked respondents how and why they were involved in the blood supply, and we probed their experiences with the blood supply. Subsequently, respondents were invited to share issues concerning the blood supply, including safety issues, that worried or upset them. In the third part, respondents compared the risk of contracting a serious TTI to a number of other risks, commented on the tolerability of each risk, and offered reasons for their comparative tolerability judgments. We included three hazards to represent extremes in the main risk dimensions of risk perception theory: the risk of having a serious traffic accident represented known, controllable, but not strongly dreaded hazards; the risk of having a nuclear meltdown represented unknown, uncontrollable, and dreaded hazards; the risks of genetically modified foods represented unknown, uncontrollable, and moderately dreaded hazards. We also included a number of hazards that resembled TTI risks in some respects, while differing in others: the risk of having adverse reactions to prescription drugs; the risk of having severe complications during surgery; and the risk of contracting a dangerous infection through food. Finally, respondents commented on the tolerability of TTI risks in relation to some research-supported claims about the costs of the Dutch blood supply, including the claim that blood products are more expensive in the Netherlands than in neighbouring countries [15]; the claim that the Dutch blood services applies more safety tests than most blood services abroad [15]; and the claim that some of these tests have incremental cost-effectiveness ratios of over €1.000.000/QALY [1].

Analysis

The first 12 interviews (3 in each category) were written out verbatim, except for parts that were completely unrelated to the research topic, which were summarized. Fragments that seemed to address relevant issues were listed and coded in a separate file (using Microsoft Excel 2013). We subsequently rejected fragments that did not address reasons for tolerance or intolerance towards TTI risks, or that concerned risks taken by donors, recipients, or haematologists rather than the blood service.

The remaining fragments were open coded, i.e. given initial labels, based on their content. Fragments with related labels were grouped and captured under increasingly general categories.

From the remaining 13 interviews and the focus group discussions, we extracted fragments that seemed to add something new to our initial list of fragments, whether in terms of the topic addressed, in terms of the view expressed about this topic, or in terms of wording. A revised list of fragments and categories was obtained by incorporating these additional fragments and revisiting the passages from our initial analysis.

RESULTS

We extracted 414 relevant passages from 25 interviews and 2 group discussions. We identified clusters of passages in which similar arguments for risk tolerance or intolerance were addressed (whether or not these arguments were considered valid). These clusters were captured under seven headings: 'clinical impact of infection'; 'probability of infection'; 'avoidability of infection'; 'costs and health benefits of safety measures'; 'miscellaneous consequences of safety measures (logistics, supply, and clinical effectiveness)'; 'non-consequentialist ethical arguments'; and 'stakeholder interests'. The arguments involved are summarised in Tables 2 – 8. Below, we follow these headings and discuss remarkable or controversial arguments captured under them.

1. Clinical impact of infection

Arguments that related to the clinical impact of TTIs are presented in table 2.

Table 2: Arguments for tolerance or intolerance toward TTI risks: clinical impact

Argument:	*Tolerance or intolerance:*
The disease is/is not serious	—/+
The disease is/is not lethal	—/+ | x
The disease is/is not curable	+/—
Some patients are especially vulnerable	—
Without the TTI, patients have a good/bad prognosis	—/+
Infection does not imply disease	+ | x

Legend:
/: Separates alternative values of variables
+: Argument for risk tolerance
—: Argument for risk intolerance
X: Argument or variable deemed irrelevant
|: Separates alternative evaluations of arguments

That the seriousness, lethality and curability were considered relevant variables for the tolerability of TTI risks, and that the vulnerability of specific patient groups was offered as an argument for risk intolerance, seems unsurprising. Non-lethality was sometimes denied to be relevant for risk tolerability, which was supported by arguing that even non-lethal TTI could be serious, or by calling attention to especially vulnerable groups of patients, to whom TTIs that are generally non-lethal might prove fatal. Most interesting, there were some respondents who seemed to deny that the special vulnerability of certain patients groups supports intolerance towards TTI risks. Upon closer consideration, however, these respondents argued that having a poor prognosis even without a TTI justified tolerating some TTI risks. In the words of respondent D01:

> "If you lose a lot of blood while giving birth, and need a transfusion because of that, that is something entirely different than if someone needs his third transfusion that week. (…) When you're dealing with a bottomless pit, you could accept some more risk. (…) [Whether someone] needs a blood transfusion just one or two times, but whose life-expectancy is not affected, or whether you're talking about someone whose life expectancy is very limited anyway." (Fragments D01-19 & D01-20)

A further argument in this cluster is that someone who becomes infected need not develop disease symptoms. This argument was offered to support risk tolerance, but its relevance can be contested, as respondent P08 did, by highlighting that the infection could be transmitted further, that carrying the infection affects one's social interactions, and that the infection might develop into disease later in life.

2. Probability of infection

The probability of acquiring a TTI was another unsurprising consideration behind our respondents' views on the tolerability of TTI risks. Still, some interesting arguments were offered (see table 3, next page).

One notable finding is that although the risk (in terms of the possibility of becoming infected) varies per TTI, many respondents considered this risk small in general. As respondent R01, a polytransfusee, said:

> "If you consider how much blood is collected in the Netherlands, and how few people have the bad luck of experiencing an adverse event, that is such a minimal amount, it's negligible." (R01-03)

Table 3: Arguments for tolerance or intolerance toward TTI risks: probability of infection

Argument:	*Tolerance or intolerance:*
The risk of infection is/is not large	−/+
TTI risks are conditional risks	+ | −
Further transmission is not probable	+
Other risks are larger	+
Other non-medical risks are larger	+ | x
Other medical risks are larger	+
Other risks of blood products are larger	+
Different modes of transmission are more probable	+
Many safety measures are already in place against TTIs	+
Some (small) risks must be accepted	+
(Small) risks are part of daily life	+
(Small) risks are part of medicine	+
A line must be drawn somewhere	+
TTI Risks are not distributed evenly	
The at-risk group is/is not a small portion of society	+/−
Certain patient groups run more risk	−

Respondents regularly stated that TTI risks are small and well-managed compared to many day-to-day risks, medical risks, transfusion hazards other than TTIs, and infection risks with other modes of transmission (e.g. eating). They also recognized that some small risk should be tolerated, as risk is ubiquitous and TTI risks cannot be eliminated completely. These views were typically, but not always, offered as arguments for TTI risk tolerance. Some respondents stressed that TTI risks are unevenly distributed. The risk may be small for many patients, but patients who need blood products regularly, like haemophiliacs and polytransfusees, run significantly more risk. This was considered an argument for intolerance towards TTI risks.

Various respondents noted that TTI risks are conditional upon the risk of getting health problems that require blood product therapy, but conflicting conclusions were drawn from this insight. Small risks per blood product translate into even smaller risks for random persons, most of whom never need blood products, which according to some respondents is an argument for risk tolerance. According to others, though, this is an argument for risk intolerance. In the words of respondent R11, who has a rare clotting disorder:

> "The chance of having what I have is one in a million. And the chance that, if I need a transfusion, it is the one transfusion in ten years where something goes wrong, that is just... That is very nasty." (R11-11)

On this view, a small risk is not more tolerable if it is conditional upon another small risk; to the contrary, being stricken by a small conditional risk means one suffers from extreme bad luck, which is a dramatic and undeserved fate. A related view is that risk is especially intolerable when it frustrates attempts to remedy someone's bad luck. As respondents R11 and D11 explain:

> "You see, the reason you receive blood products, something is going on already, something has happened to you, something is wrong that might already be unfair. If you get an infection on top of that, that's like kicking someone when he's down." (R11-10)
> "If you need drugs or an operation, you are in a situation and you are dependent, for instance on medication. If that goes wrong, or you develop nasty adverse reactions, that is just very... Because you already are a victim, actually, you become a double victim." (D11-09)

3. Avoidability of infection

A third cluster of arguments regarded the avoidability of TTI risks.

Table 4: Arguments for tolerance or intolerance toward TTI risks: avoidability of infection

Argument:	*Tolerance or intolerance:*
TTI risks are/are not avoidable	−/+
Recipients can/cannot choose to avoid TTI risks	+/−
Getting a transfusion is/is not a choice	+/−
There are no alternatives for blood products	−
There are no alternative suppliers of blood products	−

Clearly, risks that cannot be avoided must be tolerated (or accepted). However, respondents differed on whether TTI risks are avoidable. Some claimed that TTI risks are typically foreseeable and can be ruled out by taking adequate safety measures. Others argued that TTI risks are unavoidable due to unforeseeable epidemiological developments and technological limitations of safety measures. These claims may hint at different interpretations of the notion of avoidability: if avoiding risk means reducing risk drastically, many TTI risks may be avoidable, but not if avoiding risk means reducing risk to zero.

Another issue was whether individuals (blood product recipients and their clinicians) had options to avoid TTI risks. Various respondents claimed that blood product recipients had no choice but to undergo treatment, although some respondents argued that receiving blood products in the context of elective surgery is avoidable, and one respondent argued that even risks relating to life-saving treatments are avoidable, insofar as such treatments can be refused. Similar arguments were that there are no treatment alternatives for blood products, and that blood product users cannot choose among suppliers, given Sanquin's monopoly in the Netherlands. Lacking choices to avoid TTI risks was considered an argument for risk intolerance.

4. Costs and health benefits of safety measures

A fourth cluster of arguments concerned the costs and (health) benefits of safety measures.

Table 5: Arguments for tolerance or intolerance toward TTI risks: costs and (health) benefits of safety measures

Argument:	*Tolerance or intolerance:*
The absolute costs of safety measures are/are not high	+/− | x
The budget impact of safety measures is/is not high	+/−
Other medical procedures are more expensive	−
Preventing infections saves costs	−
Taking safety measures means the price of blood products will increase	+ | x
The absolute health benefits of safety measures are/are not high	−/+
Health benefits are very valuable	−
The value of health cannot be expressed in monetary terms	−
Safety measures are/are not a beneficial use of resources	−/+
Some safety measures are not cost-effective	+ | x
Resources can/cannot be used to benefit more people	−/+ | x
Resources can be used to save more life-years	+
Other patients have a claim on health care resources too	+
Resources should not go unused	−
Alternative savings are/are not possible	−/+
Costs of safety measures are borne collectively	+ | x

Relating costs to health benefits was a common strategy to put the former into perspective. Some respondents denied the relevance of cost-effectiveness data by arguing that someone's life is extremely valuable or that the value of life cannot be translated into monetary terms. Various respondents would tolerate TTI risks, however, if resources needed to reduce TTI risks could be applied more efficiently elsewhere in the health care system, thus helping more people or saving more life-years. Interestingly, this included recipients of blood products, for example respondents R07 and R12:

> "Of course I want to run as little risk as possible. But I am realistic in understanding that it's not only about me. And that what matters is always how you can help the most people. (…) You can't expect society to spend its money on an individual rather than helping a larger group." (R07-27 & R07-28)

> "If it's indeed like, six million, one life, if we spend that six million in some other way we save ten lives, well, ok, then you have a point. (…) But you have to show that with facts, you have to be transparent about that." (R12-57)

As other respondents expressed, stacking inefficient blood safety measures is difficult to defend if other patients lack adequate care, because those patients have a claim on health care funds too:

> "To be honest, I think that [safety measures costing over one million per QALY] is a little too much, because health care is wildly expensive, and I think everyone has a right to health care, and not just a few people on whom lots of money are spent." (P05-26)

> "What if there's someone who needs a heart transplant, for which you don't have the money, but you would apply these safety measures. That would be very odd. (...) Then you're telling a patient getting a transfusion: you are more valuable." (P04-48)

One respondent deepened this argument by relating other patients' claim on resources to the way health care is funded:

> "It's public money, which means that you want to help as many people as possible, or reduce disease burden to a minimum. (...) We have a social principle that we all pay for it, and that we all want to reap the benefits." (P06-77)

However, various respondents argued that the choice between applying blood safety measures or helping other patients is a false dilemma. One argument was that the budget impact (and thus the opportunity cost) of blood safety measures is negligible in the Netherlands. As respondent P07 stated:

> "If I start calculating and cut costs seriously, I say it's all going well, and we can cut about half our expenses. Then I end up saving around 20 million euros. 20 million in public health care, well, what would you like to use it for? (…) 20 million is nothing in public health care." (P07-28)

Another argument was that freeing health care funds does not require cutting costs on blood safety measures. Other inefficient processes within or outside the blood service should be optimized instead:

> "I would like to visit Sanquin and go through your business process, see if we can make it more efficient. (...) Creativity gets you far. But don't get creative with our safety." (R12-49)

These passages deny that taking blood safety measures excludes supplying other types of health care. Some respondents denied that being able to supply care to more patients is relevant at all, for example:

> "I think that [by saving money on blood safety measures and spending it elsewhere in the health care system, more patients could be helped] is a bit of a platitude, because it applies to a lot of things, right? Like, you know what, let's just leave that patient who costs 150.000 euros a month. Couldn't we do much better things with those 150.000 euros? Actually, couldn't we do much better things, on a global scale, with the 100 billion we spend on health care in the Netherlands? Such questions can be developed indefinitely." (P08-21)

Another way to put the costs of blood safety measures into perspective was to compare them to the costs of other medical procedures. Respondents who chose this framing downplayed the relevance of the costs of blood safety measures:

> "Compared to blood products, there are so much more expensive drugs. A haemophilia patient, for example, costs 150.000 euros a year, you know, and we spend that too. So if it's really necessary, we should do it." (H05-28)

> "If we would all consider how many sports-related injuries there are, and how much costs these injuries entail, I would like to compare that to this figure. (…) You would have to consider carefully why you would do the one thing, but wouldn't do the other." (R10-45)

5. Miscellaneous consequences of safety measures

Besides costs and health benefits, some other consequences of safety measures were considered relevant (see table 6).

Table 6: Arguments for tolerance or intolerance toward TTI risks: miscellaneous consequences of safety measures

Argument:	*Tolerance or intolerance:*
Safety measures do/do not cause logistical problems	−/+
Safety measures do/do not threaten the supply of blood	−/+
Safety measures do/do not threaten clinical effectivity of blood products	−/+
Safety measures do/do not invade donors' privacy	−/+
Safety measures do/do not decrease the market value of plasma	−/+

Logistical problems, supply problems, diminished clinical effectivity of blood products, and invasions on donors' privacy were mentioned as reasons not to take safety measures, and thus as arguments to tolerate some risk.

6. Non-consequentialist ethical arguments

A sixth cluster of arguments comprises non-consequentialist ethical arguments for risk intolerance (confer table 7, next page).

That these arguments are non-consequentialist means that they appeal to other ethical concerns than the (balance of) good and bad effects of decisions. A number of arguments revolved around the ethical premise harm is especially objectionable, from an ethical perspective, if it is caused by human action (compared to harm not prevented by human action). Some respondents argued that taking TTI risks means inflicting harm upon patients who contract a TTI:

> "Risks in traffic are things that if, well, if you're the one stricken by risk, you've done it to yourself. This is a risk that you, as a doctor, inflict on someone through your treatment. It does not strike you

> because you're just unlucky, it strikes you because someone else is actively doing something to you." (H03-12)

> "If I am administered something, uh, like blood, then I feel that I should not contract some kind of disease, which I did not have in me, but which is thus administered, in fact." (D04-44)

Table 7: Arguments for tolerance or intolerance toward TTI risks: Non-consequentialist ethical arguments

Argument:	*Tolerance or intolerance:*
Do no harm	
Taking TTI risks means being causally responsible for harm	−
TTIs are a serious breach of bodily integrity	−
Blood products are traceable sources of harm	− | x
Taking TTI risks is contrary to the aims of giving blood transfusions	−
Someone has been made responsible for avoiding TTIs	− | x
Stopping safety measures is particularly objectionable	
The status quo should be cherished	−
Stopping safety measures feels unsafe	x
Stopping safety measures is an active decision	−
(Potential) patients have acquired a right to the continuation of safety measures	−
Reintroducing safety measures is/is not problematic	− | +

One recipient argued that harms caused by taking TTI risks are especially serious, compared to harms caused by other medical procedures, because administering blood products constitutes an active and serious breach of bodily integrity:

> "You violate a body's integrity, and that calls for extra safeguards. (…) By infusing something, a barrier is crossed that normally remains untouched. Swallowing, eating and drinking, is something we all do. In that sense it goes further than taking a pill." (P01-12 & P01-14)

Blood products were considered easily traceable and well-delineated causes of harm; blood products, whether specific products or blood products in general, are easy to point at as the source of TTIs. Whether respondents accepted this argument was somewhat unclear, but they did offer it as an explanation of risk intolerance:

> "The question is: what is the cause? The cause could be the patient's natural disease progression. Here, [in the case of TTIs], it's quite clear that the cause is not the patient's natural disease progression." (H05-17)

> "It's administered, so it seems easier to pinpoint, like you can say, something was amiss there. That was what went wrong. You've externalized it, so to speak. It's someone else's, who gives it to you, who is therefore also guilty." (P06-41)

Several respondents noted that tolerating risks to patients conflicts with the aim of medicine, which is to improve patients' health. Thus, even if not construed as causing harm, taking TTI risks was considered inconsistent with the rationale of providing blood product therapy in the first place:

> "A serious infection through blood products is something you want to avoid at all times, because you want to help someone by giving blood products, and things go completely in the opposite direction if you do this." (D08-09)

> "It's a medical necessity for you, but it turns against you." (H05-13)

Some other ethical arguments applied specifically to TTI risks that result from discontinuing blood safety measures, which on these arguments are particularly intolerable (compared to TTI risks that persist because safety measures are not introduced). Various respondents indicated that the status quo should be maintained even if current safety measures are inefficient, although the rationale was sometimes unclear. One respondent explained and criticized this standpoint by arguing that maintaining ineffective safety measures just feels safe:

> "Take safety seats for children in the backs of cars, suppose that research would show they do not contribute to safety. Suppose that research would emerge, you would still see safety seats for children. (…) It still feels safe. (…) It feels like a loss." (P04-52)

Two respondents related stopping safety measures to being causally responsible for harm patients suffer:

> "If you really remove tests, then someone has consciously made a decision, and that influences your health. I think that is the point. (…) Something's afflicted upon you." (R11-45)

> "The one is an active decision, the other is passive. In the one case you really do something, you remove that, eh, that test, in the other you leave the situation as it is. Of course you could say that you do something by not introducing that test, and it's a decision not to make a decision. But emotionally, it's different." (D03-51)

The latter respondent also suggested that (potential) recipients of blood products had acquired a right to the continuation of inefficient safety measures:

> "Withdrawing funds from blood safety, if applying it elsewhere benefits more people. (…) Instinctively, I say no. (...) It's a bit like the idea of acquired rights, you see? (…) I think everybody [has acquired this right]. Everyone who could come into contact with the blood supply." (D03-46)

An important factual issue for the tolerability of withdrawing safety measures was whether these safety measures could, if necessary, be reintroduced easily and quickly. Competing views towards this issue were expressed.

7. Stakeholder interests

Arguments in the final cluster referred to the position or interests of specific stakeholders in the blood system (see table 8, next page).

Clearly, arguments in the preceding clusters already related, in some way, to the interests of blood product recipients. The current cluster comprises arguments that fit the previous clusters poorly but do address stakeholders' interests, where not only recipients' interests but all stakeholders' interests are included.

A diversity of arguments addressed the interests of blood product recipients and their families, or the special situation they are in. Respondents argued that recipients of blood products are in a dependent position, because they must entrust their safety to clinicians and have little control over their own safety. In addition, respondents argued that recipients of blood products deserve solidarity because their health is priceless to them and their loved ones, and because everyone could have been or could become a blood product recipient.

Table 8: Arguments for tolerance or intolerance toward TTI risks: interests/position of stakeholders

Argument:	*Tolerance or intolerance:*
Recipients' interests/position	
Recipients deserve solidarity	
Recipients' health is priceless to them (and to their loved ones)	−
Everyone could have been and may become a recipient	−
TTIs affect recipients' families	−
Families of infected recipients do/do not get adequate support	+/−
Recipients are in a dependent position	
Recipients must entrust their health to physicians	−
Recipients have limited influence on their safety	−
Recipients have more serious health-related worries	+
Blood products do/do not benefit the recipient significantly	+|− / −
Recipients should accept (some) bad luck	+ | x
Donors' interests/position	
Donors' blood should be used beneficially	
Donors' altruism should be supported or rewarded	−
Products for which donors have made an effort should not be spilled	−
Donors do not always take their responsibility for safety	−
Safety measures should not prevent donors from donating	
Donors want to donate	x
Donors have a right to donate	x
Rejecting donors is discrimination	x
Haematologists' interests/position	
Haematologists must trust in the safety of blood products	−
Haematologists have a special relation with recipients	
Haematologists are personally involved with recipients	−
Haematologists have a relationship of trust with recipients	−
Haematologists are (or feel) responsible for recipients	−

Table 8: Arguments for tolerance or intolerance toward TTI risks: interests/position of stakeholders (continued)

Argument:	*Tolerance or intolerance:*
Policy-makers' interests/position	
Policy-makers are empathetic with recipients	—
Policy-makers do not want to be responsible for TTIs	—
Policy-makers fear reputational damage	x
Policy-makers do not bear the costs of safety	x
Policy-makers are liable for TTIs	— | x
Policy-makers should be follow procedures and be consistent	
Tolerating TTI risks is/is not consistent with expressed values	+/—
Tolerating TTI risks is/is not consistent with democratic procedures	+/—
Tolerating TTI risks is/is not consistent with safety policies abroad	+/—
Society's interest/perspective	
Public acceptance of TTI risks is low	
The public expects blood to be safe	— | x
The public fears TTIs	— | x
Blood is special to the public	x
Safety policies affect public perception of blood safety	— | +

Another argument for risk intolerance, offered by recipients, was that TTIs affect victims' families. This argument was made by several recipients who had been infected by TTIs in the past, who expressed worrying for their loved ones rather than for themselves:

> "My first response [when I learned I had HIV] was: shit, how about my wife? (…) And how about my parents? I wasn't thinking about myself at all. Not at that point." (R09-02)

> "I have never really been afraid of what happens to me. I have never been afraid of death or whatever. Yes, I've feared for my relatives more, right. As I said, when the doctor told me, you are indeed infected, the first thing I thought was, oh great, how about her?" (R12-12)

One recipient explained that financial and practical problems for his family were intolerable to him:

> "If a father has a family, and that father has contracted something, then you can say, we couldn't help it. But still, such a family has a huge problem, if that father gets seriously ill at some point, or dies. (…) You're in fact saying, I'm exaggerating: if something happens, it's your problem. Then I think that as a recipient you're entitled to say: but then I want you to put maximum effort into keeping it safe." (R10-33 & R10-34)

Upon further questioning, this respondent stated that if families were offered more security against such problems, he would be more tolerant towards TTI risks:

> "You would have to consider carefully how much trouble this causes in the family, and how one can help out there. (…) OK if you do something on this side, but then do something on the other side as well. If you do this [remove safety measures], then take responsibility for problems you might cause." (R10-39 & R10-44)

Blood product recipients explained the limited concern for their own safety by appealing to their medical histories and prospects:

> "Maybe that's also something, as a haemophilia patient you've gone through so many things early in life, I think your coping mechanism works differently than for someone else who learns a shocking fact about his health." (R12-12)

> "If I would have no problems, would be completely healthy, and would have to imagine: I will get a blood transfusion, and I know it might not be tested for this or for that – wait, I won't accept that. While from my current perspective I'm saying, it means nothing. What I have is much more serious, and it won't get worse because of that." (R13-20)

Several respondents noted that blood products are very beneficial, or indeed life-saving, to recipients. Some saw this as an argument for the tolerability of TTI risks, others saw it as an argument for their intolerability. The latter view, expressed most clearly by respondent H05, seems surprising:

> "You might die if you do not get these drugs, that operation or that blood product, so your life might depend on it. (…) And you might also die because of adverse reactions, serious complications during surgery, or an infection. That makes it very dramatic, and that's why something needs to be done." (H05-16)

Contracting a TTI was also considered dramatic in another sense, namely that because the risk is small, contracting a TTI means being extremely unlucky. One recipient suggested that he would accept being stricken by bad luck:

> "If that happens, than maybe it's my time. Then I've just been unlucky." (R01-02)

This view was opposed by another recipient, who appealed to the personal tragedy of becoming a victim of risk:

> "Some risk you can always, right, you can live with that, but if you happen to be that one person who suffers from it, then you feel totally shit." (R11-37)

A few arguments related to donors' and haematologists' interests. Some respondents discussed and rejected the argument that certain TTI risks should be tolerated because donors have a right to donate, or because rejecting donors from high-risk groups is discrimination. One respondent suggested that donors' altruistic motives and the effort required for donating are reasons for risk intolerance:

> "The donor gets no remuneration, does it voluntarily, so you must ensure that the product he supplies is used optimally, and does not pose risks to the recipient. (…) To reward his altruism, so to speak." (H03-06)

> "You don't want to waste blood. Not because it costs money, but because someone made time to donate blood, and accordingly loses half a point or a full point of Hb." (H03-07)

On this respondent's view, these arguments apply not just to the use of blood by clinicians, but also to safety decisions at blood services.

Arguments relating to haematologists' interests centred on haematologists' relation with blood product recipients. Haematologists stressed that they feel responsible for their patients' safety, with whom they have a fiduciary relationship, and with whom they are personally and emotionally involved. Policy-makers were taken to have an interest in not being responsible for TTIs, and some respondents seemed to consider this a legitimate reason for risk intolerance:

> "You don't want anyone getting sick from an infected blood product or something like that. Think of HIV or things like that, you wouldn't want to have that on your conscience, would you? (P01-05)"

> "One patient with AIDS a year, although it's very subjective, I can't explain it to him. Like: I could have prevented it, but we thought that was too expensive." (H04-34)

These arguments seem to relate primarily to policy-makers empathy with recipients. Respondents also mentioned motives to avoid responsibility that they considered inappropriate: policy-makers' fear for reputational damage, their fear for liability, and the fact that policy-makers do not pay safety measures out of their own pockets. Some further arguments revolved around the idea that policy-makers (being in a political position) should follow procedures and be consistent. On this idea, policy-makers' tolerance or intolerance towards TTI risks must square with the values they express:

> "If you say (...) we place high value on safety, then you should not take measures that are only or mostly intended to improve efficiency. Then you should say: no, we're opting for safety. If it can be done more effectively, fine, but then you must say: we place high value on effectivity." (H04-46)

Also, risk tolerance or intolerance must be democratically legitimate. Any change in direction therefore requires political legitimation:

> "We have collectively decided to apply those safety tests, based on an attitude, one which we discuss each time, and that is evaluated by external parties. If that's the outcome, then that's a given. Of course you can say: perhaps these committees should apply different safety criteria, but that's something they must decide on." (P03-23)

Finally, certain arguments addressed the interests and concerns of the general public. The general public was stated to fear TTIs, to expect that blood products are safe, and to attach a special meaning to blood. Respondents usually, but not always, seemed to reject these public views as reasons for risk intolerance. The influence of risk tolerant or intolerant safety policies on the public perception of blood transfusion was considered important. A lack of trust in the safety of blood products was considered problematic, for example for public health:

> "If someone becomes infected with HIV, then that causes an enormous amount of problems for Sanquin's reputation and for the trust in blood products. People will no longer want to use them. So then the very treatment of all sorts of diseases is endangered." (H05-36)

Public trust was mentioned by some respondents as an argument for risk intolerance, but also, by one respondent, as a possible reason for risk tolerance. Safety measures might in this respondent's view have an adverse effect on public trust:

> "If a blood bank has to do this often, tell donors: we do not want to draw your blood, because you've visited this or that place, then people will become more and more aware of the kind of disease problems they have, and so will become more afraid, will think of blood as something scary. (...) If I put locks on my door, it means something's wrong outside. So if I start implementing security systems, it means that I don't, uh, that what I supply can't be good." (P02-25)

DISCUSSION

The aim of this study was to identify and understand the spectrum of arguments regarding the tolerability or intolerability of TTI risks, providing perspectives that deserve closer consideration in research and policy-making. Because the study design was strictly qualitative, the views expressed by our respondents cannot be generalized: no conclusions can be drawn about what recipients, donors, haematologists and policy-makers think in general. Our research was limited to stakeholders in the Dutch blood supply. In a way, all citizens qualify as stakeholders: everyone may become a patient someday, and the blood supply is funded collectively. Because the public's risk perception has been addressed in previous research and because we were interested in *informed* views on TTI risks, the current study included only stakeholders with first-hand experience with the blood supply.

While the number of new arguments declined steeply as we analysed more interviews, we cannot claim to have reached saturation. Now and then, new arguments arose, some of which were expressed by only one or two respondents. In spite of the high number of arguments we have found, it is conceivable that additional arguments for the tolerability or intolerability of TTI risks can be retrieved by further research.

We found some undertheorized arguments for tolerance or intolerance towards TTI risks. We had expected to find more appeals to what is 'special' about blood (e.g. its symbolic significance) and blood donation (e.g. its social function and the distribution of responsibility between donors and the blood service). Although blood and blood donation were framed in diverse ways, this framing rarely connected to the tolerability of TTI risks. Still, some

interesting new perspectives were opened. Whether these perspectives are valid and persuasive deserves further reflection.

An important insight is that recipients may not be primarily concerned about their own health. Some recipients said that they were accustomed to facing health risks and that blood products brought them much good, but said they did fear the (medical and practical) impact of TTIs on their families. Understanding such perspectives is necessary to engage stakeholders in constructive deliberation about TTI risks and to develop safety policies they can accept.

A remarkable argument for risk intolerance was that because TTI risks are small, contracting a TTI is a dramatic and undeserved fate. A related argument was that TTIs frustrate attempts to remedy patients' bad luck, whose bad luck thus strikes in two steps. One may perhaps support these arguments by appealing to luck egalitarianism: the idea that justice requires neutralizing the effects of bad luck on peoples' lives [16]. Building on this idea, one could argue that tolerating TTI risks *reinforces* some patients' bad luck and is therefore unjust. But perhaps we should acknowledge the sense of tragedy behind these arguments without granting it ethical weight. Allocating scarce health care resources is inherently tragic: if providing care to some patients means that others must forego care, every allocation decision will have losers. At least on a societal level, some bad luck must be accepted, as neutralizing everyone's bad luck is beyond our means.

Respondents offered some non-consequentialist ethical arguments for risk intolerance. Some respondents argued that taking TTI risks means causing harm or defended the view that terminating safety measures is more objectionable than not introducing them. These views have been discussed and criticized elsewhere [6, 17]. Respondents also argued that taking TTI risks is contrary to the aims of providing blood transfusions, that blood products are traceable or recognizable sources of harm, and that TTIs are a serious breach of bodily integrity. An important question in evaluating these arguments (which is beyond the aims of this paper) concerns their scope. Taking health risks is always contrary to the aims of medicine but is inevitable in many medical interventions – this does not only apply to administering blood products. In addition, other iatrogenic harms may also involve violations of bodily integrity and have traceable sources (e.g. surgical errors). Thus, these arguments might not support stronger intolerance towards TTI risks than towards other iatrogenic risks.

A remarkable argument for risk tolerance applied to patients with a poor prognosis. The respondent who expressed this view argued that patients with bad prospects might not live long enough for a TTI to develop into disease, for which reason the TTI would have little

impact. The rationale behind this view, which is similar to triaging in emergency settings, is that scarce resources should not be 'wasted' on patients with bad prospects if that excludes helping patients with better prospects. It might then be reasonable to allow somewhat higher TTI risks in the context of high-risk surgery or when treating severe haematological malignancies than, for example, in the context of haemophilia treatment or blood loss after delivery. But even if this sort of risk stratification is ethically acceptable, which would be an issue for further research, the question remains whether having different safety policies for different groups of recipients is logistically feasible.

On the assumption that resources spent on inefficient blood safety measures could be applied more beneficially, to help more people or save more life-years, various respondents expressed tolerance for TTI risks. Respondents also offered reasons to doubt that assumption, though: the amount of resources spent on blood safety measures might be too small to make a difference somewhere else, and alternative ways to save and reroute money might be available. Initiatives to contain the costs of blood safety measures should address these doubts. Perhaps it should be conceded that saving costs on blood safety measures will be neither sufficient nor necessary to reap substantial benefits elsewhere. Still, one might argue that taking responsibility for efficiency is important because inefficient forms of health care *collectively* disallow achieving better health outcomes. But then initiatives to increase efficiency in blood safety should be matched by similar initiatives in other domains of health care.

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