Is it safe for epilepsy patients to donate blood?

Alyssa Kellens, MD

Dissertation presented in fulfillment of
the requirements for the degree of
Master of Family Medicine

Supervisor:
Philippe Vandekerckhove, MD, PhD (KU Leuven, Belgian Red Cross-Flanders)

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Preface

A wise man once said that 'the best preparation for good work tomorrow is to do good work today'. That man was Elbert Hubbard, an American writer and philosopher who lived and worked at the end of the nineteenth and the beginning of the twentieth century. The reason I chose this quote, is because I believe it can be perfectly applied to science. After all, science is, mostly, done in small steps and each step can be a base for future clues. All these clues together can mean a solution to unravel scientific puzzles. It's like building a wall, where every brick brings you closer to building a home.

As a medical doctor and therefore a scientist, it has given me great pleasure to work on this dissertation and to do my part to contribute to science. Needless to say that the process of writing this dissertation couldn't have gone smoothly without help. Therefore, I would like to thank a few people:

At first, my thanks go to my supervisor Philippe Vandekerckhove, my co-supervisors and all the staff members of the Centre for Evidence-Based Practice (CEBaP) of Belgian Red Cross-Flanders. They have given me the opportunity to make a dissertation in an ideal atmosphere, guided by people who are really passionate about their work. Special thanks go to Emmy De Buck, who has stood by my side during this whole process as a mentor. She really did a wonderful job in guiding and teaching me.

I also wish to thank Mark Peeters, my supervisor as a general practitioner, for his interest in my dissertation and his useful feedback.

Last but not least, I wish to thank the people in my immediate environment: my friends and my family. I would like to thank them for their unconditional support. Special thanks go to my parents, who have given me the chance to fulfill my dream to become a medical doctor. A simple 'thank you' isn't enough to express my gratitude towards them.

I hope you will enjoy reading this dissertation.

Summary

Epilepsy is a common neurological disorder that is characterized by the appearance of seizures. Often, epilepsy patients are temporarily or permanently excluded from blood donation. This exclusion is not based on solid evidence, but rather influenced by other considerations. A survey that was performed to map this problem, as part of this dissertation, confirms that there is indeed inconsistency in worldwide policies.

A systematic review was performed to collect and critically examine the evidence with regard to the safety of blood donation in epilepsy patients. Five databases (MEDLINE, Embase, The Cochrane Library, Web of Science and CINAHL) were searched for studies from the date of inception until December 2014, which yielded 7283 references. Following title and abstract screening in the first phase, and full text screening in the second phase, only three observational studies were finally withheld: two case series and one cohort study. All studies were of poor methodological quality and none included a solid statistical analysis.

Based on the available evidence, a significant increased risk of adverse events in blood donors could not be demonstrated in case of a history of epilepsy. The strength of the available evidence should however be classified as very low. Future studies are necessary to further investigate this area.

Samenvatting

Epilepsie is een vaak voorkomende neurologische aandoening, die gekenmerkt wordt door stuipaanvallen. Vaak worden epilepsiepatiënten tijdelijk of definitief geweigerd als bloeddonor. Deze uitsluiting is niet zozeer gebaseerd op wetenschappelijke evidentie, dan wel beïnvloed door andere overwegingen. Een vragenlijst, opgesteld in het kader van deze thesis om dit probleem in kaart te brengen, bevestigt dat er inderdaad een inconsistentie bestaat tussen de verschillende bloedinstellingen wereldwijd.

Er werd een systematische review verricht om wetenschappelijke evidentie met betrekking tot de veiligheid van epilepsiepatiënten bij bloeddonatie te zoeken en kritisch te beoordelen. In vijf databanken (MEDLINE, Embase, The Cochrane Library, Web of Science en CINAHL) werd er van bij het ontstaan van de databank tot december 2014 gezocht naar studies, met 7283 referenties als resultaat. Na titel en abstract screening in een eerste fase, en screening van de volledige tekst in een tweede fase, konden uiteindelijk slechts drie observationele studies weerhouden worden: twee casusreeksen en één cohortstudie. Alle studies waren van slechte methodologische kwaliteit en geen enkele studie bevatte een degelijke statistische analyse. Op basis van de beschikbare wetenschappelijke evidentie, kon er geen significant verhoogd risico op neveneffecten worden aangetoond bij patiënten met een voorgeschiedenis van epilepsieaanvallen. De bewijskracht moet echter als zeer laag worden geclassificeerd. Verder onderzoek in dit domein is dan ook nodig.

List of abbreviations

AGREE	Appraisal of Guidelines for Research and Evaluation
BRC-F	Belgian Red Cross-Flanders
CEBaP	Centre for Evidence-Based Practice
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CT	Computed Tomography
EBM	Evidence-Based Medicine
EBP	Evidence-Based Practice
EEG	Electroencephalogram
GAP	Global Advisory Panel on Corporate Governance and Risk Management of Blood Services in Red Cross and Red Crescent Societies
GRADE	Grading of Recommendations Assessment, Development and Evaluation
IOM	Institute of Medicine
MeSH	Medical Subject Headings
MRI	Magnetic Resonance Imaging
PICO	Patient; Intervention; Comparison; Outcome
WoS	Web of Science

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1. General introduction

Blood donation is of key importance in our modern society. Indeed, blood products are used for (bio)medical and pharmaceutical purposes in a range of different ways. All these applications are intended to improve the life and health of humans.
This implies that there is a high demand for blood products. Until today, blood donation is still the only way to obtain human blood components. Synthetic forms of human blood components (i.c. red blood cell substitutes) are currently only being used in an experimental setting and not suitable yet to be used as an alternative for human red packed cells (1).

Although blood donation is promoted, only a small number of people donate blood in comparison to the number of people who will ever need blood. The annual report of Belgian Red Cross-Flanders (BRC-F) 2014 shows that in that year, a total of 372759 blood products was donated by 184734 people; 87.18% of these donations were full blood donations, 11.05% and 1.77% were blood plasma and blood platelet donations respectively (2). These numbers indicate that only a small percentage (i.e. 2.87 %) of the inhabitants of Flanders donate blood, knowing that Flanders has over 6.4 million inhabitants (3). Media campaigns result in new blood donors every year, but the number is rather limited. The annual report of BRC-F 2014 shows that there was a total of 41339 new donors that year (2).
A medical questionnaire is being used to exclude people from blood donation for different reasons, in order to guarantee safety for both donor and recipient. An example is the exclusion of epilepsy patients until they are 3 years free of medication and epileptic attacks. Medical questionnaires worldwide are based on expert opinion, internal regulations, law, or medical guidelines. However, it is not always based on proven scientific data, which results in a lot of variation in donor selection questionnaires worldwide. A thorough analysis of the medical questionnaire and supporting it with scientific studies could lead to a more accurate policy on donor eligibility and possible a larger group of potential donors. It is the aim of BRC-F to scientifically support all its activities with evidence-based practice, including the donor eligibility questionnaire.

In this dissertation, an attempt will be made to answer the question: Is it safe for epilepsy patients to donate blood? To frame the problem, a survey was performed to have a clear understanding of the policies that are currently being applied in blood donation centers around the world. Subsequently, a systematic review was performed to search for evidence to confirm or deny this question. The results will be described below and in the discussion section specific recommendations will be made.

2. Background information

2.1. Evidence-based medicine/practice (EBM/EBP)

2.1.1. History and definition

The term evidence-based medicine (EBM) has been introduced during the 1990's by investigators at McMaster University in Canada (4,5). Initially, it was defined as 'a systematic approach to analyze published research as the basis of clinical decision making' (5). In 1996, however, a more formal definition was formulated by David Sackett and colleagues at Oxford University in Great-Britain (6). Sackett stated that EBM can be defined as 'the conscientious and judicious use of current best evidence from clinical care research in the management of individual patients' (5,6). These definitions concern the modern interpretation of EBM.

After its introduction in medical literature, it took some time for the term EBM to spread itself globally, but now, it has been accepted and applied widely (5). The sources where clinical evidence can be retrieved nowadays, are very extensive (e.g. internet, journals, etc) (7). This makes integrating EBM into clinical practice more easy. David Sackett stated the following about the practice of EBM in 1996: 'It means integrating individual clinical expertise with the best available clinical evidence from systematic research. Individual clinical expertise can be understood as proficiency and judgment that individual clinicians acquire through clinical experience and clinical practice. Best available clinical evidence can beside be understood as clinically relevant research, especially from patient centered clinical research. Neither alone is enough. Clinicians who practice EBM, will identify and apply the most efficacious interventions to maximize the quality and quantity of life for individual patients' (6).

Following the introduction of EBM, this concept also found its way in other domains than medicine, resulting in evidence-based practice (EBP), which can also be applied to other disciplines (e.g. social work, psychology, etc.) (8). Around the same time as David Sackett's publication, Haynes and colleagues published about the development of a conceptual model for EBP: the transdisciplinary model (see figure 1) (9,10). This model was later alternated by Satterfield and colleagues after some criticism (8) (see appendix (figure 1)).

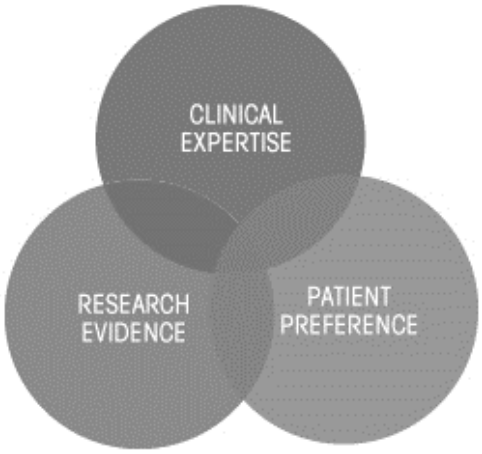


Figure 1 *(adapted from (8))**: The transdisciplinary model of evidence-based practice (9). The model is composed of 3 circles, that are connected with each other. Each circle represents an equally important feature of evidence-based practice, although under some circumstances, clinical expertise and/or patient preferences may override research evidence (8).*

2.1.2. EBM/EBP and guidelines

Guideline development is a process that can be done in several ways. In the past, most guidelines were drafted by a group of experts during round table discussions. These guidelines were mainly based upon the knowledge and opinion of these experts, which holds an important intrinsic risk for bias. A more formal way to apply this so-known 'Good Old Boys Sat Around The Table' principle is the making of 'consensus-based guidelines'. These kind of guidelines are based upon a formal consensus technique, which, however, still holds a big risk for bias. In contrast to this expert-based principle of guideline development, guidelines can also be based upon the best available scientific evidence. These guidelines are called 'evidence-based guidelines', which use existing and/or new systematic reviews. The fact that they systematically integrate the scientific evidence, makes them more valid than consensus-based guidelines. However, since there are inevitable gaps in research, expert opinion and judgment are still necessary to fully formulate an evidence-based guideline (11-18).

To bridge the gap between theory and practice, the IOM (Institute of Medicine) has made an overview about the process of developing a clinical practice guideline (CPG). This is a guideline, which is defined by the IOM as 'a statement that includes recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options'. This enables clinicians to choose the best care for a patient, based on his/her preferences (18,19). The AGREE website states that these CPG's are evidence-based 'if they undertake a review of the literature and link their concluding recommendations to the evidentiary base identified through the literature search' (18).

To develop a trustworthy CPG according to the IOM, a series of intricate steps has to be followed by the developers. First, a guideline development group needs to be formed. This group has to be multidisciplinary and balanced. All groups that are expected to be affected by the CPG have to be represented. Any conflict of interest has to be disclosed. Second, the guideline development group has to use good quality systematic reviews as evidence. If a systematic review about the same subject is developed at the same time as the guideline, both groups have to collaborate. Third, expert opinions have to be incorporated and an assessment of the benefits and harms of care options for an individual patient has to be appraised. Fourth, the CPG can be made, with an explanation of the reasoning behind the recommendations, a rating of the level of confidence or certainty of the evidence and a rating of the strength of the recommendations (19). To frame this process of guideline development, the IOM has set up a list of 8 standards, that has to be followed during the process (see appendix (figure 2)).

To keep the quality of the developed guidelines of high standards, methodological instruments have been made available by different organizations, that are primarily involved in guideline development. The AGREE II checklist (Appraisal of Guidelines for Research and Evaluation) is another example of these instruments. This checklist can be applied to guidelines that deal with just about any topic in the healthcare continuum. It is composed of 23 items that are sorted into 6 categories (see appendix (figure 3)). Besides, it contains 2 final overall assessment items to make overall judgments. The checklist can be used when developing as well as when reviewing a CPG. In other words, it helps the developers as well as the appraisers consider their answers on the questions (20,21).

2.1.3. EBM/EBP and systematic reviews

A systematic review is defined by The Cochrane Collaboration as 'a review of a clearly formulated question that uses systematic and explicit methods to identify, select and critically appraise relevant research and to collect and analyze data from the studies that are included in the review' (18,22). Often, a meta-analysis component is included, which involves using statistical techniques to synthesize the numerical data of the studies (23). The use of a systematic method results in reliable scientific information.

The Cochrane Collaboration is the organization that uses the strictest methodological criteria for the development of systematic reviews. The organization has been founded by Archibald Cochrane, an

epidemiologist originating from Great-Britain, in 1993. The mission of the organization is to widespread qualitative and relevant systematic reviews and other synthesized research evidence in the domain of healthcare. The logo of the Cochrane Collaboration has been inspired by its mission (see figure 2).
The development of a systematic review according to the rules of The Cochrane Collaboration is comprised of the following steps. First, the review question has to be defined and the selection criteria for including studies have to be formulated. Second, databases of scientific literature have to be searched. Third, studies that meet the selection criteria are withheld and data are collected. Fourth, the risk of bias in the included studies has to be assessed. Fifth, the data have to be analyzed and a meta-analysis has to be undertaken, if possible, to statistically combine the results of the included studies. Sixth, reporting biases have to be addressed. If sufficient studies are included, a funnel plot can be used to do so. Seventh, the results have to be presented. A level of evidence has to be assigned to the body of evidence using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach (24,25). Eight and last, the result have to be interpreted and a final conclusion has to be drawn about the practical usefulness (22,26).



Figure 2 *(adapted from The Cochrane Collaboration)**: The logo of The Cochrane Collaboration is comprised of two C's, representing the name 'Cochrane Collaboration', and a forest plot in the middle. This forest plot belonged to a very important meta-analysis that was conducted around the time of the foundation of the organization. Each line represents the individual results from the included studies and the diamond represents the combined result from all studies (27).*

2.1.4. Centre for Evidence-Based Practice (CEBaP), Belgian Red Cross-Flanders

The Centre for Evidence-Based Practice (CEBaP) at BRC-F has been founded in 2009 to bridge the gap between science and practice in this non-profit organization. Its role is to scientifically underpin all activities of BRC-F to support policy making in the institution. The activities of BRC-F cover many areas that are sorted under the headings of humanitarian aid and blood services.
To perform their task, the members of the CEBaP use high quality methods to develop reviews and guidelines. The exact steps in both processes are summarized in a methodological charter that guarantees transparency and uniformity (18,26).
The high quality methods that are used often result in scientific publications, which ensures dissemination of knowledge.

2.2. Blood donation and donor health

2.2.1. Donor eligibility criteria

Blood donation and transfusion is an intricate process, in which safety for both the donor and the recipient is of paramount importance. The European legislation provides a framework to make sure that all safety measures are taken into account. All countries that are part of the European Union have to respect this legislation. However, the interpretation of it can and may differ from country to country and even from region to region (28).
In general, every step of the blood donation process needs to be looked at and controlled adequately. An important feature in this hemovigilance process is selecting donors that are eligible for blood donation.

Donor eligibility is a complicated concept that comprises several aspects. In Flanders, blood donors are eligible if they meet a list of criteria. First, blood donors have to meet age criteria. They have to be between the age of 18 and 66. In case of experienced donors, blood donation is even possible until the age of 71. Second, blood donors have to meet weight criteria. They have to weigh at least 50 kg. Third, the appropriate time between donations needs to be respected. Full blood donations can be done to a maximum of 4 times a year. An interval of at least 2 months has to be respected between 2 donations. Blood plasma and blood platelet donations on the other hand, can be done every 2 weeks.
If all these criteria are met, blood donors have to fill in a medical questionnaire (see appendix (figure 4)). This questionnaire contains items about their medical history (including drug and/or alcohol abuse), their medication history, their travel history and their sexual history. The purpose of these questions is to search for events that can mean a safety threat. The list is looked through and discussed during a consultation with a physician. During this consultation, the donor's vital parameters are also checked.
When the physician finds no items that can potentially cause problems for the donor or recipient, the donor is declared eligible for that donation. It is important in this context to notice that donor eligibility can vary and that a onetime positive advise does not result in a guaranteed free pass the next time (29).

2.2.2. Donor adverse events

Donor adverse events are inherently associated with blood donation. These adverse advents can happen during or sometime after the blood donation process. The most common adverse events during the blood donation process are vasovagal reactions (2.5%) and hematomas (0.35%). The most common adverse events sometime after the blood donation process are bruises (22.7%), sore arms (10.0%), fatigue (7.8%) and vasovagal reactions (7%). In extremely rare cases, blood donation can lead to life-threatening illnesses or even death. In addition, there are some donor characteristics that also influence the risk of adverse events: gender, age, donation status (30).
When all adverse events are taken into account, about one in every three donors will experience one or more adverse events. In some cases, donors who experience adverse events will seek outside medical care (31,32).
To prevent adverse events, every donor has to follow the donor protocol. This protocol enhances the period before, during and after the donation. The precautions which are contained in the protocol are designed to minimize the number of adverse events (e.g. medical questionnaire, medical consultation, et cetera).

2.3. Epilepsy

Epilepsy is a common neurological disorder, that in most cases starts during childhood. The disease is known to have an incidence of 50 new cases per year per 100000 people. The prevalence of the disorder in the general population is about 1%.
Epilepsy is characterized by the appearance of seizures, which are caused by abnormal neuronal firing in the brain, which happens when there is an imbalance between excitation and inhibition.
When seizures are recurrent and unprovoked, they can be classified as epilepsy. After all, seizures can also be provoked because of other numerous causes (e.g. fever, brain tumor, etc).
Seizures can be classified into two types: generalized seizures and focal seizures. A generalized seizure is characterized by abnormal neuronal firing in the two cerebral hemispheres, whereas a focal seizure is characterized by abnormal neuronal firing in one of both cerebral hemispheres. A focal seizure can however turn into a generalized seizure when the abnormal firing spreads from one hemisphere to the other. The exact location of the origin of the firing can be found in the cortex or subcortical structures of the brain.
Generalized seizures can be divided into four subtypes: tonic-clonic seizures (formerly known as grand-mal seizures), absence seizures (formerly known as petit-mal seizures), myoclonic seizures and atonic seizures. Tonic-clonic seizures are characterized by bilateral symmetric convulsive movements. Absence seizures can be described as staring with unresponsiveness. Sometimes, eye blinking or head nodding is involved. Myoclonic seizures consist of brief, sudden muscle contractions without loss of consciousness. These

movements can be generalized or focal, which makes this subtype of seizures harder to classify. At last, atonic seizures are characterized by loss of body tonus. This can result in a head or body drop.

The cornerstones of the diagnosis of epilepsy are a detailed history and clinical examination. Besides, other tests can be performed to further investigate the diagnosis. Possible routine supplementary tests are laboratory tests, electroencephalogram (EEG) and/or neuroimaging i.c. computed tomography (CT) or magnetic resonance imaging (MRI). An EEG is a recording of the brain's electrical activity. This test can, if necessary, be performed with simultaneous video monitoring.

In most cases, epilepsy can be managed with drugs. There are numerous anti-epileptic drugs that can be tried in monotherapy or combined if necessary. When two or more appropriate anti-epileptic drugs are not sufficient to control the appearance of epileptic seizures, the disease can be classified as refractory (33).

2.4. Blood donation and epilepsy: the current situation in Belgian Red Cross-Flanders (2015)

The rationale for exclusion of epilepsy patients as blood donors is two-fold: (1) Historically, it is believed that giving blood could evoke a new epileptic seizure, (2) Medication in the blood of epilepsy patients could have a negative effect on the recipient of the blood (34,35).
Currently, epilepsy patients in Flanders are temporarily excluded from blood donation. They have to be seizure- and medication-free for at least three years before they can donate blood. This policy is applied in all blood donation centers of Belgian Red-Cross Flanders.
The temporary exclusion of epilepsy patients as blood donors has only been around for a short amount of time. Before the year 2015, epilepsy patients were permanently excluded from blood donation in Flanders. This policy was based on one donor, who had an epileptic seizure during the blood donation process. Retrospectively, this donor should, however, have been excluded from blood donation, because he/she was not medication-free at the time of donation.

3. Survey

3.1. Introduction

It is still unclear if epilepsy patients are potential eligible blood donors. As a consequence, there is a large discrepancy in policies worldwide. Some blood institutions accept epilepsy patients as blood donors, whereas others temporarily or even permanently exclude them. The decision to accept or exclude an epilepsy patient as a blood donor, has so far not been based on proven scientific data, but rather seems to be influenced by other motives. To frame the current situation with regard to blood donation and epilepsy, a study has been set up, using a web-based questionnaire. In this study, the policies from different blood institutions around the world were gathered and evaluated.

3.2. Materials and methods

3.2.1. Participants

A cross-sectional questionnaire using the online Questback© tool was distributed in May 2015 to 46 representatives of blood services worldwide. The questionnaire was sent out to the representatives by personal e-mail or by web link. The applied method for sending the invitation to each representative was based on international agreements (i.e. the representatives of blood services in Africa, America and Europe were contacted by personal e-mail and those in Asia and Oceania by web link). The data were collected and analyzed from June 2015 until September 2015. Descriptive analysis was used to evaluate the data.

3.2.2. Questionnaire

The questionnaire was composed of 9 multiple choice questions with the ability to select multiple answers and/or add a comment if necessary in selected questions. Each participant only received those questions to answer that were relevant and logical to him/her. The questions that were submitted to a certain participant were i.c. dependent on his/her answer on the initial question 'Do you accept patients with epilepsy for blood donation, assuming that all other requirements for blood donation are fulfilled?'. If a participant answered the initial question with 'they are permanently excluded', that participant only had to answer question 1 and 2 to complete the questionnaire. If the participant answered the initial question with 'they are temporarily excluded', he/she had to answer question 1 to 9. If the participant finally answered the initial question with 'they are permanently accepted', the participant had to answer question 1 to 5 and 8 to 9. The final question of the survey was drawn up in two versions, also dependent on the answer on the initial question, but the content of the question was similar.

The final goal of the questionnaire is to gain insight into to the different policies and the rationale behind it. Different aspects are assessed to do so. Question 1, 2, 6 and 7 are meant to understand if epilepsy patients are accepted or excluded, as well as for what time and what reason. Questions 3, 4, 5 and 8 are designed to gauge for different aspects that could possibly play a role in preventing donor adverse events. Question 9 at last, is meant to investigate if blood services have the experience (if possible supported with data) that epilepsy patients experience more syncopes than healthy donors.

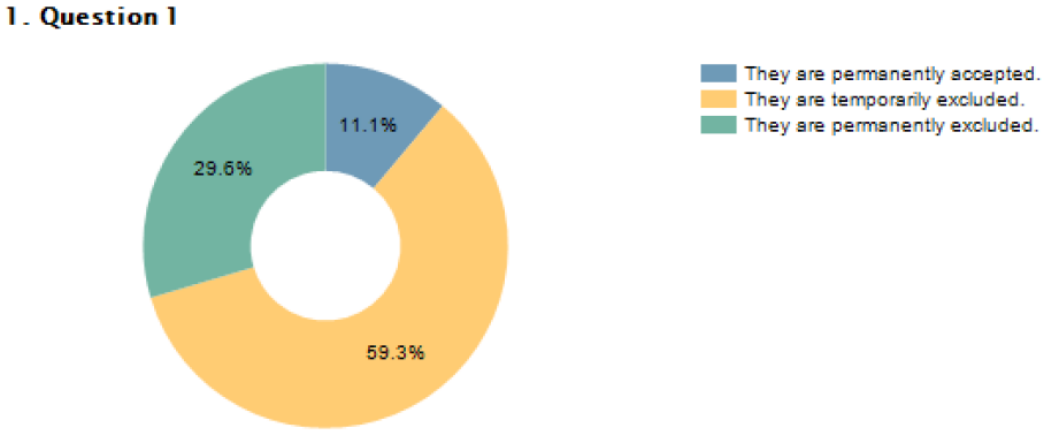
3.3. Results

A total of 27 respondents, representing blood services in 26 countries on five continents (Africa, America, Asia, Europe and Oceania), participated in the survey, which means a response rate of 27/46 or 59%. Of these 27 respondents, one participant only partially completed the survey. The list of respondents is presented in appendix (table 1)).

Question 1: 'Do you accept patients with epilepsy for blood donation, assuming that all other requirements for blood donation are fulfilled?'

The policies that can be applied are permanent exclusion, temporary exclusion or permanent acceptance. The results show that there is a significant global disagreement. In 59.3% of the cases, epilepsy patients are temporarily excluded from blood donation. In 29.6% of the cases, they are permanently excluded. In 11.1% of the cases at last, epilepsy patients are permanently accepted as blood donors.

In Europe, 9 of the 15 respondents selected temporary exclusion, whereas 6 of the 15 respondents selected permanent exclusion. Permanent acceptance is never applied on this continent. In Asia, there is a great division. All three policies are applied on this continent, to a greater or lesser extent. In America, the results show that epilepsy patients are always temporarily excluded from blood donation. The respondents from Africa and Oceania, at last, both selected permanent acceptance.

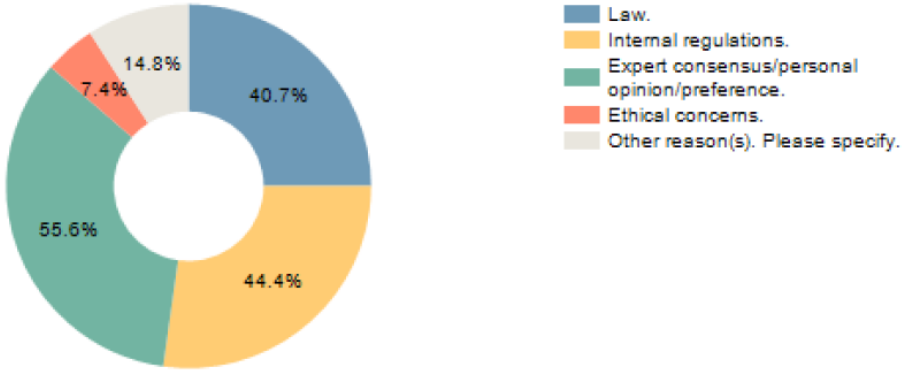


Question 2: 'Why do you accept/refuse patients with epilepsy as blood donors?'

The results show that there are numerous reasons to accept or refuse epilepsy patients as blood donors. In some cases, respondents only chose one reason for acceptance or deferral, whereas in others, multiple reasons were cited. Analysis of the results shows that there is no correlation between the specific reason for acceptance or exclusion and the policy that is being applied.

When the results are studied in detail, 55.5% of the respondents provides expert consensus/personal opinion/preference as a reason for acceptance or exclusion. Other reasons are internal regulations (44.4%), law (40.7%) and ethical concerns (7.4%). Some respondents even provide other reasons (e.g. acceptance or exclusion is a medical decision). It is remarkable that most respondents who provide law as a reason for acceptance or deferral, originate from European countries (Austria, Belgium, Estonia, Great-Britain, Ireland, Italy, the Netherlands, Spain, Sweden). Taiwan and Japan are the only non-European countries who also provide law as a reason for acceptance or deferral. When we look at the policy that is currently being applied in these blood institutions, temporary exclusion is the most represented.

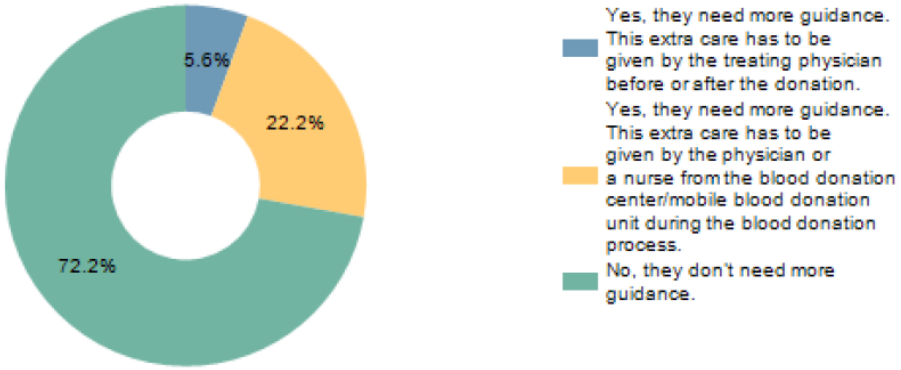
2. Question 2



Question 3: 'In those countries/states/blood transfusion services were epilepsy patients are accepted as blood donors, either permanently or after temporary exclusion: Do epilepsy patients need more guidance (e.g. clinical/technical investigations, follow-up before/during/after the donation, etc.) compared to otherwise healthy donors?'

In 72.2% of the cases, respondents agree that there is no need for extra guidance of epilepsy patients before/during/after the donation compared to otherwise healthy donors. However, 27.8% of the respondents think that epilepsy patients actually do need extra care, especially during the blood donation process. One respondent also sees a role for the treating physician of the donor, who can provide extra care before or after the blood donation process.

3. Question 3



Question 4: 'In those countries/states/blood transfusion services were epilepsy patients are accepted as blood donors, either permanently or after temporary exclusion: Does the blood donation center require the waiting period between blood donations to be longer in epilepsy patients compared to otherwise healthy donors?'

All respondents unanimously agree that the waiting period between blood donations doesn't need to be longer in epilepsy patients compared to otherwise healthy donors.

4. Question 4



Question 5: 'In those countries/states/blood transfusion services were epilepsy patients are accepted as blood donors, either permanently or after temporary exclusion: Are there any extra laboratory tests done afterwards (e.g. to detect levels of anticonvulsants in blood samples)?'

All respondents, except for one, agree that extra laboratory tests are not necessary for epilepsy patients. From the respondent indicating that extra laboratory test should be done, it is not clear which test(s) is (are) appropriate.

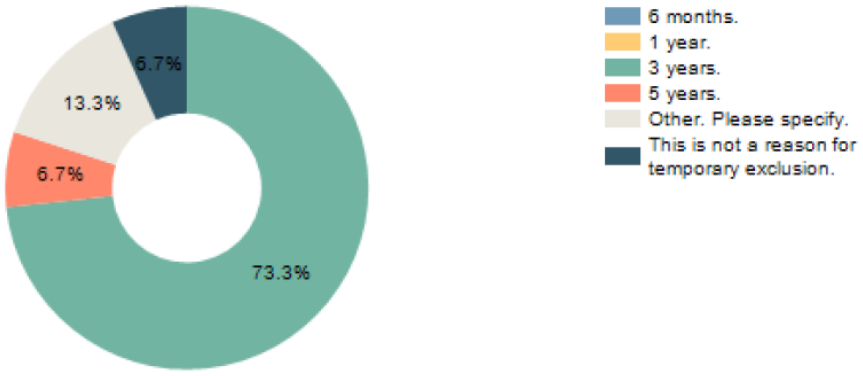
5. Question 5



Question 6: 'In those countries/states/blood transfusion services were epilepsy patients are temporarily excluded from blood donation: How long (at least) do they have to be medication-free before they can donate blood?'

Most respondents (73.3%) agree that epilepsy patients should be medication-free for at least three years before they can donate blood. However, other time frames are also applied, mostly outside of Europe. They range from two (6.7%) to five (6.7%) years, except in the United States of America, where the time frame is variable (6.7%) or being off medication is not a reason for temporary exclusion (6.7%).

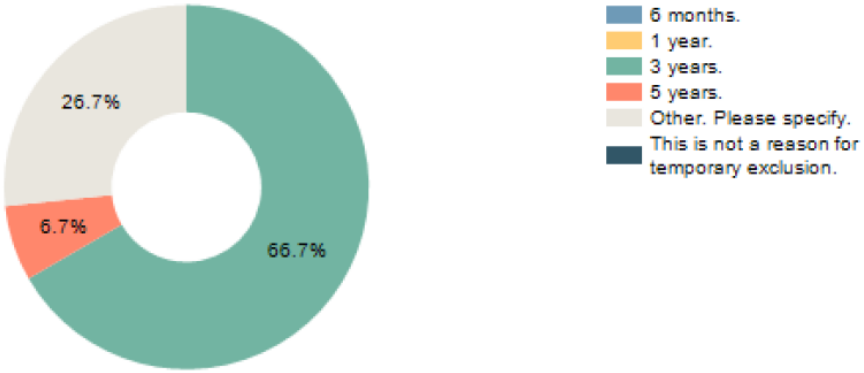
6. Question 6



Question 7: 'In those countries/states/blood transfusion services were epilepsy patients are temporarily excluded from blood donation: How long (at least) do they have to be seizure-free before they can donate blood?'

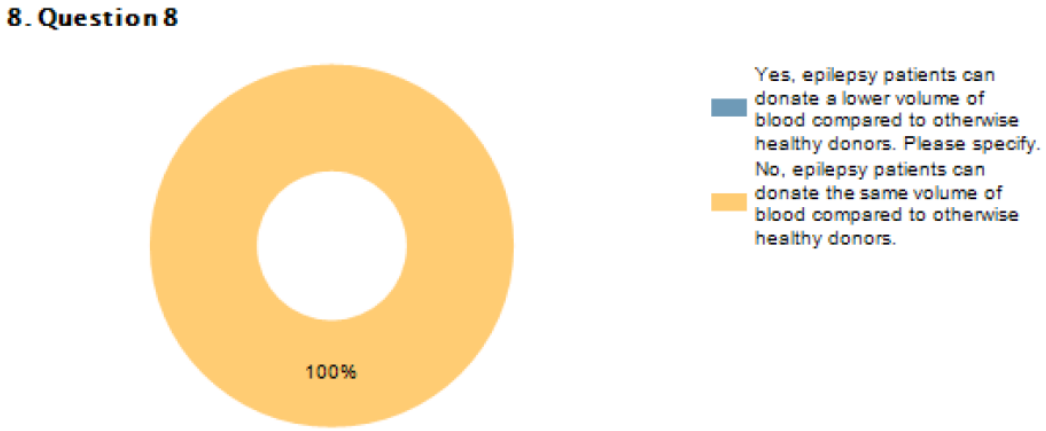
Most respondents (66.7%) agree that epilepsy patients should be seizure-free for at least three years before they can donate blood. When the results are compared to the period that epilepsy patients have to be medication-free, there is a slightly larger disagreement here. The other time frames that are being applied are one or a few months (6.7%), two years (6.7%), five years (6.7%) and a variable time frame between six month and a year (6.7%). These other time frames are mostly applied outside of Europe.

7. Question 7



Question 8: In those countries/states/blood transfusion services where epilepsy patients are accepted as blood donors, either permanently or after temporary exclusion: Is there a difference in the volume of blood that epilepsy patients can donate in comparison to otherwise healthy donors?'

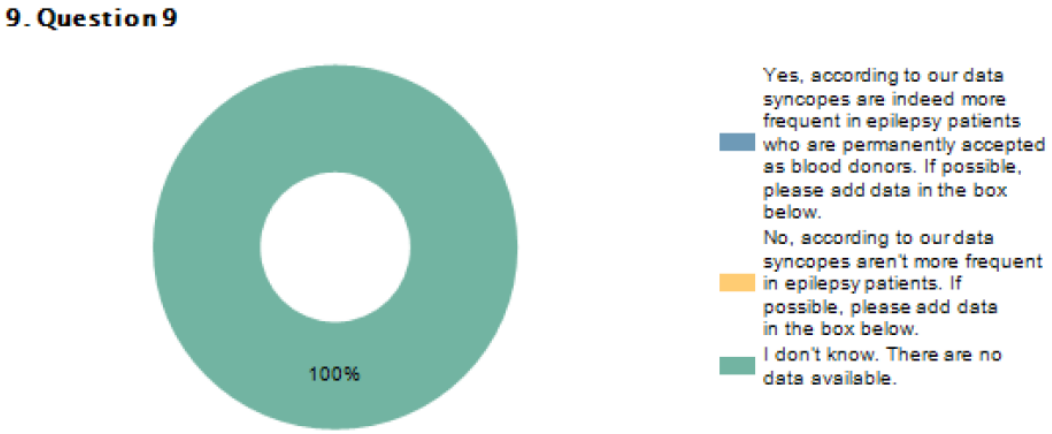
All respondents unanimously agree that epilepsy patients can donate the same amount of blood in comparison to otherwise healthy donors.



Question 9: 'In those countries/states/blood transfusion services were epilepsy patients are accepted as blood donors, either permanently or after temporary exclusion: Are syncopes during the blood donation process more frequent in blood donors with a history of epilepsy compared to otherwise healthy donors?'

This question was used to gauge for data with regard to adverse events in epilepsy patients. Since syncopes are a frequent adverse event during blood donations, this event was used as an example.

The results show that none of the respondents had data available to show if this particular adverse event is or is not more frequent in epilepsy patients.



3.4. Discussion

In this study, policies regarding the eligibility of blood donors with a history of epilepsy were assessed. 26 respondents from five continents (partially) completed the questionnaire. Although this survey does not present a complete overview of all blood donation services in all countries, it can be considered as representative for the current policies that are being applied worldwide. The results of this survey indicate that there is a large discrepancy in policies worldwide, which most likely suggests that there is no clear scientific evidence available that can serve as a basis for policy making. This expected lack of evidence implies that policy makers nowadays have to base their decision to follow a certain policy on other arguments, as indicated in the survey. These arguments differ from blood institution to blood institution and hold an intrinsic risk for an in- or overcautious attitude. Being overcautious can theoretically mean missing blood donations from patients that are potential eligible blood donors. Being incautious can on the other hand mean inducing unnecessary risks for donor and/or recipient.

The variety in policies regarding the different aspects of the medical questionnaire is further displayed in two other studies. In 2011, Benjamin and colleagues published an article reporting about a survey concerning blood donor eligibility policies for men having sex with men, and in 2013, Pauwels and colleagues published on a similar survey concerning the use of blood of hemochromatosis patients as donor blood (36,37). The findings in these articles are similar to the findings presented in this article, i.c. there is no uniformity in worldwide policies. Furthermore, there is a small survey from van der Linden and colleagues about epilepsy patients and blood donation in the Netherlands (34). This survey concluded that a greater risk of seizures in blood donors with a history of epilepsy could not be demonstrated.

Other comparable studies in medical literature are difficult to find, so there is only a very small number of articles to draw conclusions. Presumably, these articles just show the tip of the iceberg. The problem of discrepancy in policy making with regard to the different aspects of transfusion medicine might be of even larger extent. Further medical research and effort is therefore needed for homogenisation of the worldwide policies on blood donor selection. This will ultimately lead to a safer approach of transfusion medicine and a safer process for both donor and recipient. Possibly, there can be an important role for the 'Global Advisory Panel on Corporate Governance and Risk Management of Blood Services in Red Cross and Red Crescent Societies' (GAP). This is a partnership between several blood institutions worldwide. According to their website (www.globaladvisorypanel.org), their mission is to 'support Red Cross/Red Crescent blood services in risk management and corporate governance of blood programmes and promote good practices and knowledge exchange'. An international cooperation in guiding medical research to scientifically underpin all aspects of the medical questionnaire could be a project to support. After all, joined forces can lead to important changes that are urgent and necessary.

3.5. Conclusion

This study confirms that there is indeed a large discrepancy in policies that are being applied worldwide with regard to epilepsy patients and blood donation. This discrepancy seems to be caused by a lack of studies, that can serve as a base for policy making. A standardization of the worldwide policies, based on evidence, will lead to a more safe and effective blood transfusion program, which will benefit the outcome in donor and recipient. Further medical research is necessary and urgent.

4. Systematic review

4.1. Introduction

To scientifically underpin the eligibility of epilepsy patients as blood donors, we addressed the question whether it is safe for epilepsy patients to donate blood. A systematic review was performed to answer the question.

4.2. Materials and methods

4.2.1. PICO

Is there a higher risk of donor adverse events (O) in blood donors (P) who have had (an) epileptic attack(s) in the past (I) compared to blood donors who never had an epileptic attack (C)?

4.2.2. Search strategy

All searches for evidence were performed between November 2014 and December 2014. The following sources were searched: MEDLINE (using the PubMed interface), Embase (using the Embase.com interface), The Cochrane Central Register of Controlled Trials, Web of Science and CINAHL (see appendix (figure 5)).

The references were extracted from each database on the 30th of December 2014 and stored as text files. Then, they were imported in Reference Manager 12® and sorted alphabetically. Subsequently, a duplicate search was performed on the list of references in a three-phase way. Reviewer 1 (A.K.) and reviewer 2 (E.D.B.) then each received a copy of the database after duplicate removal.

4.2.3. Selection criteria

The following selection criteria have been applied to the full texts of the articles:

Study design:

Included: Experimental studies: (non-)randomized controlled trials, non-controlled experimental studies; Observational studies: cohort studies, case-control studies, cross-sectional studies (surveys/questionnaires), non-controlled observational studies, case series; conference abstracts describing one of the previous study types;
Excluded: case reports, letters, comments, opinion pieces, narrative reviews

Population:

***Included*:** blood donors (no geographic limitations; whole blood/blood platelets/plasma; autologous/allogenic);
Excluded: deferred donors

Intervention/risk factor:

Included: (former) epileptic attacks; patients taking medication, or who are medication-free;
Excluded: none

Comparison: healthy donors

Outcome: new epileptic attack; adverse events for donor

4.2.4. Study selection

The list of references has been screened separately by reviewer 1 and reviewer 2, first by title and then by abstract. After this scanning process, the list of residual references has been imported in a Microsoft Excel® file by each reviewer. A full text search of the references has been performed as a next step. The Adobe PDF®-files of these articles were stored in a documents folder. Full texts were found and opened by using the Limo Libris® system that is provided by the KU Leuven. Full texts that could not be retrieved immediately due to accession rights, were ordered at the university library and sent to the reviewers by mail. A referential number was used to identify the queried articles.
All collected full texts were screened to see if the articles met the in- and exclusion criteria. Articles that met these criteria, were studied in detail. The result of this process was deliberated by reviewer 1 and reviewer 2. In case of a disagreement, a third reviewer was involved.
To search for additional related articles, the citation lists of the selected articles were checked for potentially missed articles that met the selection criteria. Besides, the first 20 related items in PubMed were also screened, even as references by which the included studies were cited.

4.2.5. Data extraction

Study characteristics and study findings were extracted and tabulated.

4.2.6. Quality of the data

The quality of the data was judged by using the GRADE approach. GRADE considers limitations of study design of the individual studies (i.c. inappropriate eligibility criteria, inappropriate measures for exposure and outcome variables, no control for confounding, incomplete or inadequate follow-up and other limitations), imprecision (i.c. lack of data, large variability of data and limited sample size), inconsistency, indirectness and publication bias. All these factors can lead to a down- or upgrading of the level of evidence. Experimental studies inherently start at a higher level of evidence than observational studies. After taking all considerations into account, the level of evidence can result in being high, moderate, low or very low (25).

4.3. Results

4.3.1. Study characteristics

Figure 3 provides a flowchart of the identification and selection of studies. 7283 studies have been screened. After duplicate removal, 5184 studies have been withheld. Evaluation of title and abstract subsequently resulted in 186 studies for reviewer 1 and 71 studies for reviewer 2. After full text evaluation, 4 studies were included by reviewer 1 and 3 were included by reviewer 2 (see appendix (table 2)). After deliberation, 3 studies were finally withheld. Van der Linden et al. 1986 was finally not included, because the data in the study are retrospective.

All of the included studies are observational studies. Two studies (38,39) are case series and one study (35) is a cohort study. The population in Krumholz et al. 1988 consisted of 314 blood donations done by 297 donors with a history of epilepsy/seizures. Approximately one quarter of these blood donors was taking

anti-epileptic drugs at the moment of donation and about one in ten has had a seizure in the year before the donation. There was no mention of the population's gender. Subsequently, the population in Krumholz et al. 1995 is comprised of 723 blood donations done by 613 donors with a history of epilepsy/seizures versus 328420 blood donations done by donors without a history of epilepsy/seizures. In the group of blood donors with a history of epilepsy/seizures, approximately one quarter was taking anti-epileptic drugs at the moment of donation and about one in ten still had active seizures. In this study there was no difference in the amount of male blood donors versus female blood donors. The population in Illies et al. 2000, at last, is comprised of 26 autologous blood donors with a history of refractory epilepsy. Approximately six out of ten of these blood donors were symptomatic and four out of ten were idiopathic. Besides, there is a difference in the amount of female donors versus male donors, i.c. 17 females versus 9 males. Except for one, all blood donors are taking anti-epileptic drugs at the moment of donation.

All study characteristics are summarized in appendix (table 3).

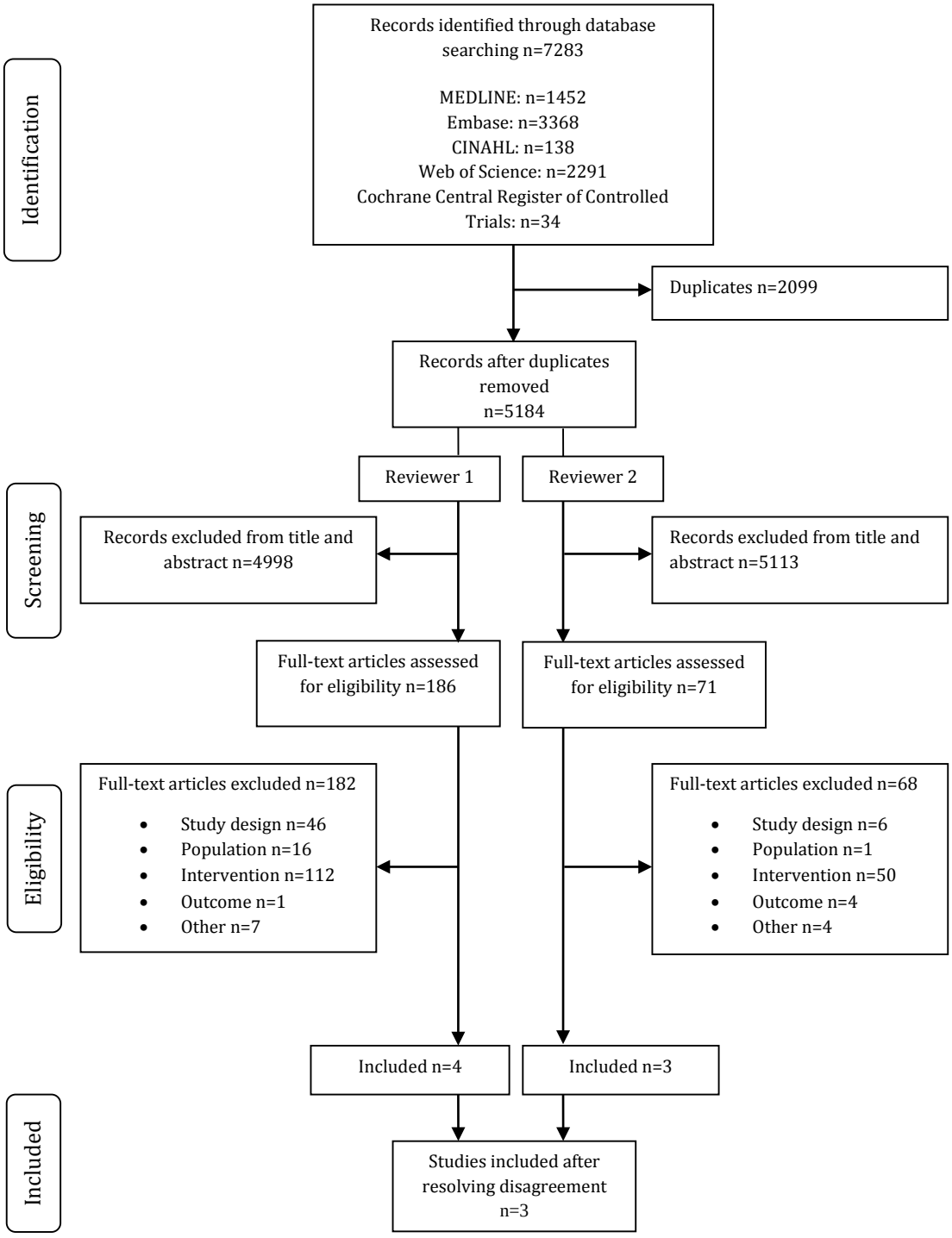


Figure 3: *Flowchart of the study selection (reviewer 1= A.K.; reviewer 2= E.D.B.). A total of 7283 articles has been screened. After duplicate removal, 5184 studies were withheld. Reviewer 1 selected 4 articles after the title and abstract screening. Reviewer 2 selected 3 articles after the title and abstract screening. After resolving disagreement, 3 studies were finally withheld.*

4.3.2. Study findings

All three included studies have poor statistical analyses and only contain descriptive numbers: Krumholz et al. 1988, a study with 297 participants, showed a total of 4.10% adverse events in blood donors with a history of seizures/epilepsy. 3.50% of these adverse events were slight, 0.60% were moderate and

none were severe. Krumholz et al. 1995 was comprised of two groups of blood donors. 328420 donations were done by persons without a history of seizures/epilepsy, while 723 donations were done by persons with a history of seizures/epilepsy. Based on the descriptive numbers in the article, it was possible to calculate the risk ratio and the appurtenant confidence interval, using Review Manager 5® (see appendix (figure 6)). The study showed a total of 7345 adverse events in the group of 328420 blood donors and a total of 24 adverse events in the group of 723 blood donors. Calculations show that that these numbers are not statistically significant. Similar results can be found in appendix figure 5 for the subdivision in slight; moderate and severe adverse events. Illies et al. 2000, a study with 26 participants, shows no adverse events in blood donors with a history of epilepsy/seizures.

4.3.3. Quality of the data

All three included studies have serious limitations in study design. Krumholz et al. 1988 is a case series and is not controlled for confounding. Additionally, the appropriateness of eligibility criteria cannot be judged, because there is no control group. Illies et al. 2000 has similar limitations. Krumholz et al. 1995 is unclear with regards to the control for confounders. One possible confounder has been mentioned in the article, but this confounder has not been statistically studied.

To determine the level of the body of evidence, the GRADE approach has been applied. Because there are only observational studies and no experimental studies, we started at the level of evidence 'low' [C]. Points have been subtracted for limitations of study design (as discussed above) and imprecision. These subtractions lead to the final grading 'very low' [D], which means that there is very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

4.4. Discussion

For many years, there has been a debate whether epilepsy patients are potential eligible blood donors. In some blood institutions, epilepsy patients are accepted as blood donors, whereas in others they are temporarily or even permanently excluded. This ambiguity indicates that current policies are not based on proven scientific data, but are rather influenced by other motives. In the past, there have been numerous reasons mentioned in the medical literature that were considered a possible safety treat for both the donor and the recipient. They served partially as a base for current policy making, next to other reasons, as discussed in the survey. Therefore, we addressed the question whether it is safe for epilepsy patients to donate blood, by using the methodology of evidence-based practice, taking into account (1) the best available evidence, (2) expert opinion, and (3) preferences of the target group.

First, we performed a systematic review, according to the principles of the Cochrane Collaboration. We set up a broad search strategy and screened five databases for evidence. There were no language barriers. During our search, we screened 5184 unique articles. After the title and abstract screening, four studies were withheld by the two reviewers, but only three articles were finally selected. The study from Van der Linden et al. 1986 has been excluded after resolving the disagreement, since the data in the study are retrospective. All three included studies have serious limitations that should be taken into account: (1) All studies are observational studies. Experimental studies with regard to this subject could not be found. (2) None of the studies contained an appropriate statistical analysis. Based on the numbers that were presented in Krumholz et al. 1995, it was however possible to calculate crude risk ratios, however without confounding factors taking into account. Krumholz et al. 1988 and Illies et al. 2000 did not even contain the necessary information to make these calculations. This serious lack of statistical numbers makes it very difficult to draw robust conclusions. (3) Two of the three studies are uncontrolled studies, which is an intrinsic characteristic of case series. Based on the three included studies, we can conclude that a significant increased risk of adverse events in blood donors could not be demonstrated in case of a history of epilepsy. However, evidence is scarce and more research is desirable.

The lack of strong scientific evidence to support the blood donor eligibility criteria is a recurrent finding in other systematic reviews. A scoping search of the literature has learned that there are two systematic reviews available with evidence to support blood donor eligibility criteria concerning the safety of the donor (40,41). These articles provide an overview of studies that looked at the relationship between hypotension and hypertension in blood donors and adverse donor reactions. In addition, two systematic reviews searched for evidence to support blood donor selection criteria with regard to the safety for the recipient of donor blood (42,43). One review studied men having sex with other men as blood donors, and one review collected evidence concerning hemochromatosis patients as blood donors. All mentioned systematic reviews contained only a very limited number of studies of a low to very low quality. Other elements of the medical questionnaire have not been reviewed yet for the best available evidence to support them. A scientific underpinning of all aspects of the medical questionnaire could be of paramount importance though. It can mean a(n) (even) more safe and effective approach of transfusion medicine, which will benefit the health of donors and recipients.

Second, we collected expert opinion and practice experience concerning this subject. Safety has always been an important goal in transfusion medicine. Possible safety treats could explain why many blood institutions apply a careful policy in epilepsy patients. Theoretically, there are after all many adverse advents in donors and recipients that can mean a possible safety treat during the blood donation process. (1) When an epilepsy patient donates blood, there is a loss of blood volume, that could hypothetically induce a seizure through hypotension and bradycardia. However, if a normal amount of blood is withdrawn from the donor, no acute disturbances in the blood flow are expected. (2) When an epilepsy patients donates blood, the level of anti-epileptics in the donors blood can drop, which could evoke a seizure. Since the donors blood will only recover relatively slowly, a sudden change in the concentration of anti-epileptic drugs in the donors blood is not expected. (3) When a recipient receives blood from an epilepsy patients, there is a possibility to transmit anti-epileptic drugs. This should however not pose problems, since the concentration of anti-epileptic drugs is almost negligible (34,35). Furthermore, the list of excluded studies did not contain an article about recipient outcomes.

Furthermore, if an (epilepsy) patient has a seizure during the blood donation process, it is questionable if it is indeed an epileptic seizure or a convulsive syncope. The onset of a convulsive syncope is similar to that of a syncope, but the reaction is followed by back, head and limb spasms as a response to cerebral ischemia. Since both an epileptic seizure and a convulsive syncope can look similar at first sight, it can sometimes cause a misinterpretation. However, their pathophysiological mechanism is completely different . So, they are generally distinct and different disorders that should not be confused with one another (34,35,39,44).

Third, we take into account the preferences of the target group. Nowadays, when looking at patient forums, epilepsy patients are a requesting party for blood donation. To be able to donate blood would give a satisfaction sense to a lot of epilepsy patients. We must not forget that these are only assumptions about the target populations opinion towards blood donation, since we only see the opinion of a small portion of epilepsy patients. A broader universal patient forum could be a future project to further implicate the concerns and interests of this group.

4.5. Conclusion

We can conclude that a significant increased risk of adverse events in blood donors could not be demonstrated in case of a history of epilepsy. So, permanent exclusion seems to be overcautious. Temporary exclusion seems to be a more reasonable policy. More studies are however necessary to determine how long epilepsy patients have to be excluded from blood donation.

5. General conclusion and link with general practitioners

In this dissertation, an attempt was made to answer the question: 'Is it safe for epilepsy patients to donate blood?' To answer this question, a survey and systematic review were performed. The survey showed that that there is a large discrepancy in worldwide policies regarding epilepsy patients and blood donation. The systematic review of the available scientific literature showed that a significant increased risk of adverse events in blood donors could not be demonstrated in case of a history of epilepsy.
We can therefore conclude that there is no clear reason to exclude epilepsy patients from blood donation. However, one must be cautious to draw robust conclusions, since evidence is scarce. Therefore, this dissertation is a call for further research concerning all aspects of the medical questionnaire. Homogenisation of this medical questionnaire can after all be the solid base for a more safe and efficient transfusion medicine.
Since transfusion medicine is performed by many different types of physicians, there is a need for all physicians to take their responsibility and do their part. There can be two important roles for general practitioners, since they mostly have a closer relationship with their patients than a specialist. First, they should be able to explain to their patients the different aspects of blood donation. To give correct information, it is important that this information is scientifically underpinned. Second, the general practitioner can play a role in guiding patients before or after the donation.

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7. Appendices

Figure 1: The alternated transdisciplinary model.



Figure 2: Standards for developing trustworthy CPG's.

STANDARD 1: Establishing transparency.

1.1. The processes by which a CPG is developed and funded should be detailed explicitly and publicly accessible.

STANDARD 2: Management of conflict of interest (COI).

2.1. Prior to selection of the Guideline Development Group (GDG), individuals being considered for membership should declare all interests and activities potentially resulting in COI with development group activity, by written disclosure to those convening the GDG.
Disclosure should reflect all current and planned commercial (including services from which a clinician derives a substantial proportion of income), non-commercial, intellectual, institutional, and patient/public activities pertinent to the potential scope of the CPG.
2.2. Disclosure of COIs within GDG
All COI of each GDG member should be reported and discussed by the prospective development group prior to the onset of their work.
Each panel member should explain how their COI could influence the CPG development process or specific recommendations.
2.3. Divestment
Members of the GDG should divest themselves of financial investments they or their family members have in, and not participate in marketing activities or advisory boards of, entities whose interests could be affected by CPG recommendations.
2.4. Exclusions
Whenever possible GDG members should not have COI.
In some circumstances, a GDG may not be able to perform its work without members who have COIs, such as relevant clinical specialists who receive a substantial portion of their incomes from services pertinent to the CPG.

Members with COIs should represent not more than a minority of the GDG.
The chair or co-chairs should not be a person(s) with COI.
Funders should have no role in CPG development.

STANDARD 3: Guideline development group composition.

3.1. The GDG should be multidisciplinary and balanced, comprising a variety of methodological experts and clinicians, and populations expected to be affected by the CPG.
3.2.Patient and public involvement should be facilitated by including (at least at the time of clinical question formulation and draft CPG review) a current or former patient and a patient advocate or patient/consumer organization representative in the GDG.
3.3. Strategies to increase effective participation of patient and consumer representatives, including training in appraisal of evidence, should be adopted by GDG.

STANDARD 4: Clinical practice guideline–systematic review intersection.

4.1. CPG developers should use systematic reviews that meet standards set by the Institute of Medicine's Committee on Standards for Systematic Reviews of Comparative Effectiveness Research.
4.2. When systematic reviews are conducted specifically to inform particular guidelines, the GDG and systematic review team should interact regarding the scope, approach, and output of both processes.

STANDARD 5: Establishing evidence foundations for and rating strength of recommendations.

5.1. For each recommendation, the following should be provided:
An explanation of the reasoning underlying the recommendation, including:

- A clear description of potential benefits and harms.
- A summary of relevant available evidence (and evidentiary gaps), description of the quality (including applicability), quantity (including completeness), and consistency of the aggregate available evidence.
- An explanation of the part played by values, opinion, theory, and clinical experience in deriving the recommendation.

A rating of the level of confidence in (certainty regarding) the evidence underpinning the recommendation.
A rating of the strength of the recommendation in light of the preceding bullets.
A description and explanation of any differences of opinion regarding the recommendation.

STANDARD 6: Articulation of recommendations.

6.1. Recommendations should be articulated in a standardized form detailing precisely what the recommended action is and
under what circumstances it should be performed.
6.2. Strong recommendations should be worded so that compliance with the recommendation(s) can be evaluated.

STANDARD 7: External review.

7.1. External reviewers should comprise a full spectrum of relevant stakeholders, including scientific and clinical experts, organizations (e.g. health care, specialty societies), agencies (e.g. federal government), patients, and representatives of the public.
7.2. The authorship of external reviews submitted by individuals and/or organizations should be kept confidential unless that protection has been waived by the reviewer(s).
7.3. The GDG should consider all external reviewer comments and keep a written record of the rationale for modifying or not modifying a CPG in response to reviewers' comments.

7.4. A draft of the CPG at the external review stage or immediately following it (i.e., prior to the final draft) should be made available to the general public for comment. Reasonable notice of impending publication should be provided to interested public stakeholders.

STANDARD 8: Updating.

8.1. The CPG publication date, date of pertinent systematic evidence review, and proposed date for future CPG review should be documented in the CPG.
8.2. Literature should be monitored regularly following CPG publication to identify the emergence of new, potentially relevant evidence and to evaluate the continued validity of the CPG.
8.3. CPGs should be updated when new evidence suggests the need for modification of clinically important recommendations. For example, a CPG should be updated if new evidence shows that a recommended intervention causes previously unknown substantial harm, that a new intervention is significantly superior to a previously recommended intervention from an efficacy or harms perspective, or that a recommendation can be applied to new populations.

Figure 3: The AGREE II checklist.

DOMAIN 1: Scope and purpose
1. The overall objective(s) of the guideline is (are) specifically described.
2. The health question(s) covered by the guideline is (are) specifically described.
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.

DOMAIN 2: STAKEHOLDER INVOLVEMENT
4. The guideline development group includes individuals from all relevant professional groups.
5. The views and preferences of the target population (patients, public, etc.) have been sought.
6. The target users of the guideline are clearly defined.

DOMAIN 3: RIGOUR OF DEVELOPMENT
7. Systematic methods were used to search for evidence.
8. The criteria for selecting the evidence are clearly described.
9. The strengths and limitations of the body of evidence are clearly described.
10. The methods for formulating the recommendations are clearly described.
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.
12. There is an explicit link between the recommendations and the supporting evidence.
13. The guideline has been externally reviewed by experts prior to its publication.
14. A procedure for updating the guideline is provided.

DOMAIN 4: CLARITY OF PRESENTATION
15. The recommendations are specific and unambiguous.
16. The different options for management of the condition or health issue are clearly presented.
17. Key recommendations are easily identifiable.

DOMAIN 5: APPLICABILITY
18. The guideline describes facilitators and barriers to its application.
19. The guideline provides advice and/or tools on how the recommendations can be put into practice.
20. The potential resource implications of applying the recommendations have been considered.
21. The guideline presents monitoring and/or auditing criteria.

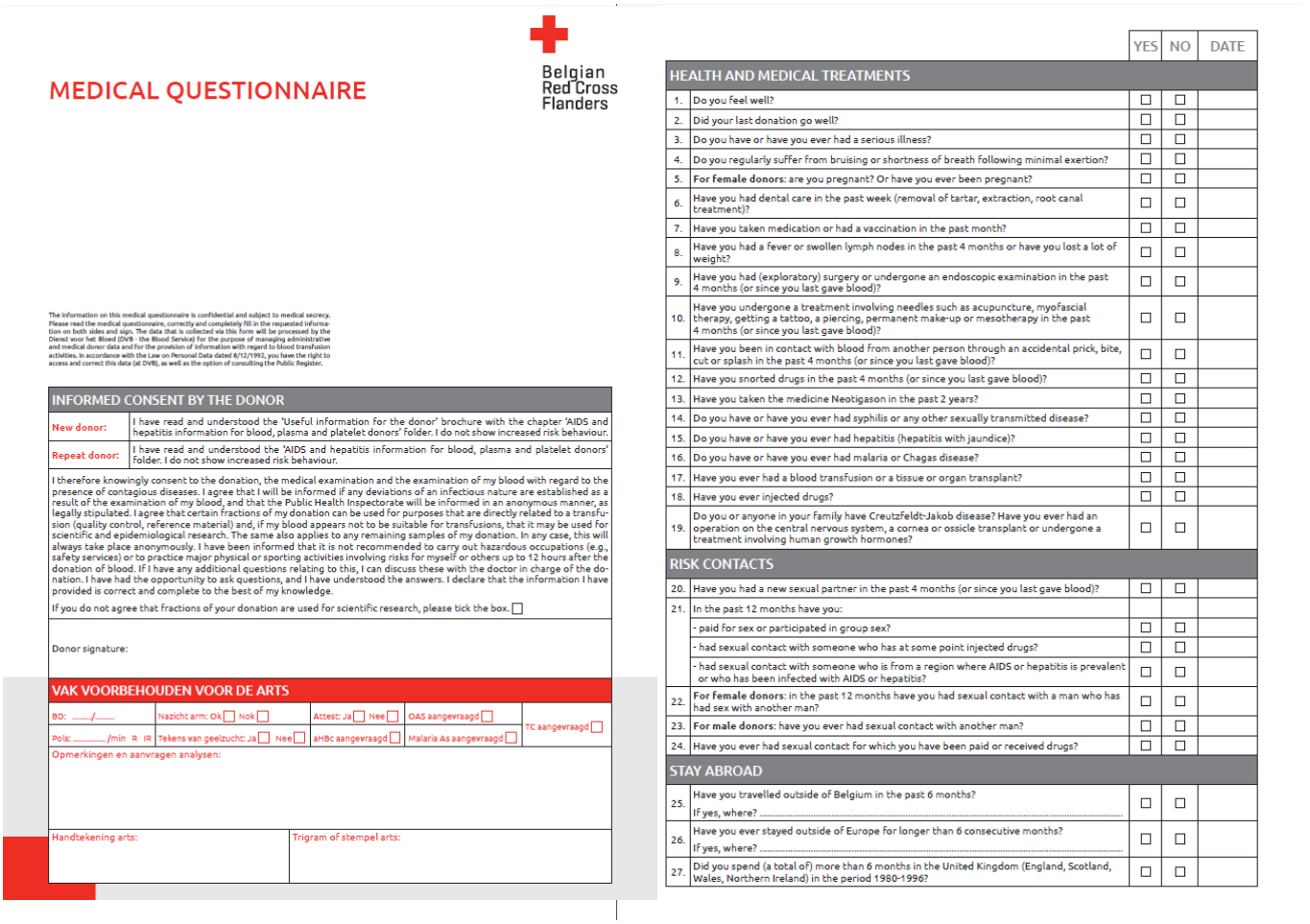
DOMAIN 6: EDITORIAL INDEPENDENCE

22. The views of the funding body have not influenced the content of the guideline.
23. Competing interests of guideline development group members have been recorded and addressed.

OVERALL GUIDELINE ASSESSMENT
For each question, please choose the response which best characterizes the guideline.

1. Rate the overall quality of this guideline.
2. I would recommend this guideline for use.

Figure 4: The medical questionnaire used by Belgian Red Cross-Flanders.



MEDICAL QUESTIONNAIRE

Belgian Red Cross Flanders

The information on this medical questionnaire is confidential and subject to medical secrecy. Please read the medical questionnaire, correctly and completely fill in the requested information on both sides and sign. The data that is collected via this form will be processed by the Dienst voor het Bloed (DVB - the Blood Service) for the purpose of managing administrative and medical donor data and for the provision of information with regard to blood transfusion activities. In accordance with the Law on Personal Data dated 8/12/1992, you have the right to access and correct this data (at DVB), as well as the option of consulting the Public Register.

INFORMED CONSENT BY THE DONOR	
New donor:	I have read and understood the 'Useful information for the donor' brochure with the chapter 'AIDS and hepatitis information for blood, plasma and platelet donors' folder. I do not show increased risk behaviour.
Repeat donor:	I have read and understood the 'AIDS and hepatitis information for blood, plasma and platelet donors' folder. I do not show increased risk behaviour.

I therefore knowingly consent to the donation, the medical examination and the examination of my blood with regard to the presence of contagious diseases. I agree that I will be informed if any deviations of an infectious nature are established as a result of the examination of my blood, and that the Public Health Inspectorate will be informed in an anonymous manner, as legally stipulated. I agree that certain fractions of my donation can be used for purposes that are directly related to a transfusion (quality control, reference material) and, if my blood appears not to be suitable for transfusions, that it may be used for scientific and epidemiological research. The same also applies to any remaining samples of my donation. In any case, this will always take place anonymously. I have been informed that it is not recommended to carry out hazardous occupations (e.g., safety services) or to practice major physical or sporting activities involving risks for myself or others up to 12 hours after the donation of blood. If I have any additional questions relating to this, I can discuss these with the doctor in charge of the donation. I have had the opportunity to ask questions, and I have understood the answers. I declare that the information I have provided is correct and complete to the best of my knowledge.

If you do not agree that fractions of your donation are used for scientific research, please tick the box. ☐

Donor signature:

VAK VOORBEHOUDEN VOOR DE ARTS				
BD: ...../.....	Nazicht arm: Ok ☐ Nok ☐	Attest: Ja ☐ Nee ☐	OAS aangevraagd ☐	TC aangevraagd ☐
Pols: ...../min R IR	Tekens van geelzucht: Ja ☐ Nee ☐	aHBc aangevraagd ☐	Malaria As aangevraagd ☐	
Opmerkingen en aanvragen analysen:				
Handtekening arts:		Trigram of stempel arts:		

		YES	NO	DATE
HEALTH AND MEDICAL TREATMENTS				
1.	Do you feel well?	☐	☐	
2.	Did your last donation go well?	☐	☐	
3.	Do you have or have you ever had a serious illness?	☐	☐	
4.	Do you regularly suffer from bruising or shortness of breath following minimal exertion?	☐	☐	
5.	**For female donors**: are you pregnant? Or have you ever been pregnant?	☐	☐	
6.	Have you had dental care in the past week (removal of tartar, extraction, root canal treatment)?	☐	☐	
7.	Have you taken medication or had a vaccination in the past month?	☐	☐	
8.	Have you had a fever or swollen lymph nodes in the past 4 months or have you lost a lot of weight?	☐	☐	
9.	Have you had (exploratory) surgery or undergone an endoscopic examination in the past 4 months (or since you last gave blood)?	☐	☐	
10.	Have you undergone a treatment involving needles such as acupuncture, myofascial therapy, getting a tattoo, a piercing, permanent make-up or mesotherapy in the past 4 months (or since you last gave blood)?	☐	☐	
11.	Have you been in contact with blood from another person through an accidental prick, bite, cut or splash in the past 4 months (or since you last gave blood)?	☐	☐	
12.	Have you snorted drugs in the past 4 months (or since you last gave blood)?	☐	☐	
13.	Have you taken the medicine Neotigason in the past 2 years?	☐	☐	
14.	Do you have or have you ever had syphilis or any other sexually transmitted disease?	☐	☐	
15.	Do you have or have you ever had hepatitis (hepatitis with jaundice)?	☐	☐	
16.	Do you have or have you ever had malaria or Chagas disease?	☐	☐	
17.	Have you ever had a blood transfusion or a tissue or organ transplant?	☐	☐	
18.	Have you ever injected drugs?	☐	☐	
19.	Do you or anyone in your family have Creutzfeldt-Jakob disease? Have you ever had an operation on the central nervous system, a cornea or ossicle transplant or undergone a treatment involving human growth hormones?	☐	☐	
RISK CONTACTS				
20.	Have you had a new sexual partner in the past 4 months (or since you last gave blood)?	☐	☐	
21.	In the past 12 months have you:			
	- paid for sex or participated in group sex?	☐	☐	
	- had sexual contact with someone who has at some point injected drugs?	☐	☐	
	- had sexual contact with someone who is from a region where AIDS or hepatitis is prevalent or who has been infected with AIDS or hepatitis?	☐	☐	
22.	**For female donors**: in the past 12 months have you had sexual contact with a man who has had sex with another man?	☐	☐	
23.	**For male donors**: have you ever had sexual contact with another man?	☐	☐	
24.	Have you ever had sexual contact for which you have been paid or received drugs?	☐	☐	
STAY ABROAD				
25.	Have you travelled outside of Belgium in the past 6 months? If yes, where?	☐	☐	
26.	Have you ever stayed outside of Europe for longer than 6 consecutive months? If yes, where?	☐	☐	
27.	Did you spend (a total of) more than 6 months in the United Kingdom (England, Scotland, Wales, Northern Ireland) in the period 1980-1996?	☐	☐	

Figure 5: Search strategy.

The following search strategy was used to search the **MEDLINE** database:

1. "Blood Donors"[Mesh] OR blood don*[TIAB] OR "Blood Banks"[Mesh] OR blood bank*[TIAB] OR blood service*[TIAB] OR blood center*[TIAB] OR blood centre*[TIAB] OR transfusion service*[TIAB] OR transfusion cent*[TIAB]
2. "Epilepsy"[Mesh] OR epilep*[TIAB] OR seizure*[TIAB] OR convuls*[TIAB] OR "Anticonvulsants"[Mesh] OR fits[TIAB]
3. "Risk" [Mesh:NoExp] OR "Risk Factors"[Mesh] OR risk factor*[TIAB] OR "Risk Assessment" [Mesh:NoExp] OR deferral*[TIAB] OR referral*[TIAB] OR inclusion*[TIAB] OR exclusion*[TIAB] OR "Donor Selection" [Mesh] OR donation history[TIAB]

4. "Syncope"[Mesh] OR syncop*[TIAB] OR vasovagal[TIAB] OR vaso vagal[TIAB] OR "Unconsciousness"[Mesh:NoExp] OR unconscious*[TIAB] OR conscious*[TIAB] OR "Hypotension, Orthostatic"[Mesh] OR collaps*[TIAB] OR faint*[TIAB] OR "Bradycardia"[Mesh] OR bradycardia[TIAB] OR "Urinary Incontinence"[Mesh:NoExp] OR incontinence[TIAB] OR "Sweating"[Mesh] OR diaphoresis[TIAB] OR diaphoretic[TIAB] OR sweat[TIAB] OR sweaty[TIAB] OR sweating[TIAB] OR "Dizziness"[Mesh] OR dizzy[TIAB] OR dizziness[TIAB] OR light headedness[TIAB] OR lightheadedness[TIAB] OR "Nausea"[Mesh:NoExp] OR nausea[TIAB] OR nauseous[TIAB] OR vomit[TIAB] OR vomiting[TIAB] OR vomited[TIAB] OR weak[TIAB] OR weakened[TIAB] OR weakness[TIAB] OR "Pallor"[Mesh] OR pallor[TIAB] OR side effect*[TIAB] OR adverse event*[TIAB] OR adverse effect*[TIAB] OR reaction*[TIAB] OR complication*[TIAB] OR incident[TIAB] OR incidents[TIAB] OR "Safety"[Mesh:NoExp] OR safe[TIAB] OR safety[TIAB]
5. 3 AND 4
6. 2 OR 5
7. 1 AND 6

The following search strategy was used to search the **Embase** database:

1. 'blood donor'/exp OR (blood NEXT/1 don*):ti,ab OR 'blood bank'/exp OR 'blood bank':ti,ab OR 'blood banks':ti,ab OR (blood NEXT/1 service*):ti,ab OR (blood NEXT/1 (center* OR centre*)):ti,ab OR (transfusion NEXT/1 service*):ti,ab OR (transfusion NEXT/1 cent*):ti,ab
2. 'convulsion'/exp OR convuls*:ti,ab OR 'epilepsy'/exp OR epilep*:ti,ab OR 'pseudoepileptic seizure'/exp OR 'seizure'/exp OR seizure*:ti,ab OR 'seizure susceptibility'/exp OR fits:ti,ab OR 'anticonvulsive agent'/exp
3. 'Risk'/de OR 'Risk Factor'/exp OR (risk NEXT/1 factor*):ti,ab OR 'Risk Assessment'/exp OR deferral*:ti,ab OR referral*:ti,ab OR inclusion*:ti,ab OR exclusion*:ti,ab OR 'Donor Selection'/exp OR 'donation history':ti,ab
4. 'Presyncope'/exp OR syncop*:ti,ab OR vasovagal:ti,ab OR 'vaso vagal':ti,ab OR 'Unconsciousness'/de OR unconscious*:ti,ab OR conscious*:ti,ab OR 'Orthostatic Hypotension'/exp OR 'orthostatic hypotension':ti,ab OR collaps*:ti,ab OR faint*:ti,ab OR 'Bradycardia'/de OR bradycardia:ti,ab OR 'Incontinence'/exp OR incontinence:ti,ab OR 'Sweating'/exp OR diaphoresis:ti,ab OR diaphoretic:ti,ab OR sweat:ti,ab OR sweaty:ti,ab OR sweating:ti,ab OR 'Dizziness'/exp OR dizzy:ti,ab OR dizziness:ti,ab OR 'light headedness':ti,ab OR lightheadedness:ti,ab OR 'Nausea'/exp OR nausea:ti,ab OR nauseous:ti,ab OR 'Vomiting'/exp OR vomit:ti,ab OR vomiting:ti,ab OR vomited:ti,ab OR weak:ti,ab OR weakened:ti,ab OR weakness:ti,ab OR 'Pallor'/exp OR pallor:ti,ab OR 'Side Effect'/de OR (side NEXT/1 effect*):ti,ab OR (adverse NEXT/1 event*) OR (adverse NEXT/1 effect*):ti,ab OR reaction*:ti,ab OR complication*:ti,ab OR incident:ti,ab OR incidents:ti,ab OR 'Safety'/de OR safe:ti,ab OR safety:ti,ab
5. 3 AND 4
6. 2 OR 5
7. 1 AND 6

The following search strategy was used to search the **Cochrane Central Register of Controlled Trials** database:

1. [mh "Blood Donors"] OR ("blood don*"):ti,ab,kw OR [mh "Blood Banks"] OR ("blood bank"):ti,ab,kw OR ("blood banks"):ti,ab,kw OR ("blood service*"):ti,ab,kw OR ("blood center*"):ti,ab,kw OR ("blood centre*"):ti,ab,kw OR ("transfusion service*"):ti,ab,kw OR ("transfusion cent*"):ti,ab,kw
2. [mh "Epilepsy"] OR (epilep*):ti,ab,kw OR (convuls*):ti,ab,kw OR (seizure?):ti,ab,kw OR [mh "Anticonvulsants"] OR (fits):ti,ab,kw

3. [mh ^"Risk"] OR [mh "Risk Factors"] OR ("risk factor*"):ti,ab,kw OR [mh "Risk Assessment"] OR (deferral*):ti,ab,kw OR (referral*):ti,ab,kw OR (inclusion*):ti,ab,kw OR (exclusion*):ti,ab,kw OR [mh "Donor Selection"] OR ("donation history"):ti,ab,kw
4. [mh "Syncope"] OR (syncop*):ti,ab,kw OR (vasovagal):ti,ab,kw OR ("vaso vagal"):ti,ab,kw OR [mh ^"Unconsciousness"] OR (unconscious*):ti,ab,kw OR (conscious*):ti,ab,kw OR [mh "Hypotension, Orthostatic"] OR (collaps*):ti,ab,kw OR (faint*):ti,ab,kw OR [mh "Bradycardia"] OR (bradycardia):ti,ab,kw OR [mh ^"Urinary Incontinence"] OR (incontinence):ti,ab,kw OR [mh "Sweating"] OR (diaphoresis):ti,ab,kw OR (diaphoretic):ti,ab,kw OR (sweat):ti,ab,kw OR (sweaty):ti,ab,kw OR (sweating):ti,ab,kw OR [mh "Dizziness"] OR (dizzy):ti,ab,kw OR (dizziness):ti,ab,kw OR ("light headedness"):ti,ab,kw OR (lightheadedness):ti,ab,kw OR [mh ^"Nausea"] OR (nausea):ti,ab,kw OR (nauseous):ti,ab,kw OR (vomit):ti,ab,kw OR (vomiting):ti,ab,kw OR (vomited):ti,ab,kw OR (weak):ti,ab,kw OR (weakened):ti,ab,kw OR (weakness):ti,ab,kw OR [mh "Pallor"] OR (pallor):ti,ab,kw OR ("side effect*"):ti,ab,kw OR ("adverse effect*"):ti,ab,kw OR ("adverse event*"):ti,ab,kw OR (reaction*):ti,ab,kw OR (complication*):ti,ab,kw OR (incident):ti,ab,kw OR (incidents):ti,ab,kw OR [mh ^"Safety"] OR (safe):ti,ab,kw OR (safety):ti,ab,kw
5. 3 AND 4
6. 2 OR 5
7. 1 AND 6

The following search strategy was used to search the **Web of Science** database:

1. TS=("blood don*") OR TS=("blood bank") OR TS=("blood banks") OR TS=("blood service*") OR TS=("blood center*") OR TS=("blood centre*") OR TS=("transfusion service*") OR TS=("transfusion cent*")
2. TS=("epilep*") OR TS=("convuls*") OR TS=("seizure? ") OR TS=("fits") OR TS=("anticonvulsants")
3. TS=("risk") OR TS=("deferral*") OR TS=("referral*") OR TS=("inclusion*") OR TS=("exclusion*") OR TS=("donor selection") OR TS=("donation history")
4. TS=("syncop*") OR TS=("vasovagal") OR TS=("vaso vagal") OR TS=("unconscious*") OR TS=("conscious*") OR TS=("orthostatic hypotension") OR TS=("collaps*") OR TS=("faint*") OR TS=("bradycardia") OR TS=("incontinence") OR TS=("sweat") OR TS=("sweaty") OR TS=("sweating") OR TS=("diaphoresis") OR TS=("diaphoretic") OR TS=("dizzy") OR TS=("dizziness") OR TS=("lightheadedness") OR TS=("light headedness") OR TS=("nausea") OR TS=("nauseous") OR TS=("vomit") OR TS=("vomiting") OR TS=("vomited") OR TS=("weak") OR TS=("weakened") OR TS=("weakness") OR TS=("pallor") OR TS=("side effect*") OR TS=("adverse effect*") OR TS=("adverse event*") OR TS=("reaction*") OR TS=("complication*") OR TS=("incident") OR TS=("incidents") OR TS=("safe") OR TS=("safety")
5. 3 AND 4
6. 2 OR 5
7. 1 AND 6

The following search strategy was used to search the **CINAHL** database:

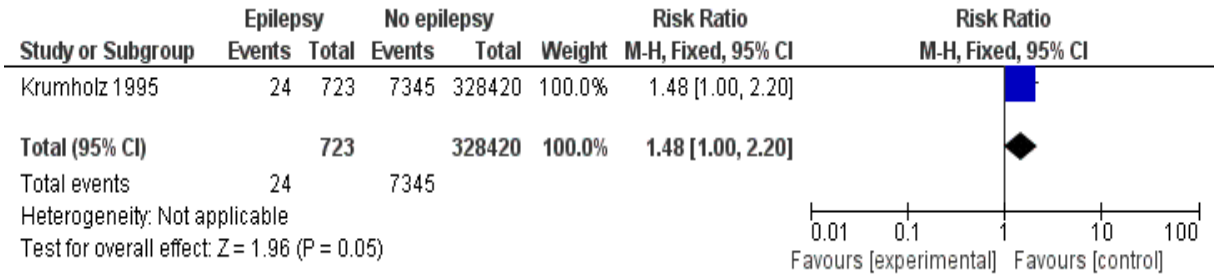
1. MH "Blood Donors" OR TI "blood don*" OR AB "blood don*"OR MH "Blood Banks" OR TI "blood bank" OR TI "blood banks" OR AB "blood bank" OR AB "blood banks" OR TI "blood service*" OR AB "blood service*" OR TI "blood center*" OR TI "blood centre*" OR AB "blood center*" OR AB "blood centre*" OR TI "transfusion service*" OR AB "transfusion service*" OR TI "transfusion cent*" OR AB "transfusion cent*"
2. MH "Epilepsy+" OR TI "epilep*" OR AB "epilep*" OR TI "convuls*" OR AB "convuls*" OR MH "Seizures+" OR TI "seizure? " OR AB "seizure? " OR TI "fits" OR AB "fits" OR MH "Anticonvulsants"
3. MH "Risk Factors" OR TI "risk factor*" OR AB "risk factor*" OR MH "Risk Assessment" OR TI "deferral*" OR AB "deferral*" OR TI "referral*" OR AB "referral*" OR TI "inclusion*" OR AB

"inclusion*" OR TI "exclusion*" OR AB "exclusion*" OR MH "Patient Selection" OR TI "donor selection" OR AB "donor selection" OR TI "donation history" OR AB "donation history"

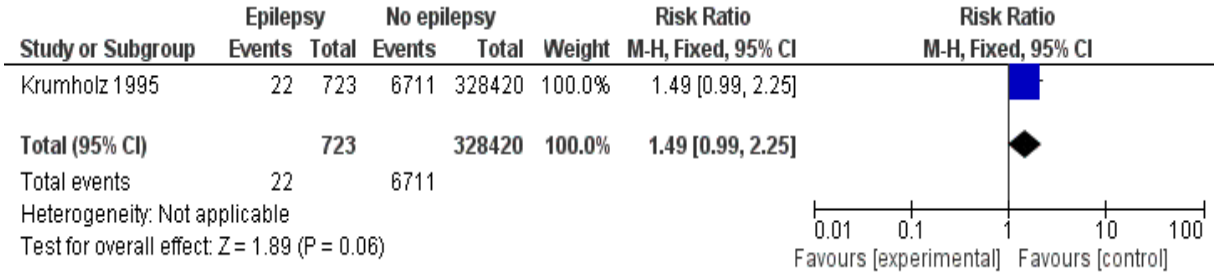
4. MH "Syncope+" OR TI "syncop*" OR AB "syncop*" OR TI "vasovagal" OR AB "vasovagal" OR TI "vaso vagal" OR AB "vaso vagal" OR MH "Unconsciousness" OR TI "unconscious*" OR AB "unconscious*" OR TI "conscious*" OR AB "conscious*" OR MH "Hypotension, Orthostatic" OR TI "collaps*" OR AB "collaps*" OR TI "faint*" OR AB "faint*" OR MH "bradycardia" OR TI "bradycardia" OR AB "bradycardia" OR MH "incontinence" OR TI "incontinence" OR AB "incontinence" OR MH "Sweating" OR TI "diaphoresis" OR AB "diaphoresis" OR TI "diaphoretic" OR AB "diaphoretic" OR TI "sweat" OR AB "sweat" OR TI "sweaty" OR AB "sweaty" OR AB "sweating" OR TI "sweating" OR MH "Dizziness" OR TI "dizzy" OR AB "dizzy" OR TI "dizziness" OR AB "dizziness" OR TI "lightheadedness" OR AB "lightheadedness" OR TI "light headedness" OR AB "light headedness" OR MH "Nausea and Vomiting" OR TI "nausea" OR AB "nausea" OR TI "nauseous" OR AB "nauseous" OR TI "vomit" OR AB "vomit" OR TI "vomiting" OR AB "vomiting" OR TI "vomited" OR AB "vomited" OR TI "weak" OR AB "weak" OR TI "weakened" OR AB "weakened" OR TI "weakness" OR AB "weakness" OR TI "pallor" OR AB "pallor" OR TI "side effect*" OR AB "side effect*" OR TI "adverse effect*" OR AB "adverse effect*" OR TI "adverse event*" OR AB "adverse event*" OR TI "reaction*" OR AB "reaction*" OR TI "complication*" OR AB "complication*" OR TI "incident" OR AB "incident" OR TI "incidents" OR AB "incidents" OR TI "safe" OR AB "safe" OR MH "Patient Safety" OR TI "safety" OR AB "safety"
5. 3 AND 4
6. 2 OR 5
7. 1 AND 6

Figure 6: Calculation of risk ratio and confidence intervals, based on the raw data provided by Krumholz et al. 1995.

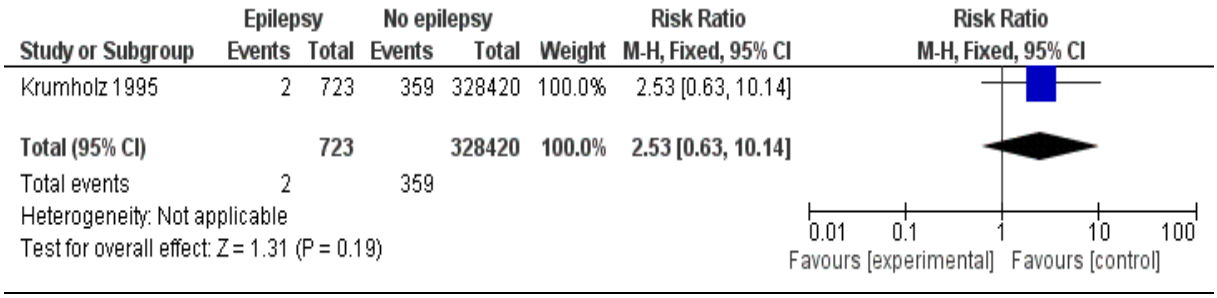
<u>All adverse events:</u>



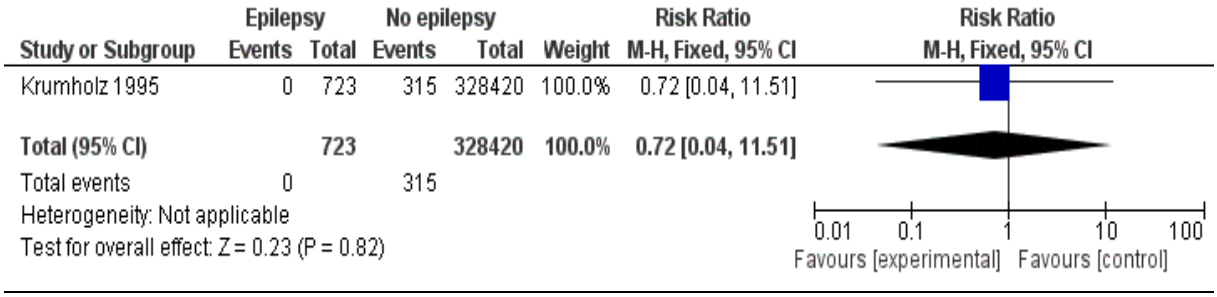
<u>Slight adverse events:</u>



Moderate adverse events:



Severe adverse events:



Moderate and severe events:

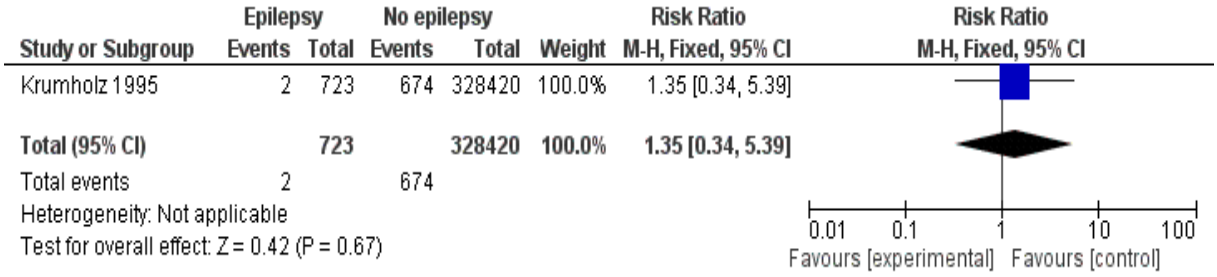


Table 1: List of the survey respondents.

Continent	Country	Respondent
Africa	South-Africa	Ravy Reddy
America	Canada	Graham Sher
	Honduras	Elizabeth Vinelli
	United States	Louis Katz
	United States	Richard Benjamin
Asia	Hong Kong	Wai Chiu Tsoi
	Israel	Eilat Shinar
	Japan	Kensyu Ketsueki
	South-Korea	So Yong Kwon
	Taiwan	Ming-Chang Lin
	Thailand	Ubonwon Charoonrouangrit
Europe	Austria	Wolfgang Mayr
	Belgium	Giovani Vandewalle
	Denmark	Jorgen Georgsen
	Estonia	Riin Kullaste
	Finland	Martti Syrjala

	France	Pierre Tiberghien
	Germany	Franz Weinauer
	Great-Britain	Lorna Williamson
	Italia	Giuliano Grazzini
	Ireland	Andy Kelly
	Latvia	Natalija Zlobina
	Malta	Alexander Aquilina
	Spain	Rosario Arrieta
	Sweden	Beatrice Diedrich
	The Netherlands	Wim De Kort
Oceania	Australia	Jennifer Williams

Table 2: Excluded studies based on the selection criteria, with the reason for exclusion.

Author	Year	Title	Type of exclusion	Reason for exclusion
Aarewatte P	2010	A study of donor deferal patterns at transfusion medicine unit Colombo South Teaching Hospital, Sri Lanka	outcome	no outcome
Abu BH	2009	Blood safety and deferred donors	population	deferred donors
Addas-Carvalho M	2010	Active haemovigilance: A efficient mechanism for identification of acute transfusion reactions (ATR) unreported	population	recipients
Alcantara R	2013	Whole blood donor return rates after a vasovagal reaction in Singapore	intervention	wrong intervention/risk factor
Allard S	2013	Blood transfusion	design	narrative review
Amorim LM	2014	Vasovagal adverse reactions in blood donors: A ten year experience in a single Brazilian Center	intervention	wrong intervention/risk factor
Amrein K	2012	Adverse events and safety issues in blood donation-A comprehensive review	design	narrative review
Anderlini P	2009	Donors, donors, and more donors	design	comment
Appalup M	2011	Reasons for absolute blood donors deferral in Moscow Blood Bank donors (Tsaritsino department) in 2010	population	deferred donors
Armstrong VA	2014	Quality in blood components-it all starts with the donation	population	no population
Bakdash S	2007	What every physician should know about transfusion reactions	population	narrative review
Behr-Gross ME	2013	[Contributions of the Council of Europe's Blood Transfusion Steering Committee to the determination of rules for the selection of donors of blood and blood components and the study of sexual behaviors having an impact on blood safety]	population	narrative review
Benjamin RJ	2010	Donor hemovigilance: Safety as the first priority of blood donor management	intervention	wrong intervention/risk factor
Bergmann H	1977	The risks of blood donation and blood transfusion for donor and recipient	design	narrative review
Bertrand O	2014	Relative blood volume: The best predictive factor associated to vasovagal blood donor reactions?	intervention	wrong intervention/risk factor
Bhardwaj K	2014	Adverse donor reactions in whole blood and blood component donors of a Tertiary Care Hospital of Punjab, India	intervention	wrong intervention/risk factor
Bhattacharya P	2010	Transfusion related adverse events at tertiary care center in north India: An institutional hemovigilance effort	intervention	wrong intervention/risk factor
Bhattacharya P	2011	Transfusion-related adverse events at the tertiary care center in North India: An institutional hemovigilance effort	intervention	wrong intervention/risk factor
Bischoff F	2014	Risk assessment process in transfusion medicine	population	no population
Bolton-Maggs PH	2013	Serious Hazards of Transfusion (SHOT) haemovigilance and progress is improving transfusion safety	design	narrative review

Bonig H	2011	Donor safety comes first	design	letter to the editor
Boonmawongsa N	2013	The prevalence of vasovagal reactions in blood donors at blood transfusion center, faculty of medicine, Khon Kaen university	intervention	wrong intervention/risk factor
Bravo M	2011	Factors associated with fainting: before, during and after whole blood donation	intervention	wrong intervention/risk factor
Bravo M	2011	Vasovagal reaction (VVR), outside medical care (OMC) and injury rates during/after whole blood (WB) and automated collections (AC)	intervention	wrong intervention/risk factor
Bujandric N	2014	Improving Blood Safety: Errors Management in Transfusion Medicine	intervention	wrong intervention/risk factor
Burkhardt T	2009	Establishment of an advanced system to register and compare side effects of whole blood and plasmapheresis donations	intervention	wrong intervention/risk factor
Burkhardt T	2012	Donor vigilance system in the german red cross blood transfusion service east	intervention	wrong intervention/risk factor
Burta OL	2011	Population study regarding the impact of blood donation eligibility and collected blood units validation, upon the transfusion self-sufficiency in different Romanian regions	intervention	wrong intervention/risk factor
Busby H	2012	Risk, safety and consent in blood services in the UK: Exploring the perspectives of patients, professionals and policy makers	population	recipients
Busch MP	1999	Oversight and monitoring of blood safety in the United States	design	narrative review
Campos MM	2009	Risk management in transfusion medicine-A Proactive Program	population	recipients
Carneiro-Proietti AB	2014	Transfusion adverse reactions and haemovigilance in a public general hospital in minas Gerais, Brazil	population	recipients
Carson JL	2012	Red Blood Cell Transfusion: A Clinical Practice Guideline From the AABB	design	guideline
Cesario E	2012	Potential adverse reactions associated with apheresis multicomponent (MAC) donors	intervention	wrong intervention/risk factor
Chawla SC	1994	Blood safety and rational use of blood	design	narrative review
Clifford P	2014	Allogeneic donor reactions in a large hospital-based donor center from 2012 through 2013	intervention	wrong intervention/risk factor
Condeco J	2014	Serious adverse reactions in portuguese blood donors (2011/12)	intervention	wrong intervention/risk factor
Cordell RR	1986	Experience with 11,916 designated donors	design	narrative review
Coutinho GF	2012	Adverse reactions during whole blood donation: A 12 years' experience from a single centre	intervention	wrong intervention/risk factor
Crocco A	2007	Adverse reactions during voluntary donation of blood and/or blood components. A statistical-epidemiological study	intervention	wrong intervention/risk factor
Crocco I	2009	Adverse reactions in blood and apheresis donors: experience from two Italian transfusion centres	intervention	wrong intervention/risk factor

Custer B	2005	Community blood supply model: development of a new model to assess the safety, sufficiency, and cost of the blood supply	design	narrative review
Custer B	2009	Associations between collection procedure type and donor adverse events	intervention	wrong intervention/risk factor
Custer B	2010	The impact of adverse reactions on future blood donation	intervention	wrong intervention/risk factor
Custer S	2011	Donor adverse events: Needle related injuries and vasovagal reactions are strongly associated	intervention	wrong intervention/risk factor
Damiano B	2012	Adverse reactions in apheresis multicomponent (MAC) donors: Percentage of risks	intervention	wrong intervention/risk factor
Danic B	2009	The contraindications in the blood donation. Impact of new rules	design	narrative review
Danic B	2010	Serious adverse effects of blood collection	design	narrative review
Danic B	2012	[Ensuring the safety of donated blood]	design	narrative review
Davey RJ	2004	Recruiting blood donors: Challenges and opportunities	design	comment
Despotis GJ	1999	Adverse events in platelet apheresis donors: A multivariate analysis in a hospital-based program	intervention	wrong intervention/risk factor
Dhidah K	2007	[Complications of blood donation in Morocco (during and immediately after the donation)]	intervention	wrong intervention/risk factor
Dhingra N	2006	Safety of blood transfusion at the international level. The role of WHO	design	narrative review
Diekamp U	1996	[Donor exclusions, discarded blood and transfusion unsuited blood conserves of 2,13 million potential blood donors 1991 to 1994]	intervention	wrong intervention/risk factor
Dinesh D	2011	The New Zealand national haemovigilance programme: The first step is the hardest	design	narrative review
Dinesh D	2012	The New Zealand haemovigilance system	intervention	wrong intervention/risk factor
Ditto B	1995	Family history of hypertension and vasovagal symptoms during blood donation	intervention	wrong intervention/risk factor
Dunbar N	2010	Implementation of height and weight criteria for young donors and impact on vasovagal reaction rates	intervention	wrong intervention/risk factor
Dunbar N	2010	Impact of donor height and weight criteria on young donor eligibility	intervention	wrong intervention/risk factor
Dunbar N	2011	The potential impact of new donor height and weight criteria on young donor eligibility and faint or prefaint reaction rates	intervention	wrong intervention/risk factor
Dzieciatkowska A	2011	Problems with identification of serious adverse events in the Polish blood transfusion service	intervention	wrong intervention/risk factor
Eder A	2010	Evidence-based selection criteria to protect blood donors	design	commentary
Eder A	2012	Can we improve safety for young blood donors?	intervention	wrong intervention/risk factor

Eder A	2012	Current efforts to reduce the risk of syncope among young blood donors	intervention	wrong intervention/risk factor
Eder A	2012	Do reactions after whole blood donation predict syncope on return donation?	intervention	wrong intervention/risk factor
Eder AF	2008	Adverse reactions to allogeneic whole blood donation by 16- and 17-year-olds	intervention	wrong intervention/risk factor
Eder AF	2008	The American Red Cross donor hemovigilance program: Complications of blood donation reported in 2006	intervention	wrong intervention/risk factor
Eder AF	2010	Improved safety for young whole blood donors with new selection criteria for total blood volume	intervention	wrong intervention/risk factor
Eder AF	2011	Improved safety for young whole blood donors with new selection criteria for total estimated blood volume	intervention	wrong intervention/risk factor
Epstein JS	2012	Best practices in regulation of blood and blood products	design	narrative review
Erraguntla M	2013	Multiple vasovagal reaction characterization	intervention	wrong intervention/risk factor
Erraguntla M	2014	Do reactions increase likelihood of vasovagal reaction in subsequent donation?	intervention	wrong intervention/risk factor
Escoval MA	2013	Improving donor safety-delayed donor adverse reactions	intervention	wrong intervention/risk factor
Fan W	2009	The eligible blood donor population in Canada	intervention	wrong intervention/risk factor
Fan W	2009	The eligible blood donor population in Canada	intervention	wrong intervention/risk factor
France CR	2008	Mitigating adverse reactions in youthful donors	design	editorial
Franchini M	2002	Frequency of adverse events during blood and apheresis donations: A single-center study	intervention	wrong intervention/risk factor
Fujii KE	2005	A pilot study on blood donors deferred for potential risk to blood safety	population	deferred donors
Fujii Y	2009	Three-year experience of a nationwide network of University Hospital Transfusion Services to investigate transfusion reactions in Japan	population	recipients
Gammon R	2009	Whole blood vs. automated donors, how do the reactions compare?	intervention	wrong intervention/risk factor
Garozzo G	2009	Adverse events of blood donation in 2386 first donors	intervention	wrong intervention/risk factor
Garozzo G	2009	Adverse reactions in 106,082 blood donations	intervention	wrong intervention/risk factor
Gavillet M	2013	Blood donation associated risks: data from a Swiss regional haemovigilance program	design	letter to the editor

Giovanni G	2010	Adverse events of blood donation in 2925 first donors	intervention	wrong intervention/risk factor
Giovanni G	2010	Adverse reactions in 120,468 blood donations	intervention	wrong intervention/risk factor
Giraud C	2002	[Blood donation]	design	narrative review
Goldman M	2013	Frequency and risk factors for donor reactions in an anonymous blood donor survey	intervention	wrong intervention/risk factor
Goldman M	2013	Donor hemovigilance	intervention	wrong intervention/risk factor
Goldman R	2012	Frequency and risk factors for donor reactions	intervention	wrong intervention/risk factor
Goncalez TT	2010	Adverse reactions in whole blood donors in Brazil	intervention	wrong intervention/risk factor
Goncalez TT	2012	Vasovagal reactions in whole blood donors at three REDS-II blood centers in Brazil	intervention	wrong intervention/risk factor
Grindon AJ	1982	Adverse reactions to whole blood donation and plasmapheresis	design	narrative review
Heery K	2010	Haemovigilance reporting in Ireland: 2000-2008	population	recipients
Hillyer CD	1994	Comparable safety of blood collection in 'high-risk' autologous donors versus non-high-risk autologous and directed donors in a hospital setting	intervention	wrong intervention/risk factor
Huestis DW	1989	Risks and safety practices in hemapheresis procedures	design	narrative review
Hume H	2012	Acute transfusion reactions in a university-affiliated hospital in sub-saharan Africa	intervention	wrong intervention/risk factor
Ilincic FL	2009	Our experience in transfusion reactions monitoring	population	recipients
Inaba S	2009	Predicting the occurrence of vasovagal reactions in blood donors: A questionnaire study by the Kanagawa Red Cross Blood Center	intervention	wrong intervention/risk factor
Inaba S	2013	Analysis of a questionnaire on adverse reactions to blood donation in Japan	intervention	wrong intervention/risk factor
Islam MA	2004	An analysis of the donor deferral pattern - A transfusion centre based study	outcome	no outcome
Jason CW	2010	Study of risk factors for vaso-vagal reaction amongst blood donors in Singapore	intervention	wrong intervention/risk factor
Jimenez-Marco T	2012	Donor hemovigilance: The usefulness of early post-donation information notification	population	deferred donors
Jones K	2011	Points of Care - A simple evidence based multidisciplinary donation pathway	intervention	wrong intervention/risk factor
Kamel H	2010	Delayed adverse reactions to blood donation	intervention	wrong intervention/risk factor

Kamel H	2010	Characteristics, prevalence and risk factors for adverse events in blood donors before venipuncture and during phlebotomy	intervention	wrong intervention/risk factor
Karim F	2014	Root cause analysis of non-infectious transfusion complications and the lessons learnt	population	recipients
Kasprisin DO	1992	Moderate and severe reactions in blood donors	intervention	wrong intervention/risk factor
Kleinman S	2013	The National Heart, Lung, and Blood Institute Recipient Epidemiology and Donor Evaluation Study (REDS-III): A research program striving to improve blood donor and transfusion recipient outcomes	design	narrative review
Kleinman S	2014	The National Heart, Lung, and Blood Institute Recipient Epidemiology and Donor Evaluation Study (REDS-III): A research program striving to improve blood donor and transfusion recipient outcomes	design	narrative review
Koistinen J	2004	[Blood transfusion safety]	other	not available
Konstantinidou A	2014	Analysis of adverse reactions in voluntary whole blood donors: Experience from a greek blood centre	intervention	wrong intervention/risk factor
Koppen A	2011	Analysis of donor adverse reactions after whole blood donation reported in the years 2005 to 2010	intervention	wrong intervention/risk factor
Krumholz A	1987	Blood Donation by Individuals with Epilepsy - Are Restrictions Necessary	outcome	no outcome
Krumholz A	1995	People with Epilepsy Are Safe Blood-Donors	other	not available
Krumholz A	1995	Regulations Restricting Blood Donations by People with Epilepsy Are Unwarranted	other	same as Krumholz 1995 'Adverse reactions in blood donors with a history of seizures or epilepsy'
Krumholz A	1997	Regulations prohibiting blood donation by individuals with seizures or epilepsy are not necessary	other	same as Krumholz 1995 'Adverse reactions in blood donors with a history of seizures or epilepsy'
Kwapisz MM	1998	[Risk factors and frequency of adverse effects after autologous blood donation]	intervention	wrong intervention/risk factor
Kyriazi V	2009	Overview of vasovagal reactions following whole blood donation: An experience from a single Greek blood bank	intervention	wrong intervention/risk factor
Langham J	2011	5 years of haemovigilance reporting to the designated UK competent authority: SABRE 2005-2010	population	no population
Lin CK	2013	Current issues in donor health and safety	intervention	wrong intervention/risk factor
Lin CL	2013	A retrospective study of adverse reactions and impact on subsequent behavior in blood donors: Contributory role of age, gender, weight, donor status and collection sites	intervention	wrong intervention/risk factor

Lin JT	1982	Convulsive syncope in blood donors	intervention	wrong intervention/risk factor
Lopez-Perez-Lancac JC	1996	Value of drug plasmatic levels in blood donors	design	narrative review
Loslier M	2004	[Current transfusion safety]	design	narrative review
Lower J	1994	[The safety of blood and blood products]	design	narrative review
Majlessi F	2008	Systemic complications and their risk factors among Tehranian blood donor, 2005	intervention	wrong intervention/risk factor
Marijt-van der Kreek T	2012	Risk factors for vasovagal reactions in a cohort of first-time donors	intervention	wrong intervention/risk factor
Masser B	2012	Experienced donors, adverse events, and retention	design	narrative review
Matsuzaki KM	2012	Investigation of delayed adverse reactions	intervention	wrong intervention/risk factor
McLeod BC	1998	Frequency of immediate adverse effects associated with apheresis donation	intervention	wrong intervention/risk factor
McLeod BC	1999	Frequency of immediate adverse effects associated with therapeutic apheresis	intervention	wrong intervention/risk factor
McVay PA	1990	Donation reactions among autologous donors	intervention	wrong intervention/risk factor
Mehra R	2014	A retrospective study of adverse events in blood donors from MGM Hospital, Kamothe	intervention	wrong intervention/risk factor
Michaelis G	1996	Quality management in autologous hemotherapy - Risks of autologous blood donations	intervention	wrong intervention/risk factor
Misso SM	2011	Prevalence of exclusion criteria for donation in a real-word centre for transfusion medicine	intervention	wrong intervention/risk factor
Momiroska T	2009	Unwanted reactions on volonteri blood donors our experience	intervention	wrong intervention/risk factor
Munasinghe SR	2011	Use of donor deferral evaluation for optimizing recruitment of blood donors	outcome	no outcome
Muylle L	2013	Donor vigilance in Belgium	intervention	wrong intervention/risk factor
Nakajima K	2009	Donor complication and donor care -vasovagal reaction and preventive measures	intervention	wrong intervention/risk factor
Nazli S	2013	Donor adverse reactions in Saudi blood donors	intervention	wrong intervention/risk factor
Newman B	2012	Syncope after whole blood donation: factors associated with increased donor injury	design	letter to the editor

Newman BH	2002	Vasovagal reactions in high school students: findings relative to race, risk factor synergism, female sex, and non-high school participants	intervention	wrong intervention/risk factor
Newman BH	2003	Vasovagal reaction rates and body weight: findings in high- and low-risk populations	intervention	wrong intervention/risk factor
Ortakovska S	2010	Unwilling reactions during blood donation	intervention	wrong intervention/risk factor
Pena C	2014	Nursing activity in management of adverse reactions during blood donation	intervention	wrong intervention/risk factor
Philip J	2014	A single-centre study of vasovagal reaction in blood donors: Influence of age, sex, donation status, weight, total blood volume and volume of blood collected	intervention	wrong intervention/risk factor
Popov R	2010	Adverse reactions during and after whole blood donation	intervention	wrong intervention/risk factor
Popov R	2012	Prognosing the risk of developing side effects in blood donation	other	not available
Popovsky MA	2002	Vasovagal donor reactions: an important issue with implications for the blood supply	design	editorial
Raj T	2013	One year experience after implementation of donor vigilance system at university hospital, Jeddah	intervention	wrong intervention/risk factor
Rauscher S	1986	Syncope and Convulsive Syncope in Blood-Donors	intervention	wrong intervention/risk factor
Rebibo D	2007	Haemovigilance donors: Methods and results	design	narrative review
Rios JA	2010	The potential impact of selective donor deferrals based on estimated blood volume on vasovagal reactions and donor deferral rates	intervention	wrong intervention/risk factor
Roddy SM	1983	Venipuncture fits: A form of reflex anoxic seizure	intervention	wrong intervention/risk factor
Rohra DK	2010	Prevalence of immediate vasovagal reaction in blood donors visiting two blood banks of Karachi	intervention	wrong intervention/risk factor
Rosiek A	2013	Identification and reporting of adverse transfusion reactions in Poland	intervention	wrong intervention/risk factor
Rupasena IP	2013	Adverse reactions during voluntary donation of whole blood-first time donors verses regular donors within 1 year experience	intervention	wrong intervention/risk factor
Sala CN	2014	Incidence and predictive features for systemic reactions during and after whole blood donation in Castilla y Leon, Spain	intervention	wrong intervention/risk factor
Samarajiwa G	2010	Audit of donor adverse events in Southern region of Sri Lanka	intervention	wrong intervention/risk factor
Sarlija D	2013	Croatian haemovigilance report 2011	intervention	wrong intervention/risk factor
Schottstedt V	2001	About safety of blood products today - Experiences from more than 800.000 blood donations per year	design	editorial

Shehata N	2004	Reaction rates in allogeneic donors	intervention	wrong intervention/risk factor
Silvergleid AJ	1992	Donor screening	design	narrative review
Sorensen BS	2008	Complications related to blood donation: A population-based study	intervention	wrong intervention/risk factor
Stichtenoth DO	2001	Blood donors on medication. Are deferral periods necessary?	design	narrative review
Stichtenoth DO	2002	Blood donors on medication: Are deferral periods necessary?	design	narrative review
Strauss RG	2002	Rationale for medical director acceptance or rejection of allogeneic plateletpheresis donors with underlying medical disorders	intervention	wrong intervention/risk factor
Symvoulakis EK	2008	Adverse reactions to blood donation among adolescents	design	letter to the editor
Szelei-Stevens K	2006	Reactions to blood donation in Caucasian teenagers	design	letter to the editor
Takanashi M	2010	Complications following voluntary blood donations at The Japanese Red Cross Tokyo Blood Centre	intervention	wrong intervention/risk factor
Takanashi M	2012	Risk factor analysis of vasovagal reaction from blood donation	intervention	wrong intervention/risk factor
Tawfik H	2009	Blood safety and deferred donors	population	deferred donors
Tomasulo A	2010	Blood donor loss-of-consciousness VVS: Duration and magnitude of risk	intervention	wrong intervention/risk factor
Tomasulo P	2009	Faint and prefaint reactions in whole blood donors: Predictive value of pre-donation measurements	intervention	wrong intervention/risk factor
Tomasulo P	2009	Faint and pre-faint reactions in whole blood donors: predictive value of pre-donation measurements	other	presentation
Tomasulo P	2010	Time course of vasovagal syncope with whole blood donation	other	presentation
Tomasulo P	2014	Do we select donors thinking especially about donor welfare? Are more efforts needed to protect donor health?	intervention	wrong intervention/risk factor
Tomasulo PA	1980	A study of criteria for blood donor deferral	intervention	wrong intervention/risk factor
Tomonko M	2006	Principles and national regulations of blood donor qualification	design	narrative review
Tondon R	2008	Vasovagal reactions in 'at risk' donors: a univariate analysis of effect of age and weight on the grade of donor reactions	intervention	wrong intervention/risk factor
Trouern-Trend JJ	1999	A case-controlled multicenter study of vasovagal reactions in blood donors: influence of sex, age, donation status, weight, blood pressure, and pulse	intervention	wrong intervention/risk factor

Vanderlinden GJ	1984	Blood Donation, A Risk for Persons with Epilepsy	design	opinion piece
Vanderlinden GJ	1986	Blood donation, a risk for epileptic patients?	design	opinion piece
Vasiljevic JB	2013	Transfusion adverse reactions and events in Serbia-first results of mandatory reporting	intervention	wrong intervention/risk factor
Veldhuizen I	2012	Irons status and vasovagal reactions in non-deferred whole blood donors	intervention	wrong intervention/risk factor
Vrielink H	2014	Side effects of blood donation by apheresis	intervention	wrong intervention/risk factor
Waiswa MK	2014	Acute transfusion reactions at a national referral hospital in Uganda: a prospective study	intervention	wrong intervention/risk factor
Wenk RE	1988	Whose blood is safe?	design	comment
Wiersum-Osselton JC	2012	Donor vigilance: what are we doing about it?	design	narrative review
Wiersum-Osselton JC	2013	Plasmapheresis in healthy donors in the Netherlands: cohort study of risk factors for donor complications	intervention	wrong intervention/risk factor
Wiersum-Osselton JC	2014	Risk factors for complications in donors at first and repeat whole blood donation: a cohort study with assessment of the impact on donor return	intervention	wrong intervention/risk factor
Wiltbank TB	2008	Faint and prefaint reactions in whole-blood donors: an analysis of predonation measurements and their predictive value	intervention	wrong intervention/risk factor
Wong HK	2012	Vasovagal reaction among young first-time donors:Prediction by body dimension and reduction and less collection	intervention	wrong intervention/risk factor
Yuan S	2008	Risk factors for acute, moderate to severe donor reactions associated with multicomponent apheresis collections	intervention	wrong intervention/risk factor
Yuan S	2010	Moderate and severe adverse events associated with apheresis donations: incidences and risk factors	intervention	wrong intervention/risk factor
Zervou EK	2005	Vasovagal reactions in blood donors during or immediately after blood donation	intervention	wrong intervention/risk factor
Ziegler DK	1978	Convulsive syncope: relationship to cerebral ischemia	design	narrative review

Table 3: Synthesis of the study characteristics of the included studies.

Author, year, country	Study design	Population	Risk factor	Remarks
Krumholz, 1988, USA	**Observational**: case series	314 blood donations in a 9-month period 297 blood donors with a history of seizures in Maryland - 24% is taking antiepileptic drugs - 11% has had at least 1 seizure in the past year	History of epilepsy/ seizures	Adverse events were defined as follows: Slight adverse events: dizziness and nausea without loss of consciousness Moderate adverse events: syncope Severe adverse events: convulsive syncope
Krumholz, 1995, USA	**Observational**: cohort study	329143 blood donations in a 2-year period 328420 blood donations by a donor without a history of epilepsy/seizures 723 blood donations by 613 donors with a history of epilepsy/seizures in Maryland - Males: 297 (48.5%) - Females: 316 (51.5%) - Active seizures: 61 (8.4%) - Taking antiepileptic drugs: 186 (25.7%) - First-time donors: 185 (25.6%)	Epilepsy/ seizure patients vs. non-epilepsy patients	Adverse events were defined as follows: Slight adverse events: shock-like symptoms such as pallor, dizziness, and nausea without unconsciousness Moderate adverse events: a progression of symptoms associated with a slight reaction to unconsciousness (syncope) Severe adverse events: unconsciousness accompanied by convulsions (convulsive syncope) The blood donors with a history of epilepsy/seizures were actively recruited; this effort was supported by the American Red Cross by allowing a policy variance for these patients. There was a physician in attendance for all blood donors with a history of seizures/epilepsy. An informed consent was obtained from all blood donors with

				a history of seizures/epilepsy. There was a higher number of first-time blood donors in the group of blood donors with a history of seizures/epilepsy (25.6%) compared to the group of blood donors without a history of seizures/epilepsy (11.4%); first-time blood donors have a significantly higher incidence of adverse reactions than veteran donors (4.4% vs. 1.5%; p<0.01).
Illies, 2000, Germany	**Observational**: case series	26 autologous blood donors with a history of refractory epilepsy in a 2-year period - Symptomatic: 15 (57.7%) - Idiopathic: 11 (42.3%) - Males: 9 - Females: 17 - Taking antiepileptic drugs: 25 *	History of epilepsy/ seizures	Each patient was examined by a neurologist prior to blood donation. Depending on body weight, the volume of blood taken varied from 300 to 520 ml.

Table 4: Synthesis of the study findings of the included studies.

Outcome	Risk factor	Effect Size	#studies, # participants	Ref
Donor adverse events - Slight - Moderate - Severe	History of epilepsy/seizures	4.10% (all adverse events) † 3.50% (slight adverse events) † 0.60% (moderate adverse events) † 0.00% (severe adverse events) †	1, n=297	Krumholz, 1988
	Epilepsy/seizure patients vs. non-epilepsy patients (any form)	Not statistically significant: All adverse events: 24/723 vs. 7345/328420 RR: 1.48, 95%CI [1.00;2.20] (p=0.05) *¥ Slight adverse events: 22/723 vs. 6711/328420	1, n=723 vs. 328420	Krumholz, 1995

		RR: 1.49, 95%CI [0.99;2.25] (p=0.06) *¥ <u>Moderate adverse events:</u> 2/723 vs. 359/328420 RR: 2.53, 95%CI [0.63;10.14] (p=0.19) *¥ <u>Severe adverse events:</u> 0/723 vs. 315/328420 RR: 0.72, 95%CI [0.04;11.51] (p=0.82) *¥ <u>Moderate or severe adverse events:</u> 2/723 vs. 674/328420 RR: 1.35, 95%CI [0.34;5.39]; (p=0.67) *¥		
Symptoms of confusion, convulsive attacks, petit mal seizures, or any reaction	History of epilepsy/seizures	0.00% †	1, n=26	Illies, 2000

8. Addenda

Addendum 1:

Uw aanvraag werd goedgekeurd door uw promotor en doorgestuurd naar de opleidingsspecifieke begeleidingscommissie.

Met vriendelijke groeten,

Philippe Vandekerckhove

Addendum 2:

Beste student,
Dear student,

Uw aanvraag werd aanvaard door de ethische commissie van het UZ Leuven. Dit wil zeggen dat de ethische commissie van oordeel is dat uw studie volgens de gangbare ethische normen wordt uitgevoerd. Indien u van plan bent uw masterproef te publiceren kan u deze mail als bewijs van goedkeuring door een ethische commissie aan het betreffende tijdschrift doorgeven.

Your application was accepted by the Ethics Committee of the University Hospitals Leuven. This means that the Ethics Committee acknowledges that your study is carried out according to the prevailing ethical standards.
If you plan to publish your masterthesis, you can use this mail as approval by the ethics committee.

Met vriendelijke groeten,

An Stockmans

Addendum 3:

Zie volgende pagina.

mp04974	Epilepsy and blood donation: 1) Is blood of epilepsy patients safe and effective for blood donation? A systematic review. 2) Worldwide policies on epilepsy and blood donation.

○ GOEDGEKEURD - ○ AFGEKEURD

Student(en):
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Promotor:
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Emmy De Buck (Emmy.DeBuck@kuleuven.be - u0040859 - Acad. Centr. voor Huisartsgeneeskunde)
Faculteit:
Geneeskunde
Opleiding:
Master in de huisartsgeneeskunde (Leuven e.a.)
Het onderzoek is:
monocentrisch
De opdrachtgever is:
academisch (universiteit,...)

Het onderzoek is:
Overige.

Bijkomende gegevens:

Achtergrond:

Patiënten met epilepsie worden uitgesloten van bloeddonatie. Bij de Dienst voor het Bloed van Rode Kruis-Vlaanderen kunnen ze opnieuw bloed geven in het geval ze drie jaar aanvals- en therapievrij zijn. Een onderdeel van het strategisch plan van Rode Kruis-Vlaanderen is om alle activiteiten evidence-based te onderbouwen, zo ook de uitsluitingscriteria in de medische vragenlijst, die gehanteerd worden om risico's in te schatten bij potentiële bloeddonoren.

Vraagstelling:

-Wat is de policy wereldwijd omtrent uitsluiting van epilepsiepatiënten als bloeddonor?

-Is er een hoger risico op een nieuwe epileptische aanval bij bloeddonoren die eerder al stuipen hebben gehad, in vergelijking met bloeddonoren die nooit eerder een epileptische aanval hadden?

Methodologie:

-Opstellen van een vragenlijst om te polsen naar de policy wereldwijd omtrent uitsluiting van epilepsiepatiënten als bloeddonor.

-Ontwikkeling systematische review volgens de methode van de Cochrane

KU LEUVEN
Biomedische Wetenschappen
Ethische begeleiding masterproeven

Collaboration.

Referenties:

Bijlage protocol:

Survey

1. Do you
   accept patients with epilepsy for blood donation, assuming that all other requirements for blood d onation are fulfilled?
   - o They are permanently accepted (question 1,2,3,4,5,8,9).
   - o They are temporarily excluded (question 1,2,3,4,5,6,7,8,9).
   - o They are permanently excluded (question 1,2).

2. Why do you accept/refuse patients with epilepsy as blood donors?
   - o Law.
   - o Internal regulations.
   - o Expert consensus/personal opinion/preference.
   - o Ethical concerns.
   - o Other reasons.

3. In those countries/states/blood transfusion services where epilepsy patients are accepted as blood donors, either permanently or after temporarily exclusion: Do epilepsy patients need more guidance (e.g. clinical/technical investigations, follow-up before/during/after the donation, etc.) by a physician than healthy individuals during blood donation? If so, does this extra care need to be given by the treating physician or the physician from the blood donation centre?
   - o Yes, they need more guidance. This extra care has to be given by the treating physician before or after the donation.
   - o Yes, they need more guidance. This extra care has to be given by the physician from the blood donation centre during the donation.
   - o No, they don't need more guidance.

4. In those countries/states/blood transfusion services where epilepsy patients are accepted as blood donors, either permanently or after temporarily exclusion: Are there any differences in the frequency of blood donations compared to healthy individuals?
   - o Yes, there is a lower frequency of blood donations in epilepsy patients compared to healthy individuals.
   - o Yes, there is a higher frequency of blood donations in epilepsy patients compared to healthy individuals.
   - o No, there is no difference in the frequency of blood donation in epilepsy patients compared to healthy individuals.

5. In those countries/states/blood transfusion services where epilepsy patients are accepted as blood donors, either permanently or after temporarily exclusion: Are there any extra laboratory tests done afterwards (e.g. to detect levels of anticonvulsants in blood samples)?
   - o Yes, there are any extra laboratory tests done. Please specify.
   - o No, there are no extra laboratory tests done.

6. In those countries/states/blood transfusion services where epilepsy patients are temporarily excluded from blood donation: How long do they have to be medication-free before they can donate blood?
   - o 6 months.
   - o 1 year.
   - o 3 years.
   - o 5 years.
   - o Other. Please specify.
   - o This is not a reason for temporarily exclusion.

7. In those countries/states/blood transfusion services where epilepsy patients are temporarily excluded from blood donation: How long do they have to be seizure-free before they can donate blood?

- 6 months.
- 1 year.
- 3 years.
- 5 years.
- Other. Please specify.
- This is not a reason for temporarily exclusion.

8. In those countries/states/blood transfusion services where epilepsy patients are permanently, or after temporarily exclusion, accepted as blood donors: Is there a difference in the amount of blood that epilepsy patients can donate in comparison to a an otherwise healthy donor?
   - Epilepsy patients can donate less blood.
   - Epilepsy patients can donate the same amount of blood.

9. In those countries/states/blood transfusion services where epilepsy patients are accepted as blood donors, either permanently or after temporarily exclusion: Are syncopes during or right after blood donation more frequent in blood donors with a history of epilepsy compared to an otherwise healthy donor?
   - Yes, syncopes are more frequent in epilepsy patients who are permanently accepted as blood donors.
   - Yes, syncopes are more frequent in epilepsy patients who are temporarily excluded as blood donors.
   - No, they are not more frequent.

Zoekstrategie

PubMed

1. "Blood Donors"[Mesh] OR blood don*[TIAB] OR "Blood Banks"[Mesh] OR blood bank*[TIAB] OR blood service*[TIAB] OR blood center*[TIAB] OR blood centre*[TIAB] OR transfusion service*[TIAB] OR transfusion cent*[TIAB]
2. "Epilepsy"[Mesh] OR epilep*[TIAB] OR seizure*[TIAB] OR convuls*[TIAB] OR "Anticonvulsants"[Mesh] OR fits[TIAB]
3. "Risk" [Mesh:NoExp] OR "Risk Factors"[Mesh] OR risk factor*[TIAB] OR "Risk Assessment" [Mesh:NoExp] OR deferral*[TIAB] OR referral*[TIAB] OR inclusion*[TIAB] OR exclusion*[TIAB] OR "Donor Selection" [Mesh] OR donation history[TIAB]
4. "Syncope"[Mesh] OR syncop*[TIAB] OR vasovagal[TIAB] OR vaso vagal[TIAB] OR "Unconsciousness"[Mesh:NoExp] OR unconscious*[TIAB] OR conscious*[TIAB] OR "Hypotension, Orthostatic"[Mesh] OR collaps*[TIAB] OR faint*[TIAB] OR "Bradycardia"[Mesh] OR bradycardia[TIAB] OR "Urinary Incontinence"[Mesh:NoExp] OR incontinence[TIAB] OR "Sweating"[Mesh] OR diaphoresis[TIAB] OR diaphoretic[TIAB] OR sweat[TIAB] OR sweaty[TIAB] OR sweating[TIAB] OR "Dizziness"[Mesh] OR dizzy[TIAB] OR dizziness[TIAB] OR light headedness[TIAB] OR lightheadedness[TIAB] OR "Nausea"[Mesh:NoExp] OR nausea[TIAB] OR nauseous[TIAB] OR vomit[TIAB] OR vomiting[TIAB] OR vomited[TIAB] OR weak[TIAB] OR weakened[TIAB] OR weakness[TIAB] OR "Pallor"[Mesh] OR pallor[TIAB] OR side effect*[TIAB] OR adverse event*[TIAB] OR adverse effect*[TIAB] OR reaction*[TIAB] OR complication*[TIAB] OR incident[TIAB] OR incidents[TIAB] OR "Safety"[Mesh:NoExp] OR safe[TIAB] OR safety[TIAB]
5. 3 AND 4
6. 2 OR 5
7. 1 AND 6

Embase

1. 'blood donor'/exp OR (blood NEXT/1 don*):ti,ab OR 'blood bank'/exp OR 'blood bank':ti,ab OR 'blood banks':ti,ab OR (blood NEXT/1 service*):ti,ab OR (blood NEXT/1 (center* OR centre*)):ti,ab OR (transfusion NEXT/1 service*):ti,ab OR (transfusion NEXT/1 cent*):ti,ab
2. 'convulsion'/exp OR convuls*:ti,ab OR 'epilepsy'/exp OR epilep*:ti,ab OR 'pseudoepileptic seizure'/exp OR 'seizure'/exp OR seizure*:ti,ab OR 'seizure susceptibility'/exp OR fits:ti,ab OR 'anticonvulsive agent'/exp
3. 'Risk'/de OR 'Risk Factor'/exp OR (risk NEXT/1 factor*):ti,ab OR 'Risk Assessment'/exp OR deferral*:ti,ab OR referral*:ti,ab OR inclusion*:ti,ab OR exclusion*:ti,ab OR 'Donor Selection'/exp OR 'donation history':ti,ab
4. 'Presyncope'/exp OR syncop*:ti,ab OR vasovagal:ti,ab OR 'vaso vagal':ti,ab OR 'Unconsciousness'/de OR unconscious*:ti,ab OR conscious*:ti,ab OR 'Orthostatic Hypotension'/exp OR 'orthostatic hypotension':ti,ab OR collaps*:ti,ab OR faint*:ti,ab OR 'Bradycardia'/de OR bradycardia:ti,ab OR 'Incontinence'/exp OR incontinence:ti,ab OR 'Sweating'/exp OR diaphoresis:ti,ab OR diaphoretic:ti,ab OR sweat:ti,ab OR sweaty:ti,ab OR sweating:ti,ab OR 'Dizziness'/exp OR dizzy:ti,ab OR dizziness:ti,ab OR 'light headedness':ti,ab OR lightheadedness:ti,ab OR 'Nausea'/exp OR nausea:ti,ab OR nauseous:ti,ab OR 'Vomiting'/exp OR vomit:ti,ab OR vomiting:ti,ab OR vomited:ti,ab OR weak:ti,ab OR weakened:ti,ab OR weakness:ti,ab OR 'Pallor'/exp OR pallor:ti,ab OR 'Side Effect'/de OR (side NEXT/1 effect*):ti,ab OR (adverse NEXT/1 event*) OR (adverse NEXT/1 effect*):ti,ab OR reaction*:ti,ab OR complication*:ti,ab OR incident:ti,ab OR incidents:ti,ab OR 'Safety'/de OR safe:ti,ab OR safety:ti,ab
5. 3 AND 4
6. 2 OR 5
7. 1 AND 6

Cochrane Database

1. [mh "Blood Donors"] OR ("blood don*"):ti,ab,kw OR [mh "Blood Banks"] OR ("blood bank"):ti,ab,kw OR ("blood banks"):ti,ab,kw OR ("blood service*"):ti,ab,kw OR ("blood center*"):ti,ab,kw OR ("blood centre*"):ti,ab,kw OR ("transfusion service*"):ti,ab,kw OR ("transfusion cent*"):ti,ab,kw
2. [mh "Epilepsy"] OR (epilep*):ti,ab,kw OR (convuls*):ti,ab,kw OR (seizure?):ti,ab,kw OR [mh "Anticonvulsants"] OR (fits):ti,ab,kw
3. [mh ^"Risk"] OR [mh "Risk Factors"] OR ("risk factor*"):ti,ab,kw OR [mh "Risk Assessment"] OR (deferral*):ti,ab,kw OR (referral*):ti,ab,kw OR (inclusion*):ti,ab,kw OR (exclusion*):ti,ab,kw OR [mh "Donor Selection"] OR ("donation history"):ti,ab,kw
4. [mh "Syncope"] OR (syncop*):ti,ab,kw OR (vasovagal):ti,ab,kw OR ("vaso vagal"):ti,ab,kw OR [mh ^"Unconsciousness"] OR (unconscious*):ti,ab,kw OR (conscious*):ti,ab,kw OR [mh "Hypotension, Orthostatic"] OR (collaps*):ti,ab,kw OR (faint*):ti,ab,kw OR [mh "Bradycardia"] OR (bradycardia):ti,ab,kw OR [mh ^"Urinary Incontinence"] OR (incontinence):ti,ab,kw OR [mh "Sweating"] OR (diaphoresis):ti,ab,kw OR (diaphoretic):ti,ab,kw OR (sweat):ti,ab,kw OR (sweaty):ti,ab,kw OR (sweating):ti,ab,kw OR [mh "Dizziness"] OR (dizzy):ti,ab,kw OR (dizziness):ti,ab,kw OR ("light headedness"):ti,ab,kw OR (lightheadedness):ti,ab,kw OR [mh ^"Nausea"] OR (nausea):ti,ab,kw OR (nauseous):ti,ab,kw OR (vomit):ti,ab,kw OR (vomiting):ti,ab,kw OR (vomited):ti,ab,kw OR (weak):ti,ab,kw OR (weakened):ti,ab,kw OR (weakness):ti,ab,kw OR [mh "Pallor"] OR (pallor):ti,ab,kw OR ("side effect*"):ti,ab,kw OR ("adverse effect*"):ti,ab,kw OR ("adverse event*"):ti,ab,kw OR (reaction*):ti,ab,kw OR (complication*):ti,ab,kw OR (incident):ti,ab,kw OR (incidents):ti,ab,kw OR [mh ^"Safety"] OR (safe):ti,ab,kw OR (safety):ti,ab,kw
5. 3 AND 4
6. 2 OR 5
7. 1 AND 6

Web of Science

1. TS=("blood don*") OR TS=("blood bank") OR TS=("blood banks") OR TS=("blood service*") OR TS=("blood center*") OR TS=("blood centre*") OR TS=("transfusion service*") OR TS=("transfusion cent*")
2. TS=("epilep*") OR TS=("convuls*") OR TS=("seizure? ") OR TS=("fits") OR TS=("anticonvulsants")
3. TS=("risk") OR TS=("deferral*") OR TS=("referral*") OR TS=("inclusion*") OR TS=("exclusion*") OR TS=("donor selection") OR TS=("donation history")
4. TS=("syncop*") OR TS=("vasovagal") OR TS=("vaso vagal") OR TS=("unconscious*") OR TS=("conscious*") OR TS=("orthostatic hypotension") OR TS=("collaps*") OR TS=("faint*") OR TS=("bradycardia") OR TS=("incontinence") OR TS=("sweat") OR TS=("sweaty") OR TS=("sweating") OR TS=("diaphoresis") OR TS=("diaphoretic") OR TS=("dizzy") OR TS=("dizziness") OR TS=("lightheadedness") OR TS=("light headedness") OR TS=("nausea") OR TS=("nauseous") OR TS=("vomit") OR TS=("vomiting") OR TS=("vomited") OR TS=("weak") OR TS=("weakened") OR TS=("weakness") OR TS=("pallor") OR TS=("side effect*") OR TS=("adverse effect*") OR TS=("adverse event*") OR TS=("reaction*") OR TS=("complication*") OR TS=("incident") OR TS=("incidents") OR TS=("safe") OR TS=("safety")
5. 3 AND 4
6. 2 OR 5
7. 1 AND 6

Cinahl

1. MH "Blood Donors" OR TI "blood don*" OR AB "blood don*"OR MH "Blood Banks" OR TI "blood bank" OR TI "blood banks" OR AB "blood bank" OR AB "blood banks" OR TI "blood service*" OR AB "blood service*" OR TI "blood center*" OR TI "blood centre*" OR AB "blood center*" OR AB "blood centre*" OR TI "transfusion service*" OR AB "transfusion service*" OR TI "transfusion cent*" OR AB "transfusion cent*"
2. MH "Epilepsy+" OR TI "epilep*" OR AB "epilep*" OR TI "convuls*" OR AB "convuls*" OR MH "Seizures+" OR TI "seizure? " OR AB "seizure? " OR TI "fits" OR AB "fits" OR MH "Anticonvulsants"
3. MH "Risk Factors" OR TI "risk factor*" OR AB "risk factor*" OR MH "Risk Assessment" OR TI "deferral*" OR AB "deferral*" OR TI "referral*" OR AB "referral*" OR TI "inclusion*" OR AB "inclusion*" OR TI "exclusion*" OR AB "exclusion*" OR MH "Patient Selection" OR TI "donor selection" OR AB "donor selection" OR TI "donation history" OR AB "donation history"
4. MH "Syncope+" OR TI "syncop*" OR AB "syncop*" OR TI "vasovagal" OR AB "vasovagal" OR TI "vaso vagal" OR AB "vaso vagal" OR MH "Unconsciousness" OR TI "unconscious*" OR AB "unconscious*" OR TI "conscious*" OR AB "conscious*" OR MH "Hypotension, Orthostatic" OR TI "collaps*" OR AB "collaps*" OR TI "faint*" OR AB "faint*" OR MH "bradycardia" OR TI "bradycardia" OR AB "bradycardia" OR MH "incontinence" OR TI "incontinence" OR AB "incontinence" OR MH "Sweating" OR TI "diaphoresis" OR AB "diaphoresis" OR TI "diaphoretic" OR AB "diaphoretic" OR TI "sweat" OR AB "sweat" OR TI "sweaty" OR AB "sweaty" OR AB "sweating" OR TI "sweating" OR MH "Dizziness" OR TI "dizzy" OR AB "dizzy" OR TI "dizziness" OR AB "dizziness" OR TI "lightheadedness" OR AB "lightheadedness" OR TI "light headedness" OR AB "light headedness" OR MH "Nausea and Vomiting" OR TI "nausea" OR AB "nausea" OR TI "nauseous" OR AB "nauseous" OR TI "vomit" OR AB "vomit" OR TI "vomiting" OR AB "vomiting" OR TI "vomited" OR AB "vomited" OR TI "weak" OR AB "weak" OR TI "weakened" OR AB "weakened" OR TI "weakness" OR AB "weakness" OR TI "pallor" OR AB "pallor" OR TI "side effect*" OR AB "side effect*" OR TI "adverse effect*" OR AB "adverse effect*" OR TI "adverse event*" OR AB "adverse event*" OR TI "reaction*" OR AB "reaction*" OR TI "complication*" OR

AB "complication*" OR TI "incident" OR AB "incident" OR TI "incidents" OR AB "incidents" OR TI "safe" OR AB "safe" OR MH "Patient Safety" OR TI "safety" OR AB "safety"

5. 3 AND 4
6. 2 OR 5
7. 1 AND 6