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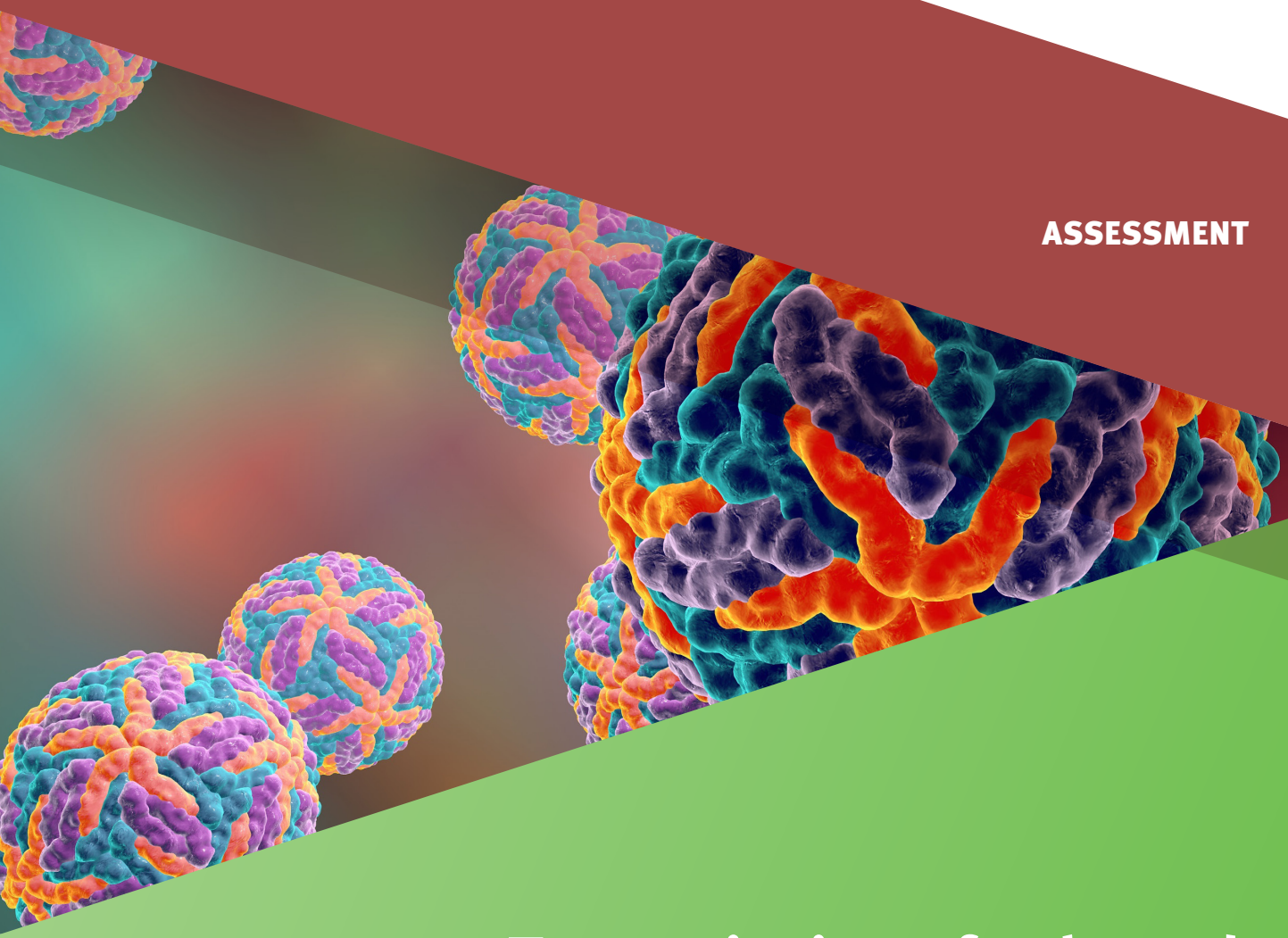

ASSESSMENT

Transmission of selected arboviruses through substances of human origin (SoHO)

A scoping review

ECDC ASSESSMENT

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A scoping review

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Abbreviations

CCHFV	Crimean-Congo haemorrhagic fever virus
CHIKV	Chikungunya virus
CRYO	Cryoprecipitate
CSF	Cerebrospinal fluid
DENV	Dengue virus
ECDC	European Centre for Disease Prevention and Control
ELISA	Enzyme-linked immunosorbent assay
EU/EEA	European Union/European Economic Area
FFP	Fresh Frozen Plasma
HSC	Haematopoietic Stem Cells
HSCT	Hematopoietic stem cell transplantation
ID NAT	Individual-donation nucleic acid testing
IFA	Immunofluorescence Assay
IgG	Immunoglobulin G
IgM	Immunoglobulin M
MAC-ELISA	Immunoglobulin M antibody capture enzyme-linked immunosorbent assay
MP-NAT	Minipool nucleic acid testing
NAT	Nucleic acid testing
PRNT	Plaque Reduction Neutralisation Test
PRISMA-ScR	Preferred Reporting Items for Systematic Reviews and Meta-Analyses Scoping Reviews
RBCs	Red Blood Cells
RNA	Ribonucleic acid
RT-PCR	Reverse transcription polymerase chain reaction
SCD	Sickle cell disease
SoHO	Substances of human origin
USUV	Usutu virus
WNV	West Nile Virus
ZIKV	Zika virus

Key findings

- In this scoping review, covering publications from January 2000 to June 2025, probable or certain transmission cases of arbovirus through substances of human origin (SoHO) were identified for West Nile virus (WNV), dengue virus (DENV) and Zika virus (ZIKV). However no transmission cases were identified for chikungunya virus (CHIKV), Usutu virus (USUV), or Crimean-Congo haemorrhagic fever virus (CCHFV).
- The review identified 77 documented cases of probable or confirmed arbovirus transmission through SoHO for WNV (47 cases), DENV (26 cases) and ZIKV (four cases).
- For WNV, forty-five cases of transmission through transfusion of blood components (platelets, red blood cells, plasma and granulocytes) were identified, along with one transmission case through haemtopoietic stem cell transplantation, and one transmission case through breastfeeding.
- For DENV, 23 transmission cases were identified through transfusion of blood components (platelets, red blood cells and plasma), two transmission cases through haemtopoietic stem cell transplantation, and one transmission case through breastfeeding.
- For ZIKV three transmission cases were identified through transfusion of blood components (platelets) and one transmission case through breastfeeding.
- There were no reports of transmission through SoHO for three of the six arboviruses considered in this review: chikungunya virus (CHIKV), Usutu virus (USUV) and Crimean-Congo haemorrhagic fever virus (CCHFV).

Introduction

Arboviruses are primarily ribonucleic acid (RNA) viruses transmitted by arthropods such as mosquitoes, ticks, and sandflies. There are hundreds of different reported arboviral diseases around the world, many of which are zoonoses and are known to cause significant morbidity in humans [1]. Human infections caused by arboviruses can result in a wide spectrum of clinical outcomes, from no symptoms or mild flu-like illness, to severe and potentially fatal haemorrhagic or neurological syndromes. Severe disease manifestations due to arbovirus infection could also lead to long-term complications [2].

The reporting of emerging arboviruses in parts of the European region, such as West Nile virus (WNV), Usutu virus (USUV), Dengue virus (DENV) and Crimean-Congo Haemorrhagic virus (CCHFV) has increased over the past decade [3]. Historically, emerging arboviruses have primarily been limited to tropical and subtropical areas. The epidemiology of arboviruses in Europe differs by virus. While the increasing transmission of WNV since the 1990s reflects complex ecological and environmental dynamics, the more recent emergence of locally-acquired dengue in Europe has been strongly influenced by the introduction and spread of invasive *Aedes* mosquitoes, together with imported cases and favourable climatic conditions. Locally-acquired transmission is now reported with increasing frequency for several arboviruses in Europe, raising concerns about further establishment in parts of the region [4-6].

Even though the major infection route of arboviruses is associated with vector transmission, pathogens could also be transmitted through non-vectorial transmission routes, such as exposure to substances of human origin (SoHO), for example, through the transfusion of blood and blood components or organ transplantation [7,8]. However, evidence regarding the risk of transmission of arboviruses via SoHO remains limited. Given the increasing frequency of locally-acquired cases in Europe and their potential impact on SoHO safety, a comprehensive overview of the transmission of relevant arboviruses through SoHO is needed.

This scoping review aims to evaluate the characteristics of transmission cases through SoHO with probable or certain imputability for six arboviruses. These six arboviruses (WNV, USUV, DENV, Chikungunya virus (CHIKV), Zika virus (ZIKV), and CCHFV) were chosen because they are of high importance for SoHO safety in the European Union/European Economic Area (EU/EEA) due to the increasing frequency of locally-acquired cases in the region. While cases of ZIKV remain rare in Europe, the potential impact of an infection on the foetus during pregnancy was considered relevant for the safety of medically assisted reproduction. The scoping review was performed using information reported in literature for the period from January 2000 to June 2025, as it represents a period of increasing arbovirus infections acquired within the EU/EEA.

The results of this scoping review are intended to support the development of ECDC guidelines on the prevention of arbovirus transmission through SoHO[1]. These guidelines are developed in support of Regulation (EU) 2024/1938 on standards of quality and safety for substances of human origin intended for human application (SoHO Regulation)[2].

[1] https://www.ecdc.europa.eu/en/topics-z/related-public-health-topics/substances-human-origin/technical-guidelines-prevention
[2] https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=OJ:L_202401938

Methods

This scoping review was conducted in accordance with the Joanna Briggs Institute (JBI) approach [9], and reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Scoping Reviews (PRISMA-ScR) extension checklist [10] to address the following review question:

> 'What are the characteristics of probable or certain transmission cases of six selected arboviruses (WNV, USUV, DENV, CHIKV, ZIKV, and CCHFV) through SoHO (excluding solid organ transplantations) reported in the literature between 2000 and 2025?'

Inclusion criteria for considering studies

The following inclusion and exclusion criteria were used to assess the eligibility of the identified studies:

- **Concept:** characteristics of probable or certain transmission cases of WNV, USUV, DENV, CHIKV, ZIKV, and CCHFV through SoHO. Eligible SoHO types relevant for this review are blood and blood components; tissues and non-reproductive cells; faecal microbiota; human breast milk; gametes or embryos for medically assisted reproduction. Human solid organs were not included as they are explicitly excluded from the SoHO Regulation. Cases of SoHO recipient infections unrelated to the SoHO application or cases where an infected donation was identified and discarded prior to application to the recipient are not of interest for this review.
- **Context:** global.
- **Study designs:** all epidemiological study designs, including case reports, case series, and observational studies. Reviews, clinical trials, modelling studies, opinion pieces, commentaries, and letters to the editor with no relevant data were excluded.
- **Publication status:** published peer-reviewed literature.
- **Timeframe:** from January 2000 to June 2025.
- **Language restriction:** no language restriction.

Search strategy for identifying studies

A comprehensive search of the literature was conducted from January 2000 to June 2025, using the following database resources:

- Published, peer-reviewed literature: Medline, EMBASE, LILACS.
- The reference list of included studies and reviews, excluded by title and abstract, was checked for relevant studies that were missing.
- Grey literature was not included.

The search strategy is presented in the annex.

Sources of evidence selection

After completing the search, all identified records were imported into EndNote for de-duplication and then imported into Rayyan [11]. A pilot screening of 100 titles and abstracts was independently conducted by two reviewers to assess the clarity of the inclusion and exclusion criteria and to suggest any required changes. Once the pilot phase was completed and a high level of agreement between the two reviewers was achieved (greater than 90%), the remaining titles and abstracts were screened by a single reviewer. Where insufficient information was available in the title and abstract, the full-text articles were screened in the subsequent stage. Studies meeting the inclusion criteria based on their title and abstract underwent full-text screening by two independent reviewers, and inter-rater agreement measures were calculated. Any disagreements were resolved by a third reviewer. The list of studies meeting the inclusion criteria upon full-text review was checked against relevant records in the Notify library (https://www.notifylibrary.org/) and reference lists of existing systematic reviews to ensure this list included all previously identified reports (e.g. [5,8]).

Data charting

Data extraction of the included studies was performed independently by two reviewers using a previously piloted data extraction template. Any disagreements were discussed or, if necessary, resolved by a third reviewer.

Extraction tables included: first author's name, year of publication, geographical area, study design, arbovirus, SoHO type and subtype, imputability grade, diagnostic test performed in the recipient(s) and donor(s) to confirm the infection, medical reason for SoHO application, reported outcomes for the recipient (mortality and morbidity – including clinical manifestations characteristics, if present) following the transmission, relevant recipient, donor and

donation characteristics (e.g. age, sex, co-morbidities, etc.), identification of the infection in the donor (e.g. selective screening, look-back procure, etc.), the interval between infection and transmission, route of transmission in the donor, viraemia around time of donation, and any processing of the donation (e.g. leucoreduction, sterilisation, storage, etc.). The imputability grade provided in the report was extracted to include only transmission cases where the imputability of a donor-derived transmission (i.e. that the transmission in the recipient was due to the use of SoHO from an infected donor) was graded as probable or certain. Possible cases were excluded. If no imputability grade was provided in the report, experts at the European Centre for Disease Prevention and Control (ECDC) performed the assessment based on available information in the report and based on the recommendations from the NOTIFY guide on Vigilance and Surveillance[3]. Where no imputability grade was provided in the report, only probable or certain transmission cases as assessed by ECDC were included. The studies included were not critically appraised as this was beyond the focus of a scoping review.

Analysis of evidence

The evidence was analysed through descriptive statistics and thematic grouping, summarising case frequencies by virus, SoHO type/subtype, transmission certainty, and recipient outcomes. Trends over time, donor-related factors, and procedural aspects were explored. SoHO types and subtypes relevant for this review are blood and blood components (subtypes: whole blood, red blood cells, platelets, plasma for transfusion, plasma for fractionation, including plasma derived medicinal products); tissues and non-reproductive cells (subtypes: ocular tissue, musculoskeletal tissue, cardiovascular tissue, skin, haematopoietic stem cells from peripheral blood, cord blood or bone marrow, foetal tissues); faecal microbiota; human breast milk (including transmission through breastfeeding, which was used as a proxy for donated milk from a milk bank) and gametes or embryos for medically assisted reproduction (subtype: sperm, oocytes, embryos).

Presentation of results

The findings from the included studies were presented using tables summarising study, donor and recipient characteristics, and bar charts showing case distribution by virus, SoHO type/subtype, and outcomes, and geographical maps of cases.

[3] https://www.notifylibrary.org/content/booklet-2018

Results

Source of evidence inclusion

A total of 6 078 hits were retrieved through the electronic database search. Of these, 1 285 were excluded as duplicates, resulting in 4 793 hits which underwent title and abstract screening. Of these, 4 613 hits were excluded based on their title and abstract, and therefore, 180 hits were assessed at the full-text stage. In total, 37 papers [12-48] were included in the scoping review (Figure 1) and 143 papers were excluded for not meeting the inclusion criteria, based on transmission not being through SoHO (this category includes transmission through solid organ transplantation) (47 papers); ineligible study design (four papers); imputability grade too low (six papers); no transmission reported (31 papers), ineligible publication types (e.g. review, letter [40 papers]), or duplicate data (preserving reports with most information on the transmission event; 15 papers) (Table 1).

Figure 1. PRISMA flow chart of selection process

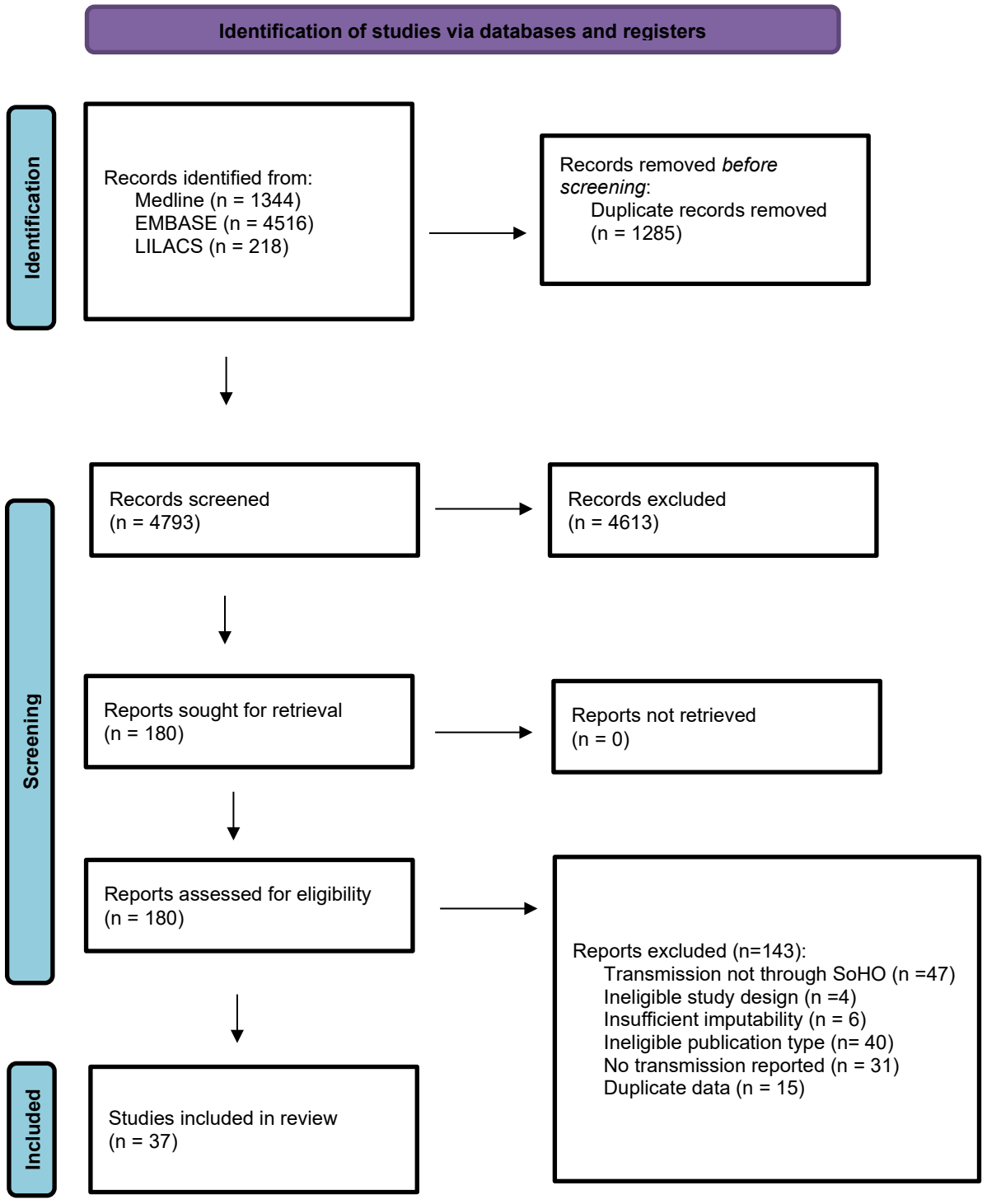


Table 1. Studies excluded at full text stage

Author, year	Reason for exclusion	Pathogen
Anonymous, 2004 [49]	Duplicate data	WNV
Ahmed, 2003 [50]	Transmission not through SoHO (vertical transmission)	DENV
Alallah, 2020 [51]	Transmission not through SoHO (vertical transmission)	DENV
Alen, 2023 [52]	Transmission not through SoHO (vertical transmission)	DENV
Almeida, 2025 [53]	Duplicate data	DENV
Anon, 2016 [54]	Ineligible publication type (review)	CHIKV,DENV, ZIKV
Araujo, 2017 [55]	Ineligible publication type (review)	WNV
Arya, 2014 [56]	Duplicate data	ZIKV
Azevedo, 2020 [57]	Transmission not through SoHO (sexual transmission)	DENV
Barroso, 2017 [58]	No transmission reported	ZIKV
Barzon, 2021 [59]	No transmission reported	DENV
Basurko, 2018 [60]	Transmission not through SoHO (vertical transmission)	DENV
Baud, 2017 [61]	Ineligible publication type (Review)	DENV
Besnard, 2014 [62]	Transmission not through SoHO (vertical transmission)	ZIKV
Bhattarai, 2023 [63]	No transmission reported	ZIKV
Bierlaire, 2017 [64]	Imputability grade too low	DENV
Blohm, 2017 [65]	No transmission reported	ZIKV
Breen, 2017 [66]	Imputability grade too low	ZIKV
Brenner, 2005 [67]	No transmission reported	WNV
Buathong, 2017 [68]	Not transmission reported	WNV
Centeno-Tablante, 2021 [69]	Ineligible publication type (review)	ZIKV
Cerdas Quesada, 2013 [70]	No transmission reported	WNV
Chancey, 2016 [71]	Ineligible study design (diagnostic)	ZIKV
Coli, 2024 [72]	Transmission not through SoHO	ZIKV
Colt, 2017 [73]	Ineligible publication type (review)	DENV
Cordeiro, 2017 [74]	Ineligible publication type (review)	ZIKV
Custer, 2014 [75]	Duplicate data	ZIKV
Custer, 2013 [76]	No transmission reported	DENV
Dedkov, 2017 [77]	Transmission not through SoHO (vertical transmission)	DENV
Desgraupes, 2021 [78]	Ineligible publication type (review)	CCHFV
Dodd, 2015 [79]	Ineligible publication type (review)	ZIKV
Dos Santos, 2016 [80]	Duplicate data	WNV
Dos Santos Bezerra, 2021 [81]	No transmission reported	ZIKV
Dupont-Rouzeyrol, 2016 [82]	Duplicate data	ZIKV
Dupont-Rouzeyrol, 2016 [83]	Insufficient imputability	ZIKV
Evans-Gilbert, 2020 [84]	No transmission reported	ZIKV
Faria, 2024 [85]	Transmission not through SoHO (vertical transmission)	CHIKV
Gallian, 2005 [86]	Ineligible publication type (review)	WNV
Gebre, 2016 [87]	Ineligible publication type (review)	ZIKV
Gimenez-Richarte, 2024 [88]	Ineligible publication type (review)	Arboviruses
Gimenez-Richarte, 2022 [8]	Ineligible publication type (review)	Arboviruses
Giovanetti, 2018 [89]	Transmission not through SoHO (vertical transmission)	ZIKV
Goldrick, 2003 [90]	Ineligible publication type (abstract only, no relevant data)	WNV
Goodnough, 2017 [91]	Ineligible publication type (review)	ZIKV
Gopakumar, 2012 [92]	Transmission not through SoHO (vertical transmission)	CHIKV

Author, year	Reason for exclusion	Pathogen
Gregory, 2017 [93]	Ineligible publication type (review)	ZIKV
Grischott, 2016 [94]	Ineligible publication type (review)	ZIKV
Guevara, 2018 [95]	Transmission not through SoHO (vertical transmission)	ZIKV
Guggenheim, 2024 [96]	Transmission not through SoHO	ZIKV
Gupta, 2016 [97]	Transmission not through SoHO	DENV
Hagmann, 2017 [98]	Ineligible publication type (Review)	ZIKV
Hayes, 2004 [99]	Ineligible publication type (Review)	CCHFV
Harxhi, 2005 [100]	Transmission not through SoHO (nosocomial transmission)	WNV
Hiatt, 2003 [101]	Imputability grade too low	WNV
Hinckley, 2007 [102]	Duplicate data	WNV
Hollinger, 2003 [103]	Ineligible publication type (review)	WNV
Inamdar, 2018 [104]	Transmission not through SoHO	DENV
Jain, 2019 [105]	Transmission not through SoHO (vertical transmission)	DENV
Jimenez, 2017 [106]	Ineligible publication type (review)	ZIKV
Joob, 2017 [107]	No transmission reported	ZIKV
Kalane, 2021 [108]	Transmission not through SoHO (vertical transmission)	DENV
Kaur, 2014 [109]	Transmission not through SoHO (vertical transmission)	DENV
Kelly, 2013 [110]	Duplicate data	WNV
Kumar, 2020 [111]	Transmission not through SoHO (vertical transmission)	DENV
Lee, 2020 [112]	Transmission not through SoHO	ZIKV
Levi, 2017 [113]	Ineligible publication type (review)	ZIKV
Liu, 2019 [114]	Ineligible publication type (review)	ZIKV
Machado, 2017 [115]	Transmission not through SoHO	CHIKV,DENV, ZIKV
Mann, 2018 [116]	Ineligible publication type (review)	ZIKV
Martin, 2004 [117]	Transmission not through SoHO	WNV
Matusali, 2018 [118]	No transmission reported	ZIKV
Mello, 2019 [119]	Imputability grade too low	ZIKV
Moayeri, 2011 [120]	Transmission not through SoHO (solid organ transplantation)	WNV
Mons, 2022 [121]	No transmission reported	DENV
Mounica, 2021 [122]	Transmission not through SoHO (vertical transmission)	DENV
Musso, 2016 [123]	Ineligible publication type (letter, no relevant data)	ZIKV
Musso, 2014 [124]	No transmission reported	ZIKV
Musso, 2016 [125]	No transmission reported	ZIKV
Joguet, 2016 [126]	No transmission reported	ZIKV
CDC, 2002e [127]	No transmission reported	WNV
American Society, 2005 [128]	Ineligible publication type (review)	WNV
CDC, 2002d [129]	Duplicate data	WNV
CDC, 2002f [130]	Duplicate data	WNV
CDC, 2002g [131]	Duplicate data	WNV
CDC, 2002b [132]	Duplicate data	WNV
CDC , 2002l [133]	Transmission not through SoHO (vertical transmission)	WNV
CDC, 2002i	Ineligible study design (Ongoing study)	WNV
NA , 2003 [134]	Transmission not through SoHO (vertical transmission)	WNV
CDC, 2004a [135]	Duplicate data	WNV
Nau, 2016 [136]	No transmission reported	ZIKV
Nemes, 2004 [137]	Transmission not through SoHO (occupational exposure)	DENV

Author, year	Reason for exclusion	Pathogen
Nguyen, 2021 [138]	Transmission not through SoHO (vertical transmission)	DENV
O'Leary, 2006 [139]	No transmission reported	WNV
Oliveira, 2018 [140]	Transmission not through SoHO (vertical transmission)	CHIKV
Pachauri, 2023 [141]	Transmission not through SoHO (vertical transmission)	DENV
Paisley, 2006 [142]	No transmission reported	WNV
Paz-Bailey, 2018 [143]	No transmission reported	ZIKV
Perez-Padilla, 2011 [144]	Transmission not through SoHO (vertical transmission)	DENV
Petersen, 2014 [145]	Ineligible study design (modelling study)	CHIKV
Pham, 2023 [146]	Transmission not through SoHO (vertical transmission)	DENV
Politis, 2014 [147]	Duplicate data	WNV
Pourahmad, 2011 [148]	Transmission not through SoHO (occupational exposure)	CCHFV
Pshenichnaya, 2016 [149]	Transmission not through SoHO (sexual transmission)	CCHFV
Razonable, 2009 [150]	Ineligible publication type (review)	Pathogen out of scope
Reddy, 2004 [151]	Imputability grade too low	WNV
Rico, 2016 [152]	No transmission reported	CHIKV,DENV
Rigau-Perez, 2001 [153]	No transmission reported	DENV
Rivadeneyra-Espinar, 2019 [154]	Transmission not through SoHO (vertical transmission)	ZIKV
Rivero Jimenez, 2016 [155]	Ineligible publication type (review)	DENV
Runge-Ranzinger, 2019 [156]	Ineligible publication type (review)	ZIKV
Ruth, 2017 [157]	Ineligible publication type (review)	ZIKV
Saa, 2017 [158]	Transmission not through SoHO	ZIKV
Sabino, 2013 [159]	No transmission reported	DENV
Sakkas, 2018 [160]	Ineligible publication type (review)	ZIKV
Salunke, 2018 [161]	Transmission not through SoHO (vertical transmission)	DENV
Sampieri, 2019 [162]	Ineligible publication type (review)	ZIKV
Sanjay, 2021 [163]	No transmission reported	DENV
Shahani, 2024 [164]	No transmission reported	DENV
Shaji, 2019 [165]	Ineligible publication type (letter, no relevant data)	DENV
Sharifov, 2025 [166]	No transmission reported	CCHFV
Sherley, 2018 [167]	Ineligible publication type (review)	ZIKV
Shrivastava, 2011 [168]	Transmission not through SoHO (vertical transmission)	CHIKV
Sotelo, 2017 [169]	No transmission reported	ZIKV
Stephens, 2018 [170]	Transmission not through SoHO (solid organ transplantation)	WNV
Stramer, 2010 [171]	Duplicate data	DENV
Stramer, 2013 [172]	No transmission reported	DENV
Stramer, 2007 [173]	Ineligible study design (implementation study)	WNV
Tan, 2024 [174]	Ineligible publication type (review)	DENV
Thokala, 2020 [175]	Ineligible publication type (review)	CHIKV,DENV, ZIKV
Traineau, 2009 [176]	Ineligible publication type (review)	CHIKV, WNV, ZIKV
Turmel, 2016 [177]	Transmission not through SoHO (sexual transmission)	ZIKV
Unlusoy-Aksu, 2014 [178]	No transmission reported	CCHFV
Vieira, 2019 [179]	Transmission not through SoHO (vertical transmission)	ZIKV
Villamil-Gomez, 2017 [180]	Transmission not through SoHO (vertical transmission)	ZIKV
Waechter, 2020 [181]	Transmission not through SoHO (vertical transmission)	CHIKV
Williams, 2004 [182]	Ineligible publication type (letter, no relevant data)	WNV

Author, year	Reason for exclusion	Pathogen
Williamson, 2017 [183]	No transmission reported	ZIKV
Witayathawornwong, 2012 [184]	Transmission not through SoHO (vertical transmission)	DENV
Wiwanitkit, 2010 [185]	Ineligible publication type (review)	DENV
Wiwanitkit, 2009 [186]	Ineligible publication type (review)	DENV
Yan, 2022 [187]	Ineligible publication type (review)	DENV
Yang, 2015 [188]	Transmission not through SoHO (vertical transmission)	DENV
Yin, 2016 [189]	Transmission not through SoHO (vertical transmission)	DENV

Characteristics of included sources

Of the 37 studies [12-48] included in the review, three studies focused on ZIKV, 14 focused on DENV, and the remaining 20 studies focused on WNV (Table 2). The year of publication of the included studies ranged from 2001 to 2025, with peaks in 2003 and 2016 (Figure 2).

No studies were identified that included cases of transmission of CCHF, CHIKV, or USUV. None of the studies excluded for failing to meet the predefined inclusion criteria addressed these three pathogens. In addition, all relevant reviews identified during the screening process, and subsequently excluded based on the scoping review's eligibility criteria, were carefully examined to identify any potentially eligible studies on these viruses, however none were found.

Table 2. Characteristics of included evidence sources

Author, year	SoHO type/subtype	Pathogen
Barjas-Castro, 2016 [12]	Blood and blood components/platelets	ZIKV
Blohm, 2018 [13]	Human breast milk	ZIKV
Motta, 2016 [14]	Blood and blood components (two cases from the same donor)/platelets	ZIKV
Almeida, 2025 [46]	Blood and blood components/RBCs, platelets, FFP, CRYO	DENV
Alves, 2016 [45]	Blood and blood components/platelets	DENV
Barthel, 2013 [15]	Human breast milk	DENV
Chuang, 2008 [16]	Blood and blood component/RBCs	DENV
Karim, 2017 [17]	Blood and blood components (two cases, same donor)/platelet, FFP	DENV
Levi, 2015 [18]	Blood and blood components/platelets	DENV
Matos, 2016 [19]	Blood and blood components/platelets	DENV
Oh, 2015 [20]	Blood and blood components/plasma	DENV
Punzel, 2014 [21]	Tissues and non-reproductive cells/HSCs	DENV
Sabino, 2016 [22]	Blood and blood components (six cases from different donors)/plasma, platelets, RBCs	DENV
Santos, 2020 [23]	Blood and blood components/RBCs	DENV
Stramer, 2012 [24]	Blood and blood components/RBCs	DENV
Tambyah, 2008 [25]	Blood and blood components (three cases from the same donor)/ RBCs, plasma, platelets	DENV
Yadav, 2021 [44]	Tissues and non-reproductive cells/HSCs	DENV
Armstrong, 2003 [26]	Blood and blood components/leucocyte-reduced RBCs	WNV
De Oliveira, 2004 [27]	Blood and blood components/platelets	WNV
Groves, 2017 [28]	Blood and blood components/plasma	WNV
Harrington, 2003 [29]	Blood and blood components/FFP	WNV
Hayes, 2020 [30]	Blood and blood components/platelets	WNV
Hong, 2003 [31]	Blood and blood components/not specified	WNV
Iwamoto, 2003 [32]	Blood and blood components/not specified	WNV

Author, year	SoHO type/subtype	Pathogen
Kightlinger, 2007 [33]	Blood and blood components/packed RBCs	WNV
	Blood and blood components/FFP	WNV
Kitagawa, 2018 [34]	Tissues and non-reproductive cells/HSC	WNV
Meny, 2011 [35]	Blood and blood components/granulocyte	WNV
Montgomery, 2006 [36]	Blood and blood components/RBCs	WNV
CDC, 2013 [37]	Blood and blood components/platelets	WNV
CDC, 2009 [38]	Blood and blood components/packed RBCs	WNV
CDC, 2004b [47]	Blood and blood components/RBCs	WNV
CDC, 2002a [39]	Blood and blood components/RBCs, FFP, not specified	WNV
CDC, 2002c [40]	Blood and blood components/RBCs case 1; human breast milk case 2	WNV
CDC, 2002h [48]	Blood and blood components/not specified	WNV
Pealer, 2003 [41]	Blood and blood components/plasma, RBCs, platelets	WNV
Politis, 2022 [42]	Blood and blood components/platelets case 1, plasma case 2, RBCs case 3 and 4	WNV
Shepherd, 2004 [43]	Blood and blood components/plasma	WNV

CRYO: Cryoprecipitate; FFP: Fresh Frozen Plasma; HSC haematopoietic stem cells; RBCs: Red Blood Cells.

Figure 2. Number of publications by publication date

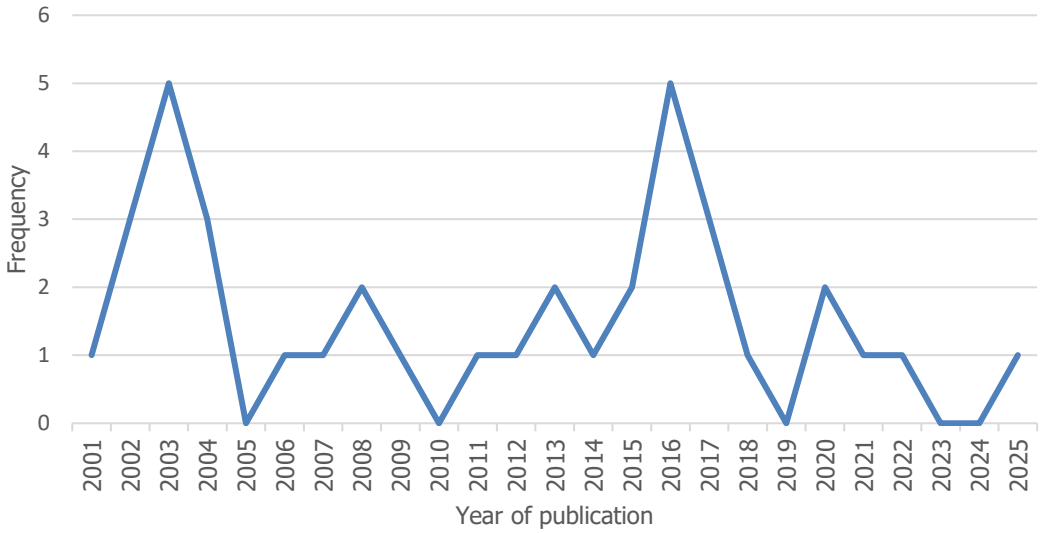


Figure 3 illustrates the number of included cases according to the year of publication of the related data, while Figure 4 shows the number of probable and certain transmission cases by pathogen. The geographical distribution of cases identified in this review, stratified by virus type, is presented in Figure 5 (data from Figure 3).

Figure 3. Number of cases reported by year of data publication and by pathogen

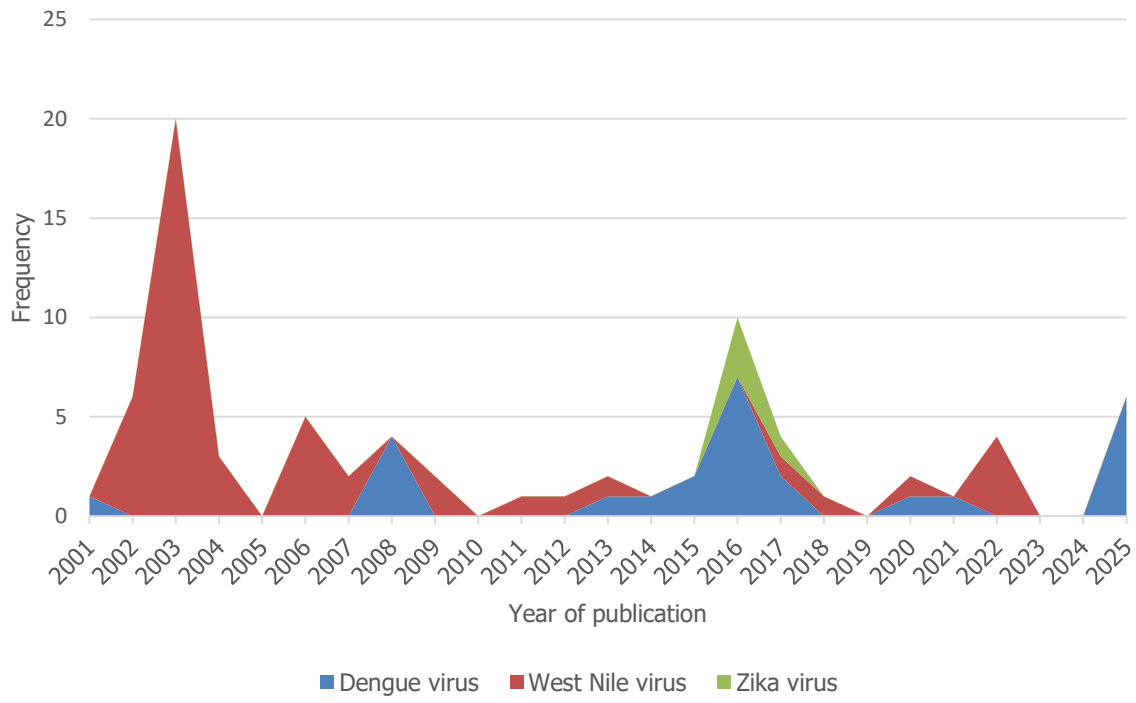
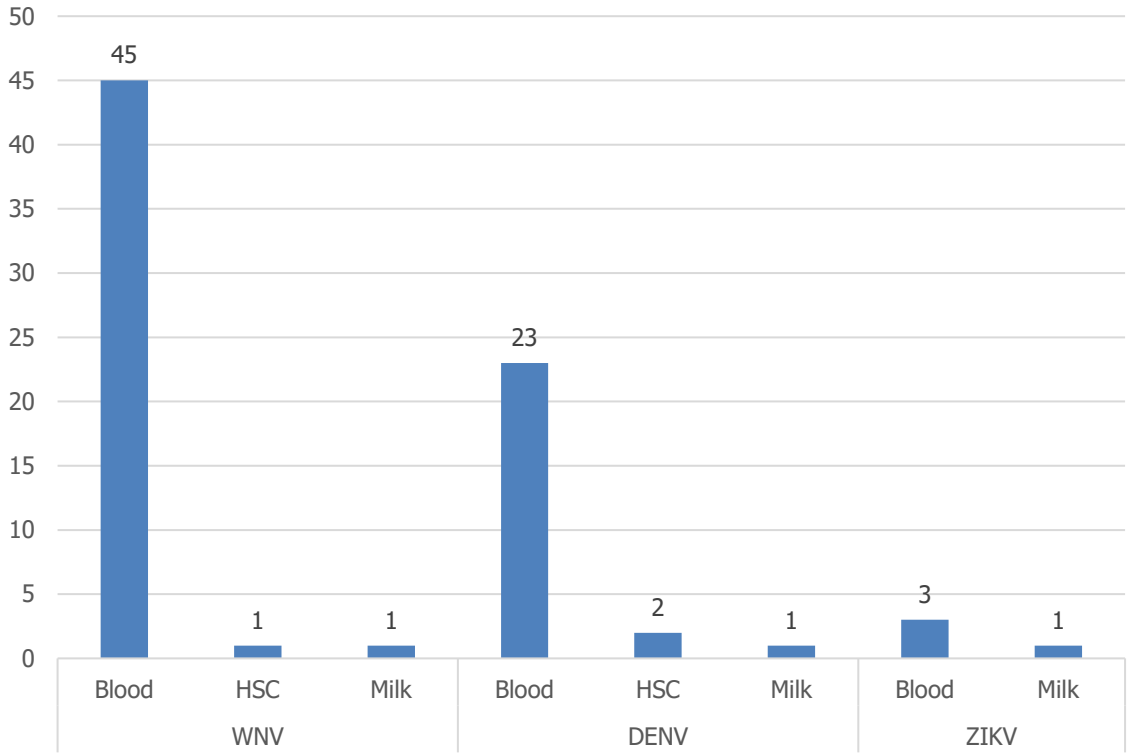


Figure 4. Reported cases of DENV, WNV, and ZIKV by SoHO type



HSC: Haematopoietic Stem Cells; Milk: Human Breast Milk.

Zika virus (ZIKV)

Of the three studies which focused on transmission of ZIKV through SoHO, two studies focused on blood and blood components and one study focused on human breast milk (Table 3).

Table 3. Characteristics of studies assessing transmission through SoHO of Zika Virus

Author, year	SoHO type/subtype	Recipient outcome	Author imputability	Country
Barjas-Castro, 2016 [12]	Blood and blood components (platelets)	Survived	Probable	Brazil
Blohm, 2018 [13]	Human breast milk	Survived	Probable	Venezuela
Motta, 2016 [14]	Blood and blood components (same donor) (platelets)	Survived	Certain	Brazil
	Blood and blood components (same donor) (platelets)	Survived	Certain	Brazil

Blood and blood components

The two studies [12,14] reporting on ZIKV transmissions through blood and blood components included transmission cases resulting from transfusion of platelets. Details of each study are reported below.

Bajas-Castro, 2016

Bajas-Castro, 2016 [12] report a probable transfusion-transmission case of ZIKV in Brazil, where a 54-year-old male donor self-reported a febrile illness three days after platelet concentrate donation. The illness started two days after donation, and was suspected to be due to DENV infection. Four days after donation, serology and molecular laboratory results excluded DENV infection, however, stored samples from the donation were positive for ZIKV on RNA Nucleic Acid Test (NAT). The recipient was a 55-year-old male who had undergone an orthotopic liver transplant and received platelet concentrate from the infected donor after transplantation. In the recipient, although laboratory investigation results were negative for DENV immunoglobulin M (IgM) antibodies, results were positive for hemagglutination-inhibiting antibodies against flavivirus in two samples collected four and 18 days after transfusion. Sequencing confirmed ZIKV in the donor and recipient samples, and a high degree of sequence homology between the two was confirmed. Therefore, the recipient had probably been transfused with an infected blood component during the incubation period after ZIKV infection but before clinical disease onset. This event occurred in a region where there was no ZIKV outbreak and the authors consider this a probable transfusion-transmission case.

Motta, 2016

The Motta 2016 [14] study reported on two certain transfusion-transmission cases from Brazil, where a donor self-reported a three-day history of retro-orbital and bilateral knee pain to the blood bank. The pain started two days after the donation of platelets by apheresis. The donated platelets were irradiated with 25 Gy and transfused into two recipients (leucoreduction). Plasma samples from the donor obtained before (Day -3) and after (Day 11) donation were negative for CHIKV and DENV RNA NAT. Plasma was positive on Day -3 but negative on Day 11, and urine was positive on Day 11, for ZIKV. Acute ZIKV infection was confirmed in the donor by serological analysis on Day 11 (Plaque Reduction Neutralization Test (PRNT) positive, titre 1:1280, Indirect Immunofluorescence Assay (IFA) positive, IgM and immunoglobulin G [IgG] positive).

The first recipient was a 54-year-old woman with primary myelofibrosis syndrome, and the second recipient was a 14-year-old girl who had undergone a haploidentical bone marrow transplantation two weeks before platelet transfusion. Pre-transfusion samples for both recipients were negative for CHIKV, DENV and ZIKV using molecular assays. Samples were then re-tested and the result was positive for ZIKV, six days post-transfusion in the first recipient and 23 and 51 days post-transfusion in the second recipient, before testing negative again on Day 31 and 71, respectively. Sequencing and phylogenetic analysis confirmed that ZIKV isolates from the donor and the two recipients were identical, with nucleotide changes in the envelope gene shared only by the donor and platelet recipients among available isolates from Brazil.

The close temporal relationship between the infection occurring shortly after ZIKV diagnosis in the donor and the phylogenetic identity of the recovered ZIKV isolates strongly supports transfusion as the source of infection. Serological findings were consistent with the molecular analyses. In the first recipient, all samples demonstrated antibody reactivity to DENV-2 using both IFA and IgG-capture enzyme-linked immunosorbent assay (ELISA), in line with the reported history of dengue infection prior to transfusion. Seroconversion to ZIKV was observed in both IFA IgG and point-of-care testing, with a PRNT titer of 1:2560 at Day +31.

In the second recipient, IFA reactivity emerged between 23 and 51 days post-transfusion, accompanied by a modest neutralising antibody response. The limited cross-reactivity to DENV-2 suggests ZIKV as the primary flavivirus infection. The attenuated antibody response in this patient was probably attributable to ongoing immunosuppressive therapy.

Although neither of the recipients reported symptoms consistent with ZIKV infection during the investigation, these findings provide evidence of ZIKV transmission through platelet transfusion.

Human breast milk

One study [13] focused on human breast milk as the type of SoHO involved in the transmission of ZIKV. No papers reporting transmission of ZIKV through donated milk were found. Details of the study are reported below.

Blohm, 2018

The study by Blohm, 2018 [13], conducted in Venezuela, described a probable transmission case of postnatal ZIKV from mother to child via breastfeeding. The 32-year-old mother experienced arthralgia and malaise for 10 days, with rash and conjunctival hyperaemia resolving four days after symptom onset. Breast milk, plasma, and urine samples were collected four days after symptom onset from the mother, and ZIKV RNA (NAT) was detected in urine. Serological testing demonstrated ZIKV-specific IgM with borderline IgG levels.

The plasma and urine samples of the five-month-old infant tested positive for ZIKV RNA; the child remained asymptomatic throughout follow-up. Although the precise source of infection cannot be definitively established, the virological and phylogenetic findings strongly support postnatal transmission during breastfeeding. The mother and child resided in an air-conditioned, screened home, minimising the likelihood of mosquito exposure. Neither had a recent travel history, and the infant spent most of the time indoors. Full-genome sequencing of ZIKV isolated from breast milk and the infant's urine demonstrated 99% nucleotide identity, differing by only two synonymous substitutions. Sequencing of the NS5 gene from additional specimens confirmed that identical viral strains were present in all samples from both mother and child. While transmission through breast milk cannot be established as certain, the authors consider it a probable transfusion-transmission case.

Dengue virus (DENV)

Of the 14 studies which reported transmission of DENV through SoHO, 11 included cases of transmission through blood and blood components, two through haematopoietic stem cells (HSCs), and one study through human breast milk (Table 4).

Table 4. Characteristics of studies assessing transmission through SoHO of dengue virus

Author, year	SoHO type/ subtype	Outcome recipient	Author imputability	Country
Almeida, 2025 [46]	Blood and blood components (RBCs, platelets, plasma)	Death	Probable	Brazil
	Blood and blood components (RBCs, platelets)	Survived	Probable	Brazil
	Blood and blood components (RBCs, platelets)	Survived	Probable	Brazil
	Blood and blood components (RBCs, platelets, plasma)	Death	Probable	Brazil
	Blood and blood components (RBCs, platelets, plasma)	Death	Probable	Brazil
	Blood and blood components (RBCs, platelets)	Death	Probable	Brazil
Alves, 2016 [45]	Blood and blood components (platelets)	Survived	Certain	Brazil
Barthel, 2013 [15]	Human breast milk	Survived	Probable	New Caledonia
Chuang, 2008 [16]	Blood and blood components (not specified)	Survived	Probable	Hong Kong

Author, year	SoHO type/ subtype	Outcome recipient	Author imputability	Country
Karim, 2017 [17]	Blood and blood components (case 1, same donor) (platelets)	Survived	Probable	Pakistan
	Blood and blood components (case 2, same donor) (plasma)	Survived	Probable	Pakistan
Levi, 2015 [18]	Blood and blood components (platelets)	Survived	Probable	Brazil
Matos, 2016 [19]	Blood and blood components (RBCs)	Survived	Probable	Puerto Rico
Oh, 2015 [20]	Blood and blood components (plasma)	Survived	Certain	Singapore
Punzel, 2014 [21]	Tissues and non-reproductive cells (HSCs)	Death	Certain	Germany
Sabino, 2016 [22]	Blood and blood components (different donors) (platelets)	Survived	Probable	Brazil
	Blood and blood components (different donors) (plasma)	Survived	Probable	Brazil
	Blood and blood components (different donors) (RBCs)	Survived	Probable	Brazil
	Blood and blood components (different donors) (RBCs)	Survived	Probable	Brazil
	Blood and blood components (different donors) (platelets)	Survived	Probable	Brazil
Santos, 2020 [23]	Blood and blood components (RBCs)	Survived	Certain	Brazil
Stramer, 2012 [24]	Blood and blood components (RBCs)	Survived	Certain	Puerto Rico
Tambyah, 2008 [25]	Blood and blood components (case 1 same donor) (RBCs)	Survived	Probable	Singapore
	Blood and blood components (case 2 same donor) (platelets)	Survived	Probable	Singapore
	Blood and blood components (case 3 same donor) (plasma)	Survived	Probable	Singapore
Yadav, 2021 [44]	Tissues and non-reproductive cells (HSCs)	Survived	Probable	India

Blood and blood components

A total of 11 publications focused on blood and blood components as the type of transmission through SoHO for DENV. Details of each study is reported below.

Almeida, 2025

The Almeida, 2025 letter [46] reported on six transfusion-transmission cases of DENV from infected blood, graded as probable by the authors but with very limited information. The specific infected blood subtype was not given as the donors were not screened before donation, and each recipient received several different components. Given the strict control measures in place against mosquito exposure in the hospital, transfusion-transmission of DENV was considered the most likely source of infection by the authors. Six paediatric recipients (age range from two months to 17 years, four females, two males) undergoing cardiac surgery received transfusions of blood/blood components from different blood donors (range 5–15 donors). All children developed clinical manifestations consistent with dengue: fever, leukopenia, thrombocytopenia, and liver damage. Four patients died, two of which can be considered as severe dengue cases. The number of days in hospital before the onset of dengue symptoms ranged from 11 to 52 days. The time between transfusion and clinical manifestations varied from one to five days, depending on the individual patient and the specific transfused component, as most patients received multiple transfusions of different components during hospitalisation (platelets, red blood cells (RBCs), pooled platelets, cryoprecipitate, FFP). Only one patient received a single type of component (five units of RBC). Dengue infection in the recipients was confirmed by positive NS1 antigen test and serology (IgM), following the onset of symptoms. Four recipients died, with clinical and laboratory findings consistent with severe dengue, including two recipients with acute liver failure. The two other recipients died from secondary bacterial sepsis.

Alves, 2016

The Alves, 2016 study [45] documented a transmission case of DENV through platelet transfusion graded as certain by the authors, based on clinical records and laboratory evidence. The report described a patient with lymphoblastic lymphoma who underwent autologous haematopoietic stem cell transplantation (HSCT). Following the procedure, the patient developed severe haemorrhagic symptoms accompanied by shock and serositis. Three days after receiving a platelet transfusion, the blood donor began to experience typical symptoms of dengue infection. This case is considered to be a severe case. Laboratory testing detected anti-DENV IgM antibodies in both donor and recipient samples. Nucleic acid testing further confirmed the presence of DENV RNA, with viral loads of 178,602 copies/mL in the donor and 8,491 copies/mL in the recipient. Transmission through platelet transfusion was verified by amplification and sequencing of the NS1 gene region. Phylogenetic analysis revealed that the viral sequences obtained from both the donor and the platelet recipient were identical within the analysed region, providing strong evidence that dengue virus transmission occurred through the platelet transfusion.

Chuang, 2008

In Chuang, 2008 [16], the medical records of all patients with laboratory-confirmed dengue admitted to public hospitals in Hong Kong from 1998 to 2005 were reviewed retrospectively.

The probable transfusion-transmission case reported in this study involved a 76-year-old woman with a history of hypertension and bronchiectasis. She was admitted to hospital in 2002 because of progressive malaise. Blood tests revealed macrocytic anaemia and pancytopenia. She was diagnosed with vitamin B12 deficiency anaemia, which was treated by vitamin B12 replacement and received a blood transfusion on 24 August 2002. On Day 2 post-transfusion, she developed low-grade fever, but no skin rash, headache, myalgia, arthralgia, or retro-orbital pain. The patient was treated with antibiotics for a urinary tract infection based on the microbiological findings. The fever subsided three days later and the patient recovered. The blood product she received (subtype not specified) was donated by a 17-year-old donor, asymptomatic at donation, living on the island of Ma Wan, Hong Kong. On 24 July 2002, he developed a generalised rash and attended the Accident and Emergency Department; in October, he was subsequently picked up through retrospective case finding as one of the dengue cases based on serology results during an active case-finding exercise in Ma Wan. RNA NAT performed on the donated blood product was positive for DENV-1. The woman who had received the blood transfusion was recalled for blood testing on 7 October 2002 and was positive for DENV IgM antibodies and had a haemagglutination-inhibition test titre of 1:2560.

Karim, 2017

The Karim, 2017 [17] study reports probable transfusion-transmission cases of DENV in two patients who received blood components from the same donor.

The two cases described illustrate a similar and unusual presentation of dengue in patients undergoing coronary artery bypass grafting, raising the possibility of transfusion-transmitted DENV infection.

A 73-year-old male and a 59-year-old male patient were admitted for evaluation and surgical management of coronary artery disease. Each patient received multiple blood components transfusions in the perioperative period. In both cases, a decline in platelet counts accompanied by the onset of fever was observed 8–9 days after surgery and transfusion, prompting further evaluation. DENV infection was confirmed in both patients by RNA NAT. Both patients had remained in closed hospital settings for several days prior to symptom onset, making mosquito-borne transmission unlikely. Given the temporal association between transfusion and the onset of symptoms, transfusion-transmission of DENV was suspected and reported to the blood bank.

All donors whose blood components had been transfused to the two patients were subsequently traced and contacted. One donor reported a history of high-grade fever beginning one day after blood donation on 16 September 2015, which persisted for one week and was associated with generalised body aches. The fever resolved with supportive care, and the donor was not tested for dengue infection at the time. It was later established that blood components from this donor had been transfused to both patients with suspected transfusion-transmitted DENV infection. The donor was recalled, and a blood sample collected on 8 October 2015 tested positive for anti-DENV IgM antibodies. DENV-specific IgM antibodies confirmed a recent dengue infection and suggested that the donor was in the incubation period at the time of donation. DENV RNA NAT could not be performed, as the donor was no longer in the acute viraemic phase. There was a very remote chance of the patients having been bitten by a mosquito. The fact that both patients shared a common donor who had a history of high-grade fever one day after donation and tested positive for dengue IgM strongly suggests that both patients had a probable transfusion-transmitted DENV infection.

Packed RBCs from the same donor were also transfused to an elderly female patient admitted with left middle cerebral artery infarction, intracranial haemorrhage, and upper gastrointestinal bleeding, who did not develop fever during hospitalisation. She remained afebrile throughout her hospital stay and was discharged without clinical evidence of dengue infection. Dengue testing was not performed on this patient, as she remained asymptomatic and was discharged before further evaluation could be undertaken.

Levi, 2015

In this study from Levi, 2015 [18], a regular plateletpheresis female donor notified the blood bank that she had been diagnosed with dengue a few days after donation, during a dengue outbreak in Brazil. On 14 April, at the time of donation, the donor tested negative for dengue IgM, IgG, and DENV RNA NAT (limit of detection: 350 copies/mL). However, a follow-up sample collected on 5 May demonstrated seroconversion, with both IgM and IgG testing positive while DENV RNA remained negative.

The donor had donated platelets on 14 April, with a negative screening test result, but was found to be IgG/IgM positive on follow-up. The epidemiologic investigation strongly supported a recent dengue infection, as multiple household members and neighbours were diagnosed with dengue during the same period. The donor resided in one of the most affected areas of a neighbouring city, further supporting community exposure.

Platelet components from this donation were transfused into two recipients. One recipient, a 56-year old man, considered to have a probable transfusion-transmission of DENV, developed clinical and laboratory evidence of dengue virus infection following transfusion. He had been hospitalised since 7 April, with no exposure to mosquito vectors. The transfusion was administered on 18 April, and he developed a high fever five days later (23 April). His pre-transfusion sample was negative for dengue IgG, IgM, and RNA. Post-transfusion testing showed a DENV RNA load of 872 100 copies/mL on 23 April, decreasing to 6 192 copies/mL on 30 April, confirming acute dengue virus infection acquired after transfusion.

Interestingly, the second platelet recipient remained asymptomatic and showed no laboratory evidence of dengue virus infection during follow-up.

Matos, 2016

In this Puerto Rico study by Matos, 2016 [19], investigators sought to determine whether patients who received blood units that were NS1-Ag–negative but RNA-positive subsequently developed post-transfusion dengue. Patients' medical records were reviewed, and recipients were followed through sample collection and interviews. This investigation identified three recipients who received blood from four DENV RNA–confirmed–positive donors. Of these only one case was recognised as a probable transfusion-transmission case of dengue virus.

The probable transfusion-transmission case involved a 75-year-old man with lung cancer and coronary heart disease who was hospitalised for symptomatic anaemia and transfused with three RBC units, one of which contained 7×10^7 copies/mL of DENV-4 RNA. Three days after transfusion, he developed fever. Blood and urine cultures were negative. Despite treatment with broad-spectrum antibiotics, he remained febrile for three days. Upon defervescence, he developed leukopenia, thrombocytopenia, melena, haematochezia, and severe plasma leakage, resulting in bilateral pleural and pericardial effusions, hypoalbuminemia, and shock. He required supportive care and was discharged after 15 days. His clinical presentation met the case-defining criteria for severe dengue haemorrhagic fever.

Oh, 2015

This work from Oh, 2015 [20] reports a transfusion-transmission case of dengue acquired through a blood transfusion in a patient in a Singaporean tertiary hospital during a dengue epidemic and considered as certain by the authors.

A 37-year-old woman with a medical history of diabetes mellitus, hypertension, and dyslipidaemia presented with signs consistent with hypertensive intracerebral haemorrhage. Ten days after admission, the patient presented with rectal bleeding due to a stercoral ulcer and haemorrhoids, accompanied by hypotension and a decline in haemoglobin. She was treated with underrunning of the rectal ulcer and transfusion of one RBC unit. Four days after the transfusion, she became febrile, while maintaining a normal platelet count. The fever persisted, and thrombocytopenia subsequently developed, with platelet counts falling two days later, prompting platelet transfusions given the recent gastrointestinal bleeding.

In the context of a national dengue epidemic, dengue serology was performed and demonstrated dengue IgM positivity with IgG negativity, consistent with a recent primary dengue virus infection. The patient did not meet the criteria for dengue haemorrhagic fever or dengue shock syndrome. Transfusion-transmitted DENV infection was suspected because she had remained continuously hospitalised in a mosquito-free, air-conditioned high-dependency unit for 10 days prior to symptom onset and had received donor blood within the usual dengue incubation period.

Investigation of the blood donor revealed that the donor developed dengue two days after donation. DENV RNA NAT was positive in both the donor's untransfused fresh-frozen plasma and the patient's plasma. Sanger sequencing confirmed DENV-2, with 100% nucleotide sequence homology.

Despite persistent thrombocytopenia over several days, the platelet count recovered spontaneously without haemorrhagic complications. By Day 20 after fever onset, the platelet count had increased. The patient was discharged 42 days after initial admission, with residual hemiparesis and a normal full blood count.

Sabino, 2016

The Sabino, 2016 [22] study was conducted in Brazil, in a DENV-endemic setting with high rates of past exposure resulting in partial immunity and large numbers of community-acquired DENV infections.

In total, 42 blood components positive for DENV RNA were transfused to 35 recipients. Among these, five recipients were considered to have had probable transfusion-transmitted DENV infection and one, a possible transfusion-transmission. No donors details were available apart from their laboratory results. For three of these recipients, pre-transfusion samples were available for testing, and all tested negative for DENV RNA; two also tested negative for IgM before transfusion. These five cases were considered probable cases of transfusion-transmitted DENV infection. One additional recipient received two RNA-positive units; the post-transfusion sample from this patient was collected on day 15 and was negative for DENV RNA, but the recipient seroconverted to DENV IgM. This case was classified as a possible transfusion-transmitted case with one exposure, because both RNA-positive units were transfused on the same day. No known fatalities occurred for the five probable or the possible cases of transfusion-transmitted DENV infection within 30 days after transfusion. Evidence of symptomatic disease consistent with dengue was present, these recipients but none developed severe dengue.

Santos, 2020

The Santos, 2020 [23] study reports a case of a 26-year-old woman with sickle cell disease (SCD) on chronic transfusion therapy who complained of severe arthralgia, myalgia, abdominal pain, headache, and fever 24 hours after transfusion of RBCs. DENV infection was suspected, and the patient was hospitalised for clinical support and given another RBC transfusion. The patient's clinical condition improved approximately eight days after the onset of symptoms. DENV-2 RNA NAT was negative in the patient's pre-transfusion sample, while the post-transfusion sample was positive (Ct: 27.8), suggesting a high viral load and an acute infection. To investigate transfusion-transmitted DENV infection, the stored donor serum was tested and was also positive (Ct: 25.8). Molecular typing confirmed the presence of DENV-2 as well. The phylogenetic analysis of the DENV-2 strains obtained from both donor and patient samples was classified as the Southeast Asia-American genotype (Genotype III) and demonstrated 100% genomic identity, supporting a certain imputability for this case of transfusion-transmitted DENV infection.

Stramer, 2012

In the Stramer, 2012 [24] study conducted in Puerto Rico, three of the 29 recipients receiving donations positive for DENV RNA were tested. Only one of the recipients (male, 80 years old) transfused with RBCs containing 10^8 copies/mL of DENV-2 became febrile three days post-transfusion and developed dengue haemorrhagic fever. The recipient was DENV-2 RNA positive by reverse transcription-polymerase chain reaction (RT-PCR). Both the donor and the recipient viruses had identical envelope sequences. Even though the recipient had no clinically significant bleeding detected, he met the criteria for severe dengue, namely, he had a fever for five days, thrombocytopenia, haemorrhagic manifestations, and plasma leakage, as evidenced by development of hypotension and hypoalbuminemia after defervescence. This case was reported as a certain case of transfusion-transmitted DENV infection.

Tambyah, 2008

The Tambyah, 2008 [25] study reports on a well-documented cluster of transfusion-transmitted DENV infections in Singapore. A 52-year-old, asymptomatic, repeat blood donor gave blood on 15 July 2007. An investigation of all recipients of his blood products was initiated after he informed the blood bank that he had a fever the day after donation.

The stored serum sample was positive for DENV-2 by RT-PCR. The recipient of the donor's RBCs (72-year-old man) had fever and myalgia two days after transfusion. The recipient of the donor's fresh-frozen plasma (64-year-old man) had fever and worsening pleural effusions the day after transfusion. Both recipients were positive for DENV-2 by RT-PCR, also with serological evidence of secondary DENV infections, and received supportive care and were discharged in good health. The last recipient of the donor's platelets (74-year old male) was asymptomatic but had serological evidence of a recent secondary DENV infection on follow-up. No molecular analysis was performed.

In this study, they were unable to perform whole-genome sequencing for definitive confirmation in the first two cases. The timing of the infections, soon after transfusion and infection in the three recipients, during a prolonged stay in an air-conditioned mosquito-free intensive care unit, supports a probable imputability for these transfusion-transmitted cases of DENV infection.

Tissues and non-reproductive cells

Two studies [21,44] focused on transmission of DENV through application of tissues and non-reproductive cells , both looking at haematopoietic stem cells (allogeneic stem cell transplantation and HSCT from a haploidentical related donor) as the subtype of SoHO. Details of each study are reported below.

Punzel, 2014

The Punzel, 2014 [21] study reported on a 51-year-old male in Germany with acute myeloblastic leukaemia, who underwent a fully matched unrelated donor stem cell transplantation. The donor was a 24-year-old woman who returned from Sri Lanka three days before donation for allogeneic stem cell transplantation. On the day of apheresis, she showed signs of respiratory infection, bone pain, and headache. Standard leukopheresis processing of blood from the donor was performed without problems. The condition of the donor worsened the same day, and a serum sample test taken three days after symptoms onset showed a weak positive result for DENV by IgM and IgG, and a strong positive result for NS1 antigen, demonstrating an acute DENV infection. DENV RNA NAT was positive with the same sequence as the recipient. On Day 3 after transplant, the patient developed painful hepatomegaly and deranged liver functions and was diagnosed with veno-occlusive disease . Blood culture showed *Staphylococcus epidermidis* growth. He was retrospectively analysed and tested negative for DENV IgM and IgG but positive for DENV NS1 antigen and DENV RNA with a DENV RNA load of 8.6×10^7 copies/mL. The patient's condition deteriorated, and he died on Day 9, probably due toxic enterocolitis and hepatic veno-occlusive disease. The authors consider this to be a certain case of DENV infection transmission by allogeneic blood stem cell transplantation.

Yadav, 2021

The Yadav, 2021 study [44] reported on a two-year-old boy in India who underwent a matched haploidentical related donor peripheral blood HSCT. The donor was his mother. The circulating peripheral blood stem cell count of the donor was unexpectedly low for a healthy donor. Apheresis was used to collect the peripheral blood haematopoietic stem cells. The recipient tolerated the stem cell infusion well. Seven days after infusion, the recipient developed high-grade fever, followed by ascites and pleural effusion on Day 8 post-infusion. The recipient was diagnosed with dengue on Day 10 following a positive result on antigen NS1, whilst dengue IgM was negative on Day 10. On Day 22, repeat dengue NS1 test came negative, and dengue IgM level became positive. The donor also had a fever a few days prior to stem cell donation; the donor's symptoms improved two days after the apheresis procedure, and the illness was later diagnosed as being due to dengue. The donor had become afebrile on Day 2 post-apheresis, and IgM was strongly positive, with NS1 antigen negative, confirming DENV infection in the donor. Therefore, a probable transmission of DENV from the donor to the recipient through haematopoietic stem cell infusion was suspected. The child had severe dengue, and experienced primary graft failure. However, he had autologous recovery of his own bone marrow and was alive on Day 200 post-transplantation.

Human breast milk

One study [15] reported DENV transmission through human breast milk. Details of the study are reported below.

Barthel, 2013

The Barthel, 2013 [15] study reported a 23-year-old Polynesian pregnant woman in New Caledonia in pre-term labour at 30 weeks and 4 days of gestation. The mother had a two-day history of fever before the start of the labour. Vaginal and blood cultures were negative. Following delivery of a healthy male infant, the mother developed a persistent fever, anaemia, and thrombocytopenia. DENV-1 was detected by RT-PCR in sequential blood samples taken from the mother (Day 0 to Day 6), the infant (Day 4 to Day 13), and in breast milk (Day 4 and Day 6). Cord blood collected at the time of delivery and infant blood samples collected at delivery (Day 0) and Day 2 post-delivery were negative for DENV by RT-PCR. Serological diagnosis was performed showing IgM seroconversion in both mother and infant, who tested positive on Day 6 and Day 25, respectively. Non–serotype specific IgG was positive on Day 0 in the mother's blood samples, reflecting a former DENV infection.

The infant was fed with expressed milk by the mother and then breastfed. DENV was detected in breast milk through RT-PCR on Day 4 after delivery. Breastfeeding was stopped on the fourth day following delivery. On the same day, the infant developed symptoms, low-grade fever (37.9°C), while on Day 9 he showed thrombocytopenia without any sign of discomfort or severity. Discharged on Day 25. His serum tested positive (RT-PCR) for DENV on Day 4. This was considered a probable transmission case of DENV transmission through breast milk.

West Nile virus (WNV)

Of the 20 studies reporting on WNV transmissions through SoHO, 19 reported cases through blood and blood components, one through breast milk, and one through tissues and non-reproductive cells (Table 5).

Table 5. Characteristics of studies assessing transmission through SoHO of West Nile virus

Author, year	SoHO type/subtype	Outcome recipient	Author imputability	Country
Armstrong, 2003 [26]	Blood and blood components (leucocyte reduced RBCs)	Death	Certain	US (Ohio)
De Oliveira, 2004 [27]	Blood and blood components (platelets)	Survived	Certain	US (Nebraska)
Groves, 2017 [28]	Blood and blood components (plasma)	Death	Probable	US (not specified)
Harrington, 2003 [29]	Blood and blood components (plasma)	Survived	Certain	US (Mississippi)
Hayes, 2020 [30]	Blood and blood components (platelets)	Death	Probable	US (not specified)
Hong, 2003 [31]	Blood and blood components (not specified)	Death	Probable	US (Illinois, spent time in Texas)
Iwamoto, 2003 [32]	Blood and blood components (not specified)	NA (deceased organ donor)	Probable	Georgia
Kightlinger, 2007 [33]	Blood and blood components (RBCs)	Survived	Probable	US (South Dakota)
	Blood and blood components (plasma)	Survived	Probable	US (South Dakota)
Kitagawa, 2018 [34]	Tissues and non-reproductive cells (HSCs)	Death	Certain	US (Texas)
Meny, 2011 [35]	Blood and blood components (granulocytes)	Death	Certain	US (not specified)
Montgomery, 2006 [36]	Blood and blood components (RBCs)	Survived	Certain	US (Texas)
	Blood and blood components (RBCs)	Death	Probable	US (Texas)
	Blood and blood components (RBCs)	Survived	Probable	US (Iowa)
	Blood and blood components (RBCs)	Survived	Probable	US (Kansas)
	Blood and blood components (RBCs)	Survived	Probable	US (New Mexico-Hospital Texas)
CDC, 2013 [37]	Blood and blood components (platelets)	Death	Probable	US (Colorado)
CDC, 2009 [38]	Blood and blood components (RBCs) (same donor)	Survived	Probable	US (Louisiana)
	Blood and blood components/plasma (same donor)	NA (deceased organ donor)	Probable	US (Louisiana)
CDC, 2004b [47]	Blood and blood components (RBCs)	Death	Probable	US (Arizona)
CDC, 2002a [39]	Blood and blood components (RBCs) (same donor)	Death	Certain	US (not specified)
	Blood and blood components (same donor) (plasma)	Survived	Probable	US (not specified)
	Blood and blood components (not specified) (different donor)	Survived	Probable	US (not specified)
CDC, 2002c [40]	Blood and blood components (RBCs)	Survived	Certain	US (Michigan)
	Human breast milk	Survived	Probable	US (Michigan)
CDC, 2002h [48]	Blood and blood components (not specified)	Survived	Certain	US (Michigan)
Pealer, 2003 [41]	Blood and blood components (platelets) (case 1)	Survived	Certain	US (not specified)
	Blood and blood components (case 2) same donor as case 3 and 4 (platelets)	Death	Certain	US (not specified)

Author, year	SoHO type/subtype	Outcome recipient	Author imputability	Country
	Blood and blood components (case 3) same donor as case 2 and 4 (plasma)	Survived	Certain	US (not specified)
	Blood and blood components (case 4) same donor as case 2 and 3 (RBCs)	Survived	Certain	US (not specified)
	Blood and blood components) (case 5) same donor as case 6 (platelets	Survived	Certain	US (not specified)
	Blood and blood components (case 6) same donor as case 5 (RBCs)	Death	Certain	US (not specified)
	Blood and blood components (case 7) same donor as in [27] (platelets)	Survived	Certain	US (not specified)
	Blood and blood components (case 8) (platelets)	Survived	Certain	US (not specified)
	Blood and blood components (case 9) (RBCs)	Survived	Certain	US (not specified)
	Blood and blood components (case 10) same donor as case 11 (platelets)	Survived	Certain	US (not specified)
	Blood and blood components (case 11) same donor as case 10 (plasma)	Survived	Certain	US (not specified)
	Blood and blood components (RBCs) (case 12) same donor as case 13	Survived	Certain	US (not specified)
	Blood and blood components (case 13) same donor as case 12 (RBCs)	Survived	Certain	US (not specified)
	Blood and blood components (case 14) (RBCs)	Survived	Certain	US (not specified)
	Blood and blood components (case 15) (RBCs)	Survived	Certain	US (not specified)
	Blood and blood components (case 16) (RBCs)	Death	Certain	US (not specified)
Politis, 2022 [42]	Blood and blood components (platelets)	Survived	Certain	Greece
	Blood and blood components (plasma)	Survived	Certain	Greece
	Blood and blood components (RBCs)	Survived	Certain	Greece
	Blood and blood components (RBCs)	Survived	Certain	Greece
Shepherd, 2004 [43]	Blood and blood components (plasma)	Death	Certain	US (not specified)

HSCs - Haematopoietic Stem Cells; RBCs: Red Blood Cells.

Blood and blood components

The 19 studies focusing on blood and blood components as the type of transmission through SoHO for WNV, looked at either platelets, RBCs, granulocytes, or plasma as the subtype. In some cases, the subtype was not specified. Details of each study are reported below.

Armstrong, 2003

The Armstrong, 2003 [26] study reports on a 74-year-old woman with a history of coronary artery bypass grafting in 1996, who was admitted to a hospital on 24 August 2002, with acute coronary syndrome. She had redo-coronary artery bypass graft on 3 September 2002. During the post-operative course she had thrombocytopenia. The patient had fever on post-operative Day 5, and two sets of blood cultures yielded methicillin-resistant coagulase-negative staphylococci. The patient subsequently had high fever, along with generalised weakness and an altered mental status by the 15th post-operative day (Day 25 of hospitalisation). The fever eventually resolved; however, the encephalopathy progressed, and she became unresponsive.

By post-operative Day 6, the patient had received a total of 28 units of blood products before the onset of encephalopathy.

Because of the possibility of transfusion-transmitted WNV infection in the recipient, their serum was tested and found positive for WNV-specific IgM and IgG antibodies. CSF tested positive for WNV-specific IgM antibody. The patient died on postoperative Day 41 due to WNV meningoencephalitis.

One of the blood donors had been implicated as a source of the infection. A retained segment from the unit contained WNV RNA. A follow-up serum sample from this donor contained antibodies to WNV. A unit of leuco-reduced RBCs from this donor had been transfused to the patient between 2 and 4 September 2002.

The extended interval between admission to the hospital and onset of encephalopathy supported a probable transfusion-transmitted WNV infection which was confirmed in subsequent investigation.

De Oliveira, 2004

The De Oliveira, 2004 [27] study describes a case of WNV encephalitis due to a transfusion of blood that tested non-reactive for WNV using six-minipool nucleic acid testing (MP-NAT).

An 80-year-old Nebraska man underwent open-heart surgery on 4 August 2003, during which he received 26 blood components because of massive bleeding. The patient recovered and was discharged 10 days later. On 19 August (13–15 days post-transfusion), he was re-hospitalised with mental confusion and fever. His condition worsened, requiring ventilatory support for three weeks, after which he gradually improved and was transferred to a rehabilitation facility.

During the second hospitalisation, WNV encephalitis was suspected, and serum and cerebrospinal fluid (CSF) collected tested positive for WNV-specific IgM. Convalescent serum testing confirmed the WNV infection. Mosquito exposure was considered unlikely.

An investigation traced all transfused blood components to their donors. Although the implicated donations were nonreactive by six-MP-NAT at the time of donation, retrospective individual donation testing identified one platelet donation as reactive for WNV RNA by transcription-mediated amplification and PCR assays. The viral load was low (estimated at 30 and 40 copies/mL through dilutional studies and at 560 copies/mL by quantitative PCR) and below the detection limit of MP-NAT. Follow-up serum testing of the associated donor demonstrated seroconversion to WNV positivity, while the donor remained asymptomatic.

These findings support a certain imputability of the transfusion- transmitted WNV infection from a low-level viraemic donor whose infection escaped detection using six-MP-NAT screening.

Groves, 2017

The Groves, 2017 [28] investigation describes a 78-year-old man with underlying cardiac disease who underwent aortic valve replacement and coronary artery bypass surgery in August 2016 and received multiple blood components from different donors. He was discharged after seven days, but rehospitalised on Day 12 with fever, altered mental status, and symptoms and subsequently diagnosed with aseptic meningitis. His clinical course worsened, and he died on Day 51.

CSF obtained on Day 14 was positive for WNV specific IgM. Serum samples collected on Days 16 and 18 were also positive for WNV IgM, with subsequent detection of WNV IgG. All blood components transfused to the patient had tested either as non-reactive using MP or individual-donation (ID) NAT at the time of collection.

Further investigation led to the identification of a donor who tested positive for WNV IgM and IgG on a follow-up sample and reported a WNV-compatible illness beginning 3–5 days after donation. The donor's initial sample was included in a 16-MP that had an elevated signal-to-cutoff ratio, but was considered non-reactive according to assay cutoff. Plasma from this donor had been transfused to the patient 12 days before onset of WNV meningoencephalitis.

Although mosquito-borne exposure could not be definitively ruled out, the case was classified as a probable case of transfusion-transmitted WNV infection.

Harrington, 2003

The Harrington, 2003 [29], study reports the case of a previously healthy 24-year-old woman who experienced severe post-partum haemorrhage, requiring extensive transfusion support, July 2002 (Mississippi State, US). Initially, she received six units of RBCs and two units of fresh frozen plasma (FFP). Following transfer to a tertiary care facility, she underwent a hysterectomy and, on post-partum Day 1, received an additional 10 blood components (six units of RBCs and four units of FFP) for ongoing bleeding. Fever was first documented on post-partum Day 2, but no bacterial infections were present and no additional symptoms, and the woman was discharged on post-partum Day 5.

On post-partum Day 6, the woman developed recurrent fever accompanied by chills, headache, fatigue, and generalised weakness. Twenty-six days post-partum, she sought medical care for ongoing symptoms. She had no meningismus, photophobia, rash, focal neurological deficits, or motor weakness. She was discharged but returned the following day due to persistent fever and headache.

Specific IgM antibodies for WNV were detected in both serum and CSF and confirmed by PRNT. The patient was hospitalised for two days with a diagnosis of WNV meningitis and subsequently made a full recovery.

An investigation was initiated due to the patient receiving multiple blood components. Donor retention segments and untransfused blood components were tested using PCR, IgM ELISA, PRNT, and viral culture. Infectious WNV was isolated by viral culture from an IgM-negative, PCR-positive non-transfused unit of FFP associated with one donor from which RBCs were transfused. Follow-up testing demonstrated WNV IgM seroconversion for this donor. The donor sought medical care for frontal headache, fatigue, and upper respiratory symptoms four days after donation. The detection of WNV RNA in a sample, the detection of IgM on the follow-up sample, and the symptoms reported by the donor after donation supported a certain imputability for transfusion-transmitted WNV infection through RBC.

Hayes, 2020

The Hayes, 2020 [30] study reports a probable transmission case of a WNV infection with a fatal outcome. The recipient was a 69-year-old man with ischemic cardiomyopathy who underwent an orthotopic heart transplantation. He received 18 blood products perioperatively, including one apheresis platelet unit that had screened non-reactive for WNV by ID-NAT.

The immediate post-operative course was unremarkable. On post-transplant Day 11, the patient developed altered mental status, tremors, fever, and progressive neurologic decline. WNV RNA was detected in the recipient's blood on Day 15 by nucleic acid testing, and WNV IgM antibodies were detected in CSF on Day 17. Despite supportive care, his condition worsened, progressing to respiratory failure, renal failure requiring haemodialysis, flaccid paralysis, loss of brainstem reflexes, and death on post-transplant Day 25.

Plasma collected on the day of death tested positive for WNV IgM by microsphere immunoassay and was confirmed by PRNT.

A suspect platelet donation was identified following notification of WNV infection in another recipient. While the initial platelet donation was non-reactive by ID-NAT (estimated 95% limit of detection of 100 copies/mL), 26 days after donation of the suspect platelet unit, a subsequent donation from the same donor tested reactive by ID-NAT and was positive for both WNV IgM and IgG antibodies, consistent with a recent WNV infection in the donor.

Pre-transplant samples from the recipient and samples from the heart donor tested negative for WNV RNA and IgM, making infection prior to hospitalisation or transmission via the organ donor unlikely. Although mosquito-borne transmission or exposure from other blood donors could not be definitively excluded, the clinical, laboratory, and epidemiological findings supported a probable transfusion-transmitted case of WNV infection. The data suggest the transmission was caused by an apheresis platelet unit, collected very early in the donor's viraemic phase, while viral RNA levels were below the limit of detection of ID-NAT screening.

Hong, 2003

The Hong, 2003 [31] study describes two cases of WNV encephalitis in HSCT recipients in the US who had received blood transfusions before transplantation. The US Centers for Disease Control and Prevention (US CDC) confirmed transfusion-transmitted WNV infection in the first case; however, transmission through blood transfusion was not confirmed in the second case. The report does not provide detailed information on the specific blood donors potentially implicated in either case.

The first patient was a 58-year-old man from Illinois with relapsed acute myeloid leukaemia who underwent a matched unrelated-donor bone marrow transplantation. During his leukaemia treatment, he received multiple blood transfusions. Five days before transplantation, he developed fever, followed by progressive upper extremity weakness that evolved into generalised weakness and confusion. CSF testing was positive for WNV by RT-PCR, leading to a diagnosis of WNV encephalitis. The patient subsequently died. A US CDC investigation determined that the infection was acquired through a blood transfusion received in Illinois. In addition, two other recipients of blood components from the same donation were also infected with WNV.

Iwamoto, 2003

In the Iwamoto, 2003 [32] study, four recipients of organs from a single donor developed fever and altered mental status, raising suspicion of WNV transmission via organ transplantation. An investigation identified WNV infection in the organ donor and in all four organ recipients. Encephalitis developed in three of the recipients, and febrile illness developed in one. Three recipients became seropositive for WNV IgM, and the fourth had brain tissue that was positive for WNV by viral isolation and nucleic acid and antigen assays. Serum specimens obtained from all organ recipients before transplantation showed no evidence of WNV infection.

The organ donor was a previously healthy woman who was hospitalised for traumatic injuries and received multiple blood transfusions before brain death. Serum samples collected before transfusion showed no evidence of WNV infection; however, serum and plasma samples obtained at the time of organ recovery were positive for WNV by quantitative polymerase chain reaction and viral culture, indicating viraemia at the time of donation. The organ donor had received blood components from 63 donors. Review of blood donors and follow-up testing identified one donor who was viraemic at the time of donation and became seropositive for WNV IgM antibodies during the subsequent two months. This blood donor reported symptoms compatible with WNV illness in the weeks before blood donation but was asymptomatic at the time of donation.

All four organ recipients developed illness within weeks of transplantation, while receiving immunosuppressive therapy. Symptoms began seven to 17 days after transplantation and ranged from febrile illness to severe neuroinvasive disease with encephalitis. One recipient died, and three survived. Laboratory and epidemiological findings demonstrated transmission of WNV through the transplanted organs, and the blood transfusion was identified as the probable source of WNV viraemia in the organ donor.

Kightlinger, 2007

The report from Kightlinger, 2007 [33] describes two cases of probable transfusion-transmitted WNV infection in immunosuppressed patients from a single infected blood donor, despite a negative six-MP-NAT result at the time of donation.

The first patient, an 82-year-old man with end-stage renal disease, received a kidney transplant on 25 August and was given two units of packed red blood cells four days later. He developed fever, lethargy, and a peri-incisional hematoma 21 days post-transplant, followed by rapid mental deterioration two days later. Anti-WNV IgM was detected in both serum and CSF by MAC-ELISA. His fever and mental status improved by discharge 36 days after surgery. The kidney donor was negative for WNV IgM and WNV RNA.

Further investigation identified one of the red blood cells units as originating from a donor positive for WNV IgM on a follow-up sample.

The second patient, a 60-year-old man with a prior kidney transplant, underwent spinal fracture repair on 10 August and received 15 blood products, including one FFP unit from the same IgM-positive donor as the first case. At Day 11 post-surgery, he developed fever, and four days later, tremors, encephalopathy, and acute left arm paralysis. CSF analysis revealed anti-WNV IgM. His fever, tremors, and encephalopathy resolved, but left arm paralysis persisted five days after symptom onset following transfer to another hospital. The patient was still in long-term care three months later.

The donor was asymptomatic, local to an endemic area, and likely had natural mosquito exposure. Transfusion-transmission could not be confirmed since the index blood samples or co-components from the implicated donation were unavailable for testing. However, evidence of WNV infections in two recipients of blood products from a common donor with serological evidence of recent infection makes transfusion-transmitted WNV infection probable.

Meny, 2011

The Meny, 2011 [35] study reports the first documented certain transmission case of WNV infection acquired through apheresis granulocyte transfusion.

A 25-year-old woman with precursor B-lymphoblastic leukaemia was admitted on 9 July 2010, for post-chemotherapy fever and found to be neutropenic. Daily granulocyte transfusions began on 7 August. As granulocytes must be transfused immediately after collection, infectious disease testing cannot be completed beforehand and screening results for WNV identified a positive donation one day after transfusion. On 25 August, 16 days after starting granulocyte transfusions, the patient developed sudden confusion and weakness. CSF tested positive for WNV RNA NAT and IgM. She was discharged but subsequently readmitted and died on 6 November from sepsis secondary to febrile neutropenia.

The donor was a 45-year-old man, asymptomatic at the time of donation, who developed fever, chills, severe fatigue, headache, joint and bone pain, tremor, rash, and cognitive difficulties on 22 August. He was hospitalised on 26 August for WNV meningitis. He cleared the infection and seroconverted at follow-up (9 August, transcription-mediated amplification: positive, IgG and IgM negative, WNV RNA NAT copies/mL: 700 and 3600, showing seroconversion at follow-up (18 October, WNV RNA NAT negative, copies/mL <5, IgG, IgM positive)).

The detection of WNV RNA in the donation supports the conclusion of a certain transfusion-transmitted WNV infection.

Montgomery, 2006

The Montgomery, 2006 [36] study presents findings from the US national blood donor screening programme for WNV, which was implemented in June 2003 following documented cases of transfusion-transmission in 2002. Among 36 investigations conducted for suspected transfusion-transmission of WNV infection, one case met criteria for certain transmission cases and five were classified as probable transmission cases. One of these cases had already been described in another paper [27]. Two of these cases (including the certain transfusion-transmission case and one probable transfusion-transmission case) were identified through blood collection agency–initiated investigations, while the remaining four probable transfusion-transmission cases were identified through public health–initiated investigations. In all six transfusion-transmitted cases, recipients had received blood components from multiple donors. However, only a single WNV RNA–positive blood component was identified in each case. The implicated donations were collected between 29 July and 18 September 2003. All had undergone six-MP-NAT, and none were detected as positive at the time of screening. The median age of the affected recipients was 63 years (range, 13–82 years). Clinical outcomes included WNV encephalitis in four recipients, West Nile fever in one, and no clearly attributable WNV illness in another critically ill patient. Seroconversion was observed in one recipient,

and all tested donations were negative for WNV-specific antibodies, suggesting that the detected antibodies were not passively transferred through transfusion from seropositive donors. Adequate samples were available to estimate donor viraemia levels in four of the six cases. The median estimated viral load of these cases was 0.1 plaque-forming units (PFU) per millilitre, with values ranging from 0.06 to 0.5 PFU/mL (with 1 PFU noted as equivalent to approximately 400 copies/mL).

CDC, 2002a

This CDC, 2002a [39] report describes three cases of transfusion-transmitted WNV infection in 2002.

One certain transfusion-transmission case involved an adolescent with a hematologic malignancy who developed WNV after receiving 93 blood components during the 30 days before illness onset. Among these donors, one tested positive for WNV RNA. The implicated donor developed fever, chills, headache, eye pain, and weakness beginning two days after donation and later seroconverted. The type of components implicated in this case was not specified.

Two additional WNV, probable transfusion-transmitted cases were linked to blood components derived from the same donation but different from the first case described here. A 60-year-old man received four units of RBCs and subsequently developed encephalitis; serum and CSF tested positive for WNV-specific IgM 8 and 16 days after transfusion, respectively, and the patient died. An associated retention segment in the donor tested positive for WNV RNA.

A second recipient from the same donor, a 40-year-old woman, received FFP from the same donor and developed fever three days after transfusion. One day before transfusion she was negative when tested using RT-PCR and IgM. Serum collected nine days after transfusion was positive for WNV RNA and negative for IgM, while serum collected 15 days after transfusion was positive for both WNV RNA and IgM, confirming recent infection.

The donor associated with these two cases later tested positive for WNV-specific IgM.

CDC, 2002c

This CDC, 2002c [40] report describes a probable transmission case of transfusion-transmitted WNV infection in a 40-year-old woman who, following the delivery of a healthy infant (September, 2002, Michigan, US), to treat anaemia received two units of RBCs from a donor who was later found to be RT-PCR WNV positive, linked to severe WNV disease in another transfusion recipient (described in [48]), and herself developed WNV encephalitis.

The woman developed a headache and photophobia shortly after delivery, with initial improvement by discharge two days post-partum. A new and more severe headache developed eight days after delivery, followed by fever 12 days post-partum, leading to hospitalisation 15 days after delivery.

CSF analysis showed pleocytosis and tested positive for WNV-specific IgM, confirming WN meningoencephalitis. The patient recovered and was discharged.

CDC, 2002h

This CDC, 2002h [48] report describes a certain case of transfusion-transmitted WNV infection in August 2002, in Michigan. A 47-year-old man underwent liver transplantation and received two blood transfusions on 14 and 24 August. He was readmitted approximately 10 days later with fever and subsequently developed encephalopathy. CSF analysis showed WNV–specific IgM antibody, confirming neuroinvasive infection. The patient recovered and was discharged.

Retention segments were available from 20 blood donors; one segment tested positive for WNV by RT-PCR.

CDC, 2004b

In the CDC 2004b [47] report, Arizona State reported a probable transmission case of transfusion-transmitted WNV infection which occurred during donor screening with MP-NAT before implementation of ID-NAT in the region for the season. The patient, a 43-year-old man, was hospitalised for an above-knee amputation and received two units of packed red blood cells. Shortly after discharge, he developed non-specific symptoms including fatigue and gastrointestinal upset, which progressed to neurological manifestations and altered mental status consistent with encephalitis. CSF analysis confirmed WNV infection, with detection of WNV-specific IgM antibodies and viral RNA by RT-PCR. Neuroimaging findings were compatible with WNV encephalitis. Despite medical care, his neurological function worsened, and he died soon after transfer to a nursing facility.

Investigation of the transfused blood products identified one plasma unit that had tested negative in a MP-NAT, but was reactive when tested individually, indicating a low-level viraemia in the donor at the time of donation. Subsequent serological testing confirmed that the donor had developed WNV-specific IgM, supporting recent infection. Given the recipient's confirmed WNV infection, the NAT reactivity of the implicated donation, and the donor's seroconversion, this event was classified as a probable case of transfusion-transmitted WNV infection. However, definitive attribution was limited by the patient's potential exposure to WNV through mosquito bites in an epidemic area.

CDC, 2009

This CDC, 2009 [38] report describes two probable cases of transfusion-transmitted WNV infections linked to a single blood donation collected in September 2008. The donor lived in an area with low reported WNV activity, but had recent outdoor exposure and developed a self-limited febrile illness with myalgias and weakness nine days after blood donation. FFP and packed red blood cells were used for donation. The packed red blood cell unit was transfused to a 76-year-old nursing home resident hospitalised for atrial fibrillation and anaemia. Although the recipient did not develop a febrile illness, her serum obtained 73 days after transfusion tested positive for WNV-specific IgM and neutralising antibodies at a titer of 1:1280, indicating the infection occurred in a time period consistent with transfusion-transmission. The timing of donor illness and recipient seroconversion supports probable transfusion-transmitted WNV infection despite the absence of retained donor samples for confirmatory testing. The FFP was donated to an 18-year-old man who subsequently died and became a heart donor. The heart recipient was infected by WNV through transplantation.

CDC, 2013

This CDC, 2013 [37] report describes a fatal case of WNV infection most consistent with transfusion- transmission, despite nonreactive ID-NAT, probably due to very low-level donor viraemia.

In August 2012, a man (age not specified) with non-Hodgkin's lymphoma in partial remission was admitted for chemotherapy and autologous stem cell transplantation. Fourteen days before stem cell collection, he underwent routine infectious screening, including WNV NAT, which was negative. HSCs were collected eight days before admission and infused on hospital Days 8 and 9. On hospital Day 14, he received a platelet transfusion. On Day 18, the patient developed gastrointestinal symptoms, followed by fever and hypotension on Day 28. On Day 29, he developed altered mental status, somnolence, and respiratory failure requiring sedation and mechanical ventilation, which limited neurological assessment.

CSF on Day 30 was negative for bacterial pathogens, cryptococcal antigen, and multiple viral PCR targets, although WNV testing was not performed at that time. A brain MRI revealed diffuse encephalopathy. Neurological status did not improve after sedation was discontinued. Life-sustaining treatment was withdrawn, and the patient died on hospital Day 47 (33 days after blood transfusion). Post-mortem examination demonstrated diffuse encephalitis. Serum collected on hospital Day 43 was positive for WNV IgM, and WNV RNA was detected by RT-PCR in brain and spinal cord tissue at autopsy.

A public health investigation found that the patient had been continuously hospitalised for four weeks before symptom onset, making mosquito exposure unlikely. He had received multiple leucoreduced, irradiated blood products, including platelets transfused on hospital Day 14, from a donor who later tested positive for WNV IgM and neutralising antibodies. The implicated donation was initially screened as part of a reactive six-MP-NAT, however all units were found to be non-reactive at individual donation level and were released. An FFP unit from the same donor, which was not transfused, tested positive for IgM but was negative for WNV RNA.

The findings support transfusion-transmitted WNV infection from a donor with low-level, intermittently detectable viraemia.

Pealer, 2003

In the Pealer, 2003 [41] report, the authors summarise the findings of an investigation of blood transfusion recipients and blood donors conducted in the US from 28 August 2002, to 15 April 2003. A total of 23 certain transmission cases of transfusion-transmitted WNV infection were described. Seven of the cases reported here have already been described in greater detail in other papers included in this scoping review [26,29,32,39,40,48].

Among 16 newly described patients with confirmed WNV infection, ages ranged from seven to 90 years (median 51), and seven were female. Eight patients were immunosuppressed due to an organ transplantation, haematological disease, or cancer. Nine cases were identified after recipients developed WNV-associated illness following blood transfusion; six were detected through linkage to co-components from viraemic donors, and one following donor self-reporting of post-donation West Nile fever.

Nine patients developed WNV-associated illness, including cases of meningoencephalitis and cases of febrile illness, with symptom onset occurring 4–21 days after transfusion. Three patients died.

Exposure sources included RBCs (5/8 leucoreduced units), platelets, and FFP.

PCR testing of stored serum was performed in six recipients, with WNV RNA detected in four. Four WNV RNA-positive recipients lacked detectable WNV antibodies in serum samples collected post-transfusion, highlighting delayed or absent seroconversion in immunocompromised individuals.

The 16 certain cases of transfusion-transmitted WNV infection were linked to blood donors with viraemia who donated blood or blood components between 22 July and 6 October 2002. One recipient received transfusions from two viraemic donors. All testable recipients who received components from viraemic donors showed laboratory evidence of WNV infection; two recipients were unavailable for testing.

The implicated donors ranged in age from 18 to 72 years, and 10 were female. Two donors did not return for follow-up serological testing and interviews. Eight donors recalled symptoms consistent with viral infection, including one on the day of donation.

On samples collected at the time of donation, all implicated donors tested negative for WNV IgM, and measured viral loads were below 80 pfu/mL. The estimated mean viral levels in available plasma units was higher in donors recalling symptoms (29.6 pfu/mL) than those remaining asymptomatic (4.3 pfu/mL), though the difference did not reach statistical significance.

Testing of retention segments and plasma samples revealed variability in viral detection. Retention segments were frequently of suboptimal quality due to homolysis, dilution, storage conditions, and leucoreduction. When multiple samples were available, PCR-positive retention segments were always associated with PCR-positive plasma; however, several plasma samples tested positive when the corresponding retention segments were negative, underscoring the limitations of segment testing.

Politis, 2022

This conference abstract from Politis, 2022 [42] summarises five cases of transfusion-transmitted WNV infection in Greece from 2010 to 2021, identified through haemovigilance review and retrospective screening of blood donations and considered as certain by the authors.

Two patients received blood components derived from the same whole blood unit: one received platelets and developed WNV neuroinvasive disease, including quadriplegia and blindness, while the other received plasma and remained asymptomatic. The donation occurred one week before preventive WNV measures were implemented in Greece.

Two patients with thalassemia were transfused with one unit each of WNV-infectious RBCs from donations made prior to WNV blood safety measures. Both patients experienced serious clinical courses of WNV infection.

A fifth patient, a 10-day-old premature infant, was transfused with a WNV-positive RBC unit. WNV infection was excluded in this case by six-month follow-up serological testing.

Shepherd, 2004

The Shepherd, 2004 [43] study reports a case of WNV encephalitis in a 54-year-old kidney transplant patient, whose illness progressed rapidly with severe neuroinvasive disease (encephalitis with tremor, hallucinations, progressive coma, brain-stem involvement) 10−12 days after transfusion and resulted in death. Sero-epidemiological analysis suggested that the infection was most probably transmitted via transfusion of FFP during the transplantation procedure. Serum samples from the recipient collected prior to transplantation and transfusion tested negative for anti-WNV IgM and viral RNA, and no evidence of infection was found in the kidney donor. Subsequent retrospective testing identified one plasma donor who later developed anti-WNV IgM antibodies, confirmed through PRNT.

The authors conclude that this case is a certain case of transfusion-transmitted WNV infection which underscores the limitations of current donor screening, as low-level viraemia can go undetected, particularly during the window period. The report also highlights that immunocompromised individuals are at higher risk of prolonged viraemia, severe neurological complications, and increased mortality.

Tissues and non-reproductive cells

One study [34] focused on the transmission of WNV through the application of tissues and non-reproductive cells, looking at HSCs as the subtype of SoHO.

Kitagawa, 2018

The Kitagawa, 2018 [34] study describes a transmission case of WNV infection via bone marrow transplant.

An eight-year-old boy with high-risk acute myeloid leukaemia underwent a haploidentical HSCT in October 2015 in Houston, Texas. Both the patient and the donor were long-term Houston residents and had not travelled in the year preceding transplantation. The patient had been hospitalised for 12 days before HSCT for conditioning therapy, and the stem cell product was collected one day prior to infusion. Eleven days after HSCT, he developed persistent fever without focal symptoms. The infectious disease evaluation was negative.

On Day 21 post-transplant, the patient developed acute slurred speech and progressive right-sided weakness. Brain MRI demonstrated signs of viral encephalitis. CSF analysis was negative for WNV antibody (not specified). By Day 22, he was comatose, with abnormal tone and a depressed and slow background activity in the electroencephalogram. A repeat CSF study on Day 30 showed negative serologies. On Day 33, ophthalmological examination revealed chorioretinal lesions characteristic of WNV. CSF PCR returned positive for WNV on Day 42, confirming neuroinvasive infection. The patient died 55 days after transplantation.

Donor screening three weeks before stem cell collection was negative for WNV IgM and IgG; however, repeat testing of the donor after the recipient's diagnosis showed high-titer IgM and IgG without detectable viraemia, suggesting recent donor infection.

The timing of symptom onset 11 days post-transplant, combined with lack of mosquito exposure due to the hospitalisation pre-transplantation, supported the conclusion of a certain transmission of WNV infection via the HSCT.

Human breast milk

One study reported a probable transfusion-transmitted case of WNV infection and subsequent probable transmission of WNV infection to an infant through breastfeeding [40].

CDC, 2002c

This CDC, 2002c [40] report describes a probable case of transfusion-transmitted WNV infection in a 40-year-old woman (see section above for details, CDC, 2002c, 3.2.3.1). Following the delivery of a healthy infant, the woman received two units of red blood cells to treat anaemia from a donor later found to be WNV RNA NAT positive. She subsequently developed WNV encephalitis.

On the day of delivery, the woman began breastfeeding and continued through 17 days post-partum. A sample of breast milk obtained 16 days after delivery tested positive for WNV RNA NAT and had detectable IgM and IgG. A subsequent breast milk specimen collected 24 days after the implicated transfusion was found to be negative by PCR but remained IgM-positive. The infant remained afebrile and healthy, but a serum sample from the infant on Day 25 tested positive for IgM. No cord blood or other products of conception were available for testing. The infant was reported to have minimal outdoor exposure. Although the vector route cannot be completely discarded, breast milk is considered the most likely source of infection in the infant. In particular, the detection of IgM in the infant is suggestive of a primary immune response in the infant rather than passive transfer from the mother, as these antibodies do not cross the placental barriers and the mother's IgM in the milk would remain in the child's gastrointestinal system. Nevertheless, definitive certain imputability is precluded by the absence of documented seroconversion of the newborn. Furthermore, while WNV nucleic acids were identified in the breast milk, the possibility of transmission mediated by blood exposure — secondary to nipple bleeding — cannot be entirely ruled out. This represents a probable transmission case of WNV infection through breastfeeding, supported by concurrent positive findings in both mother and infant and a biologically plausible transmission route.

Summary of findings

Although primarily transmitted by arthropods, arboviruses have also demonstrated the capacity for transmission through SoHO. As vector-borne transmission for some of these arboviruses is increasing in several European countries due to the expanding circulation of the viruses and their vectors, describing transmission of arboviruses through SoHO is of particular relevance to support assessment of the risk of SoHO-associated transmission in Europe.

Since the first documented case of transfusion-transmission WNV infection in 2002 [8], sporadic reports have highlighted this alternative risk. Changing environmental conditions, vector distributions and human mobility may influence the geographic range and seasonality of some arboviruses in Europe. With these changes, the risk of introducing arboviruses in the SoHO supply in Europe increases and an evidence-based review of reported cases is essential to inform risk assessments and recommendations to ensure the safety of SoHO in Europe.

This scoping review focused on six arboviruses (WNV, DENV, ZIKV, CHIKV, USUV and CCHFV). These pathogens were selected for inclusion as, with the exception of USUV (which shares reservoirs, vectors, and ecological patterns with WNV), they will be covered in the upcoming technical guidelines on the prevention of transmission of arboviruses through SoHO, developed by ECDC [190]. This review includes 37 publications reporting 77 documented cases of arbovirus transmission through SoHO application. Most cases involved WNV (47 cases), followed by DENV (26 cases) and ZIKV (4 cases). However, it should be noted that the authors of these studies only classified a subset of cases as confirmed based on criteria specified in each article: 30 cases for WNV, nine cases for DENV, and two cases for ZIKV.

Transmission occurred predominantly through transfusion of blood and blood components (71 cases), and a small number linked to HSCT (three cases) and through breastfeeding (three cases), confirming that although uncommon, SoHO transmission represents a clinically relevant threat, particularly in the area of blood safety. It is acknowledged that breast milk via breastfeeding is not considered to be a SoHO, but within this review, it was considered as a proxy for transmission of arboviruses through donor human milk since there were no studies assessing the latter.

It should be noted that there were no reports of transmission through SoHO identified for three of the six arboviruses considered in this review: CHIKV, USUV, and CCHFV. Moreover, none of the studies excluded for failing to meet the predefined inclusion criteria addressed these three pathogens. All relevant review articles identified during the screening process and later excluded in accordance with the scoping review's eligibility criteria were also examined to identify any potentially eligible studies on these viruses. However, no such studies were found. This could reflect underreporting, limited investigation, or biological factors rather than a true absence of transmission risk.

For CCHFV and USUV specifically, this could be due to the relatively low number of overall cases in Europe, underreporting and limited investigations. In addition to transmission through the bite of an infected tick, humans can acquire CCHFV through contact with the blood, secretions, organs, or other body fluids of infected animals or individuals. Consequently, people who work closely with livestock — such as pastoralists, veterinarians, and abattoir workers — as well as healthcare workers in contact with infected patients, are at increased risk of exposure to the virus [8,39,191]. In areas with higher infection rates of CCHFV, the transmission route through SoHO may not be recognised.

Detection of USUV antibodies in asymptomatic blood donors and forest workers indicates that the virus circulates in both the animal and the human populations [192]. Although no cases of transmission through transfusion or organ transplantation have been reported, the possibility of virus transfer from asymptomatic donors to recipients remains a concern. Because USUV and WNV share reservoirs, vectors and ecological patterns, some experts recommend introducing blood donor screening for USUV in endemic regions, particularly during periods of increased bird mortality and WNV outbreaks [193].

For CHIKV it is uncertain why no cases have been reported, given the very large outbreaks that have occurred in several different regions. It could be that transmissions due to SoHO were not identified as they occurred in an epidemic setting where it is not possible to differentiate vector-borne from other routes of transmission, although reports of transmission of DENV through SoHO application have been documented in epidemic settings. Lack of identification of such SoHO-transmitted cases could be due to unrecognised mild disease in transfusion recipients, due to a high proportion of symptomatic patients for this infection, making it less likely to have an asymptomatic donor presenting for donation.

Since 2007, Europe has experienced multiple local CHIKV outbreaks, notably in 2007, 2017, and 2025 [194]. Since 2004, outbreaks have been noted in more than 110 countries worldwide, with several million cases reported every year [195]. Although no transfusion-transmitted CHIKV infections have been reported, organisations warn of a theoretical risk due to the very high viraemia, including among asymptomatic individuals. Supporting biological plausibility of a transmission through blood transfusion, a case of iatrogenic CHIKV transmission occurred in France, following an accidental needle-stick injury [8], and a case of transfusion-transmission of Ross River virus (another alphavirus) occurred in Western Australia [196].

Zika virus

SoHO transmission routes: two transfusion-transmitted cases of ZIKV infections via platelets (leucoreduction) were considered of certain imputability. Transmission via breast milk remains probable rather than definitively confirmed in the literature, as the potential for transmission through blood ingestion, secondary to nipple fissures or mastitis, cannot be excluded; ZIKV RNA was detected in breastmilk.

The two transfusion-transmitted cases from the same donor showed strong evidence, supported by temporal association, molecular detection, and high phylogenetic homology between donor and recipients. On the other hand, the breastfeeding case relied on exclusion of vector exposure and the presence of high sequence similarity, highlighting methodological challenges in definitively attributing postnatal transmission.

Symptoms in recipients: all reported recipients of transfusion-transmitted ZIKV infection remained asymptomatic.

Symptoms in donors: all donors self-reported symptoms after donation (i.e. febrile illness, myalgia, arthralgia, conjunctival hyperaemia, pruritic maculopapular rash).

Reported diagnostic approaches in recipients: RT-PCR was the primary diagnostic tool across studies, often complemented by serology, IgM, IgG, and PRNT.

Reported testing approach in donors: none.

Viral loads in donors: not reported in the included studies.

Timing between transmission through SoHo, symptoms and viral detection in recipients: detection of ZIKV RNA or seroconversion in recipients ranged from six to 51 days post-transfusion, demonstrating a wide diagnostic window. No symptoms were reported in recipients.

Location of certain transmission through SoHO (endemic/non-endemic countries): Brazil only.

Dengue virus

SoHO transmission routes: transmission of DENV through SoHO in this review was mainly through transfusion of blood and blood components. Eight cases were defined as certain by authors, three of them from the same blood donor.

Among certain transmission cases, RBCs and platelets appear to have been implicated. This may be due to the fact that during platelet activation, such as an infection, DENV replicates in, and binds to, platelets. As a result, these components may be associated with an increased viraemia and are more implicated in transmission [197-199]. In addition, this could be due to tropism of the virus to platelets or surface receptor like CD42b [8]. Transmission via HSCT was confirmed in one case only.

Transmission of DENV through breastfeeding was rarely reported, but may be clinically significant, as observed with ZIKV, and available evidence supports the possibility that DENV infection could be transmitted through donated human milk. However, the single reported case documented a probable transmission through breastfeeding (and a documented presence of DENV in the breast milk). However, we cannot exclude the possibility that nipple bleeding may have contributed to the transmission.

Symptoms in recipients: all cases of transmission of DENV were associated with symptoms typical of DENV except for one, who was asymptomatic. Six cases were classified as severe cases of dengue, among these two were certain cases of transmission through SoHO. Five recipients had a fatal outcome. One death following HSCT was not directly attributed to DENV infection, but to the severe underlying health condition. In a letter to the editor, four deaths were reported following transfusion-transmitted DENV infection in children with severe underlying conditions. According to this letter, two deaths could be directly attributed to the DENV infection. It is important to note this letter to the editor includes very limited information on the assessment of the imputability of the transfusions. The authors discard the possibility of a mosquito-borne transmission as the recipients were hospitalised in intensive care units with strict environmental controls, and no dengue cases were detected in other paediatric patients in the intensive care unit. However, as noted by Wendel and colleagues [200], no investigation using molecular tests on retained donor samples or pre-transfusion samples for the recipients was reported, significantly limiting the assessment of imputability. As such there remains significant uncertainty on the actual route of transmission for these cases.

Symptoms in donors: most implicated donors in certain transmission cases were asymptomatic or presymptomatic at donation. In most reported cases, donors did not report symptoms post-donation and transmissions were identified through retrospective assessments.

Reported diagnostic approaches in recipients: a wide range of diagnostic tools was employed, including RT-PCR, NS1 antigen detection, and IgM/IgG. Evidence support imputability was strongest when molecular sequencing or phylogenetic analysis demonstrated identity between donor and recipient strains. Most reported cases were identified through retrospective assessments, reflecting limitation in the recognition of the infectious risk at time of donation.

Reported testing approaches in donors: tests employed to identify DENV infections in the donors included serology (NS1 antigen, IgM/IgG) and DENV RNA NAT.

Viral loads in donors: the reported viraemia levels showed substantial variability in both magnitude and reporting units, impeding direct comparisons.

Timing between transmission through SoHO, symptoms, and viral detection in recipients: the interval between transfusion or infusion of SoHO and symptom onset was generally short (1–9 days), consistent with dengue incubation period. In some reports, the recipients were tested a few days after symptom onset, but some studies highlighted longer delays between the transmission through SoHO application and testing and diagnosis in recipients (5-10 days). This underscores the challenges in recognising SoHO-transmitted DENV infections in hospitalised patients with overlapping clinical syndromes.

Location of certain transmission through SoHO (endemic/non-endemic countries): Brazil, Puerto Rico, Hong Kong, and Singapore.

West Nile virus

SoHO transmission routes: certain imputability for cases of transmission of WNV via SoHO typically relied on multiple infected recipients linked to the same donor, demonstration of donor WNV viraemia, and exclusion of mosquito exposure through questionnaires. Blood and blood components are by far the most frequently implicated SoHO route, with 30 cases of transfusion-transmitted WNV infection, often involving severely ill, elderly, or immunocompromised recipients, across different blood components (RBCs, platelets, plasma), highlighting the broad risk spectrum rather than a component-specific phenomenon.

One rare, but severe, certain transmission via HSCT demonstrates that WNV risk extends beyond conventional blood products.

A single probable SoHO transmission event has suggested secondary transmission via breastfeeding following transfusion-transmission of WNV infection to the mother, indicating a potential transmission pathway through human breast milk [40]. While authors suggested that translocation of maternal IgM cannot be fully excluded, this phenomenon has never been demonstrated. In contrast, maternal IgM has been shown to be detectable in infant stool, but not in blood [201]. It is appropriate to emphasise the limitations of the infant's diagnosis, which relies solely on IgM detection without virological confirmation or longitudinal follow-up. A review of five cases of mothers breastfeeding with post-partum WNV infections did not provide evidence for transmission of WNV through this route [102].

Symptoms in recipients: severe neuroinvasive disease and mortality (7/30 certain transmission cases) were observed in recipients where data were reported.

Symptoms in donors: donors most frequently contributing to transmission were asymptomatic at the time of donation and minimally symptomatic after a few days.

Reported diagnostic approach in recipients: most investigations relied on NAT, IgM/IgG serology, PRNT, and occasionally viral culture.

Reported testing approach in donors: individual donation NAT and minipool NAT (pools of six or 16). A recurring theme in this review is the failure of minipool NAT to detect low-level donor viraemia (later found to be positive at individual donation level), particularly early in infection, underscoring the window-period risk.

Viral loads in donors: data on viraemia levels in donors were rarely reported, and in many cases, adequate samples were not available to estimate these levels. Among the certain transmission cases included in this review, a wide range of values was observed, from 0.8 to 75 PFU/mL in plasma.

Timing between transmission through SoHO, symptoms and viral detection in recipients: development of symptoms after transfusion-transmission was very variable when reported and ranged from 1−16 days. When data were available, positive tests were recorded between nine and 16 days after transfusion.

Location of certain transmission through SoHO (endemic/non-endemic countries): most cases (26) were reported in the US and four in Greece.

Strengths and limitations

This scoping review was carried out in line with the methodological guidance of the Joanna Briggs Institute (JBI) [9] and is reported according to the PRISMA-ScR framework [10], thereby supporting the transparency, reliability, and reproducibility of the review process. Grey literature was not considered, as the review was intentionally limited to peer-reviewed publications to maintain a high level of methodological rigour. However, to ensure the robustness of our screening process, relevant review articles identified during the search were examined in detail to identify any potentially eligible original studies on CCHFV, CHIKV, or USUV, as no original articles meeting the inclusion criteria were retrieved.

Conclusions

This scoping review adds to the evidence of transmission of arboviruses through SoHO application. Blood and blood components were the dominant and most consistently documented route for ZIKV, DENV, and WNV. Transmission events frequently involved asymptomatic or presymptomatic donors who were not tested. When tested, detection of the virus escaped routine screening due to low-level or transient viraemia below the detection limits of tests used (e.g. in the case of tests in pools). Severe clinical outcomes were most frequently reported in immunocompromised recipients and children. Although rare, transmission via SoHO other than blood and blood components, including HSC transplantations highlights possible safety gaps.

Collectively, these findings underscore the importance of risk-based safety screening policies, testing strategies including sensitive nucleic acid testing, enhanced donor follow-up in the context of outbreaks, and targeted risk mitigation for high-risk populations.

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Annex. Search strategy

Ovid Medline (R) ALL

Line	Search term
1	exp Transplantation/
2	exp Donor/
3	exp Directed Tissue Donation/
4	exp Blood Transfusion/
5	exp "Tissue Transplantation"/
6	exp "Blood donors"/
7	exp "Cell Transplantation"/
8	or/1-7
9	(Tissue* or Cornea* or Sclera* or Valv* or Skin or bone or Tendon or Cartilage or Epiderm* or Reproductive cell* or Cord blood or Oocyte or Sperm* or Stem cell or Bone marrow or ovum* or ovule* or cyte* or egg or semen).mp
10	exp "germ cells"/
11	9 or 10
12	(donor* or donat* or transplant* or graft* or transfusion* or allotransplant* or allograft* or "assisted reproduct* techni*" or "assisted reproduct* technolog*").mp.
13	exp "transplantation"/
14	12 or 13
15	11 and 14
16	("product* of human origin" or "substance* of human origin" or "SoHO").ti,ab.
17	(FMT or IMT).ti,ab.
18	exp "fecal microbiota transplantation"/
19	((fecal or faecal or feces or faeces or stool or microbiota or gut or microbiome or microflora or intestinal or rectal) adj2 (transplant* or infus* or transfus* or implant* or instil* or donat* or donor or reconstitut* or therap* or bacteriotherapy or capsul* or encapsule* or enema)).mp.
20	exp Colostrum/ or exp Milk, Human/ or exp Breast Feeding/
21	(breastfeed* or breast feed* or breast fed or breastfed or breast milk or breastmilk* or colostrum or EBM or foremilk or hindmilk or "chest feed" or "wet nurs*" or "milk shar" or ((human or breast* or mother* or expressed or maternal or donor*) adj2 milk*)).mp.
22	or/17-21
23	8 or 15 or 16 or 22
24	exp Arboviruses/
25	(Arbovirosis or arbovirus* or arthropod-borne virus*).mp.
26	exp "Arbovirus Infections"/
27	(West Nile or WNV).mp.
28	exp "West Nile Virus"/
29	exp "West Nile Fever"/
30	(Usutu or USUV).mp.
31	(Dengue or DENV).mp.
32	exp Dengue/ or exp "Severe Dengue"/ or exp "Dengue Virus"/
33	(Chikungunya or CHIKV).mp.
34	exp "Chikungunya virus"/ or exp "Chikungunya Fever"/
35	(Zika or ZikV).mp.
36	exp "Zika Virus Infection"/ or exp "Zika Virus"/
37	exp "Hemorrhagic Fever Virus, Crimean-Congo"/ or exp "Hemorrhagic Fever, Crimean"/
38	(Crimean?Congo or CCHF or CCHFV or ((congo or crimean) adj2 (fever* or virus*))).mp
39	or/24-38
40	23 and 39

EMBASE

Line	Search term
1	exp Transplantation/
2	exp Donor/
3	exp Directed Tissue Donation/
4	exp Blood Transfusion/
5	exp "Tissue Transplantation"/
6	exp "Blood donors"/
7	exp "Cell Transplantation"/
8	or/1-7
9	(Tissue* or Cornea* or Sclera* or Valv* or Skin or bone or Tendon or Cartilage or Epiderm* or Reproductive cell* or Cord blood or Oocyte or Sperm* or Stem cell or Bone marrow or ovum* or ovule* or cyte* or egg or semen).mp
10	exp "germ cells"/
11	9 or 10
12	(donor* or donat* or transplant* or graft* or transfusion* or allotransplant* or allograft* or "assisted reproduct* techni*" or "assisted reproduct* technolog*").mp.
13	exp "transplantation"/
14	12 or 13
15	11 and 14
16	("product* of human origin" or "substance* of human origin" or "SoHO").ti,ab.
17	(FMT or IMT).ti,ab.
18	exp "fecal microbiota transplantation"/
19	((fecal or faecal or feces or faeces or stool or microbiota or gut or microbiome or microflora or intestinal or rectal) adj2 (transplant* or infus* or transfus* or implant* or instil* or donat* or donor or reconstitut* or therap* or bacteriotherapy or capsul* or encapsule* or enema)).mp.
20	exp Colostrum/ or exp Milk, Human/ or exp Breast Feeding/
21	(breastfeed* or breast feed* or breast fed or breastfed or breast milk or breastmilk* or colostrum or EBM or foremilk or hindmilk or "chest feed" or "wet nurs*" or "milk shar" or ((human or breast* or mother* or expressed or maternal or donor*) adj2 milk*)).mp.
22	or/17-21
23	8 or 15 or 16 or 22
24	exp Arboviruses/
25	(Arbovirosis or arbovirus* or arthropod-borne virus*).mp.
26	exp "Arbovirus Infections"/
27	(West Nile or WNV).mp.
28	exp "West Nile Virus"/
29	exp "West Nile Fever"/
30	(Usutu or USUV).mp.
31	(Dengue or DENV).mp.
32	exp Dengue/ or exp "Severe Dengue"/ or exp "Dengue Virus"/
33	(Chikungunya or CHIKV).mp.
34	exp "Chikungunya virus"/ or exp "Chikungunya Fever"/
35	(Zika or ZikV).mp.
36	exp "Zika Virus Infection"/ or exp "Zika Virus"/
37	exp "Hemorrhagic Fever Virus, Crimean-Congo"/ or exp "Hemorrhagic Fever, Crimean"/
38	(Crimean?Congo or CCHF or CCHFV or ((congo or crimean) adj2 (fever* or virus*))).mp
39	or/24-38
40	23 and 39

LILACS

Line	Search term
1	(soho OR breast OR milk OR microbiota OR stool OR fec* OR faec* OR "blood transfusion" OR "products of human origin" OR "substance of human origin" OR "product of human origin" OR "substances of human origin" OR "germ cells" OR "tissue donor" OR "tissue donation" OR "tissue transplantation" OR "cell transplantation" OR "blood donor") AND (arbovirus OR "west nile virus" OR dengue OR chikungunya OR zika OR crimean OR usutu OR (mh:arbovirus)) AND db:("LILACS") AND instance:"lilacsplus"

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