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Italian Blood System 2021: activity data, haemovigilance and epidemiological surveillance

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EPIDEMIOLOGIA
E SANITÀ PUBBLICA

ISTITUTO SUPERIORE DI SANITÀ

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The collection of data regarding the activities of the Italian Blood System since 2009 has been carried out through the Italian national blood information system (*Sistema Informativo dei Servizi TRAsfusionali, SISTRA*). The data collected at national level are those that are communicated to international health authorities. The data in this report are relevant to the year 2021.

Key words: Blood; Red cells; Plasma; Platelets; Blood donation; Blood donors; Self-sufficiency; Transfusion; Haemovigilance; Transfusion transmissible infections; Incidence; Prevalence; Risk factors

Istituto Superiore di Sanità
Sistema trasfusionale italiano 2021: dati di attività, emovigilanza e sorveglianza epidemiologica.
Liviana Catalano, Vanessa Piccinini, Ilaria Pati, Francesca Masiello, Francesco Barone, Giuseppe Marano, Simonetta Pupella, Vincenzo De Angelis
2022, iii, 88 p. Rapporti ISTISAN 22/25 (in inglese)

La rilevazione dei dati di attività del sistema trasfusionale italiano avviene, dal 2009, mediante il Sistema Informativo dei Servizi TRAsfusionali (SISTRA). I dati raccolti su base nazionale rispondono anche al debito informativo internazionale. Nel presente rapporto sono forniti i dati di attività del sistema trasfusionale italiano per l'anno 2021.

Parole chiave: Sangue; Globuli rossi; Plasma; Piastrine; Donazioni di sangue; Donatori; Autosufficienza; Trasfusione; Reazioni avverse; Emovigilanza; Infezioni trasmissibili; Incidenza; Prevalenza; Fattori di rischio

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ACRONYMS

AP	Autonomous Province
AVIS	*Associazione Volontari Italiani del Sangue* (Association of Voluntary Italian Blood Donors)
BCS	Blood Collection Site
BE	Blood Establishment
BSS	Blood System Service
CIVIS	*Comitato Interassociativo del Volontariato Italiano del Sangue* **(**Inter-associative Committee of Voluntary Italian Blood Donors Associations/Federations)
CNS	*Centro Nazionale Sangue* (Italian National Blood Centre)
FT	First-time tested (donor)
FIDAS	*Federazione Italiana Associazioni Donatori di Sangue* (Italian Federation of Voluntary Blood Donors Associations)
FNHTR	Febrile Non-Haemolytic Transfusion Reaction
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HIV	Human Immunodeficiency Virus
HLA	Human leukocyte antigen
HSC	Haematopoietic stem cells
CRI	*Croce Rossa Italiana* (Italian Red Cross)
ISTAT	National Institute of Statistics
NAT	Nucleic Acid Amplification Technology
NSIS	*Nuovo Sistema Informativo Sanitario* (New Health Information System)
PDMP	Plasma-Derived Medicinal Product
PTP	Post Transfusion Purpura
RBCC	Regional Blood Coordination Centre
RT	Repeat tested (donor)
SISTRA	*Sistema informativo dei servizi trasfusionali* (National Blood Information System)
TACO	Transfusion Associated Circulatory Overload
TAD	Transfusion Associated Dyspnoea
TP	*Treponema pallidum*
TRALI	Transfusion-Related Acute Lung Injury
XML	Extensible Markup Language

INTRODUCTION

The Italian National Blood Centre (*Centro Nazionale Sangue*, CNS) is in charge of the coordination of the National Blood Information System (*Sistema Informativo dei Servizi TRAsfusionali,* SISTRA), which was established by *ad hoc* Ministerial Decree (1) within the Ministry of Health's New Health Information System (NSIS). SISTRA collects the data related to the activities of the Italian Blood System and ensures that, after the validation performed by the Regional Blood Coordination Centres (RBCCs), the information from the Blood Establishments (BEs) is sent to the CNS for a final verification before its publication.

The above-mentioned data are crucial to evaluate the capacity of the National Healthcare System to respond to the needs of patients in different clinical settings. Moreover, they are an indispensable instrument for the strategic planning and coordination of the blood system.

For the purpose of this report, data concerning two SISTRA's macro areas are presented separately: activity data and haemovigilance data. The activity data contributes to planning the measures aimed to achieve self-sufficiency in blood components and plasma-derived medicinal products (PDMPs) at regional and national level. The area on haemovigilance includes data on serious adverse reactions in recipients, serious adverse reactions in donors, serious adverse events, and epidemiological surveillance of donors.

In this report, data are referred to 2021.

SISTRA operates in compliance with the technical regulations and security policies of the Public Connectivity System (PCS) (2-4). All information is encoded according to product standards established by the UNI (*Ente Italiano di Normazione*, the Italian organisation for standardization) 10529 (5), which enables the unequivocal identification and traceability of every unit of blood and blood components collected, produced, and transfused.

SISTRA collects data in two ways:

- through the regional blood transfusion information systems – by exchanging XML files (eXtensible Markup Language)
  or
- through the Blood System Services (BSSs), if a Regional/Autonomous Provincial (APs) IT system does not exist or if the Regions/APs have authorised the BEs to send data directly to SISTRA.

ACTIVITIES OF THE ITALIAN BLOOD SYSTEM

Introduction

The COVID-19 pandemic significantly affected 2020 and 2021 healthcare services. The Italian National Health System was mainly focused on fighting and tackling this disease. Compared with 2020, there is evidence of an upswing in transfusion activities. The blood transfusion system has kept up with the pandemic by guaranteeing the necessary supply of blood and blood derivatives to meet patients' needs.

Thanks to the availability of the personal data of BEs and Blood Collection Sites (BCSs) and their respective peripheral organisational sites, SISTRA is able to map the national transfusion network. The latter is subject to change given the ongoing redistribution of the production activities and rationalisation of resources.

This section of the report shows national 2021 data and compare them to the ones of the previous year (6). Data are related to blood and blood component donors, as well as to the collection, production and use of blood components, including plasma intended to PDMPs manufacture. In the tables and graphs included in Annex to this chapter, the quantitative activity indicators are reported at both regional/APs and national level in order to facilitate the network's benchmarking.

Methods

For the analysis relative to this section of the report, only quantitative indicators were used. The data regarding transfused patients were analysed according to the blood components infused.

The above-mentioned indicators are presented in graphs and according to the geographic classification specified by the UNI 10529 standard (6).

The data processing was carried out with the utilisation of "SAP Business Objects", which is the business intelligence system made available by the Ministry of Health on the NSIS. The reference population for the calculation of the indicators is that provided by the Italian National Institute of Statistics (ISTAT) as of 1st January, 2021, available at http://demo.istat.it/ (last accessed December 2021).

The data shared by the Italian Regions/APs were mainly coming from single BEs. In some cases, data from two or more BEs were incorporated in a single figure as specified here below:

a. The Veneto Region submitted 7 figures from 21 operating BEs;
b. The Friuli Venezia Giulia Region submitted 1 figure from 5 operating BEs;
c. The Latium Region submitted 22 figures from 23 operating BEs;
d. The Sicily Region submitted 25 figures from 33 operating BEs.

National data

In 2021, 250 blood transfusion activity records, which include data from 277 BEs, were validated by the RBCCs on SISTRA. Compared to 2020, the number of BEs and BCSs did not change (Table 1).

Table 1. BEs and BCSs with their respective peripheral organisational sites (2020-2021)

Blood facilities and population	2020	2021	Δ%
BEs	277	277	0.00
BEs peripheral organisational sites	849	838	-1.30
BCSs	189	189	0.00
BCSs peripheral organisational sites	1,280	1,289	0.70
Population	60,244,639	59,236,213	-1.67

BEs Blood Establishments, BCSs Blood Collection Sites (in Italy all BCSs are run by Voluntary Blood Donor Associations and Federations). Updated data 2021

Table 2 shows data concerning donors of blood and blood components per type of donation. Compared to 2020, there was a 1.65% and 2.45% increase of the total number of donors and regular donors, respectively. There was a decrease (-2.66%) in first-time donors. Table 3 shows the total number of collection procedures (carried out by both BEs and BCSs) per type.

Table 2. Donors of blood and blood components (2020-2021)

Donors	2020	2021	Δ%
First-time	**355,174**	**345,715**	-2.66
Those who re-donated in the period under examination	*80,830*	*77,766*	-3.79
Regular	**1,352,162**	**1,385,319**	2.45
Those who re-donated at least once a year in the last 5 years	*588,107*	*587,709*	-0.07
Total	**1,626,506**	**1,653,268**	1.65
Apheresis	**217,638**	**215,325**	-1.06
Those who donated only in apheresis	*114,730*	*112,865*	-1.63
Permanently deferred	**39,093**	**42,131**	7.77
Members of VBDAs	**1,490,473**	**1,519,500**	1.95

VBDAs: Voluntary Blood Donors Associations/Federations

Table 3. Collection procedures (2020-2021)

Collection procedures	2020	2021	Δ%
Whole blood	**2,438,349**	**2,566,235**	5.24
Apheresis	**454,479**	**454,908**	-0.12
Monocomponent apheresis	*393,254*	*396,826*	0.91
Multicomponent apheresis	*61,225*	*58,082*	-6.60
Total	**2,893,788**	**3,021,143**	4.40
Type			
Plasmapheresis*	382,927	386,673	0.98
Plateletpheresis	8,194	8,232	0.46
Stem Cells apheresis	1,620	1,563	-3.52
Granulocytapheresis	177	63	-64.41
Lymphocytapheresis	336	295	-12.20
Red Blood Cell/Platelet apheresis	3,450	3,185	-7.68
Double Red Blood Cell unit apheresis	224	206	-8.04
Plasma/Platelet apheresis	47,826	44,372	-7.22
Red Blood Cell/Plasma apheresis	8,600	8,313	-3.34
Double Platelet unit apheresis	1,125	1,192	5.96
Red Blood Cell/Platelet/Plasma apheresis	960	814	-15.21

* In the year 2021, plasmapheresis includes 9,301 COVID-19 convalescent plasma collections (in 2020 includes 6,952 COVID-19 convalescent plasma collections)

Table 4 shows the number of collections carried out by BCSs (total and by Association/Federation); 95% were carried out by the four Associations which are part of the

National Federation of Voluntary Blood Donors Associations (CIVIS, *Coordinamento Interassociativo Volontari Italiani del Sangue*).

Table 4. Number of collections carried out by blood collection sites (2020-2021)

Association/Federation	2020	2021	Δ%
AVIS	867,355	895,796	3.28
FIDAS	96,463	99,340	2.98
FRATRES	23,255	24,232	4.20
CRI	11,609	12,709	9.48
Other	55,683	59,875	7.53
Total	**1,054,365**	**1,091,952**	3.56

AVIS, Association of Voluntary Italian Blood Donors (*Associazione Volontari Italiani del Sangue*); FIDAS, Italian Federation of Voluntary Blood Donors Associations (*Federazione Italiana Associazioni Donatori di Sangue*); FRATRES, National Consociation of Blood Donors Groups of "Misericordie d'Italia"; CRI, Italian Red Cross (*Croce Rossa Italiana*)

Table 5 shows data concerning the production of blood components. Compared to 2020, there was an increase in the total number of units of blood components produced.

Table 5. Blood component production (2020-2021)

Blood component	2020	2021	Δ%
Red Blood Cells	**2,406,222**	**2,505,318**	4.12
Red Blood Cells from whole blood	*2,388,888*	*2,488,880*	4.19
Red Blood Cells by apheresis	*17,334*	*16,438*	-5.17
Platelets from single donors	16,006	8,670	-45.83
Platelet Pools	206,334	224,174	8.65
Platelets by apheresis	66,300	62,032	-6.44
Plasma	**2,842,096**	**2,942,474**	3.53
Recovered Plasma	*2,383,353*	*2,485,242*	4.28
*Source Plasma**	*398,149*	*399,915*	0.44
Source Plasma from multiple apheresis	*60,594*	*57,317*	-5.41
Total	**5,536,958**	**5,742,668**	3.72

* The number of aliquots of Covid-19 donor-convalescent patient plasma for the 2020 (13,731) and 2021 (14,558) are not included.

In 2021, 7,903 units of blood components were transfused per day. Compared to the previous year, there was a slight increase in the total number of units of blood components transfused (Table 6). Moreover, compared to 2020, there was:

a) an overall increase in the total number of units of discarded blood components whilst a decrease of the units of discarded plasma (Table 7);
b) an increase in the quantity of plasma for fractionation (Table 8);
c) an increase in the production of allogeneic fibrin glue and an increase of allogeneic platelets gel for non-transfusion use (Table 9);
d) an increase in the production of autologous blood components for non-transfusion use (Table 10);
e) an increase of the number of patients who pre-deposited blood components for autologous transfusion (Table 11);
f) an increase of the number of transfused patients, including those transfused in BEs (day hospital) (Table 12).

Table 6. Transfused units of blood components (2020-2021)

Blood component	2020	2021	Δ%
Red Blood Cells	**2,364,088**	**2,413,673**	2.10
Red Blood Cells from whole blood	*2,351,435*	*2,401,838*	2.14
Red Blood Cells by apheresis	*12,653*	*11,835*	-6.46
Platelets from single donors	4,118	1,088	-73.58
Platelets Pools	173,359	185,433	6.96
Platelets by apheresis	54,057	50,393	-6.78
Plasma	**219,970**	**221,638**	0.76
Recovered Plasma	*75,721*	*75,376*	-0.46
*Source Plasma**	*27,437*	*28,586*	4.19
Source Plasma from multiple apheresis	*6,321*	*5,624*	-11.03
Plasma pooled and treated for virus inactivation	*110,491*	*112,052*	1.41
Total	**2,815,592**	**2,872,225**	2.01

* "The number of aliquots of Covid-19 donor-convalescent" patient plasma for the 2020 (6,912) and 2021 (13,526) are not included

Table 7. Blood components discarded for reasons linked to health, technical issues, quality control and expiry dates (2020-2021)

Blood component	2020	2021	Δ%
Red Blood Cells	**86,477**	**73,196**	-15.36
Platelets from single donors	7,268	5,870	-19.24
Platelet Pools	33,987	33,167	-2.41
Platelets by apheresis	7,645	6,752	-11.68
Plasma	**110,439**	**114,624**	3.79
Recovered Plasma	*91,478*	*94,677*	3.50
*Source Plasma**	*15,481*	*16,973*	9.64
Source Plasma from multiple apheresis	*3,480*	*2,974*	-14.54
Total	**245,816**	**233,609**	**-4.97**

* The number of aliquots of Covid-19 donor-convalescent patient plasma for the 2020 (581) and 2021 (1,192) are not included

Table 8. Plasma for fractionation (2020-2021)

Blood component	2020	2021	Δ%
Plasma for fractionation (kg)	843,149	861,707	2.20

Data source: Pharmaceutical industry - data updated to February 2022

Table 9. Production and use of allogeneic blood components for non-transfusion use (2020-2021)

Blood component	2020	2021	Δ%
Platelet Gel			
Produced	13,048	24,647	88.89
- Used	*9,574*	*18,839*	96.77
- Not used	*3,474*	*5,808*	67.18
Fibrin Glue			
Produced	157	130	17.20
- Used	*149*	*121*	-18.79
- Not used	*8*	*9*	12.50

Table 10. Production and use of autologous blood components for non-transfusion use (2020-2021)

Blood component	2020	2021	Δ%
Platelet Gel			
Produced	**9,901**	**10,912**	10.21
- Used	*9,237*	*10,215*	10.59
- Not used	*664*	*697*	4.97
Fibrin Glue			
Produced	**188**	**254**	35.11
- Used	*188*	*253*	34.57
- Not used	*0*	*1*	

Table 11. Autologous donation and transfusion (2020-2021)

Patients and autologous donation activities	2020	2021	Δ%
Patients who predeposited blood components for autologous transfusion	11,189	12,247	9.46
Patients who underwent an autologous transfusion	9,197	10,512	14.30

Table 12. Transfused patients (2020-2021)

Patients* transfused with blood components	2020	2021	Δ%
Whole Blood^	54	34	-37.04
Red Blood Cells	566,199	610,452	7.82
Plasma	48,907	55,486	13.45
Platelets	51,519	57,868	12.32
Other	5,875	5,879	0.07
Total**	**603,352**	**656,998**	8.89

* Patients transfused once or more than once during the year under examination were counted only once.

** Patients transfused more than once during the year under examination with blood components of the same type were counted only once; patients transfused with more than one type of blood component were included in the count of each type.

^ Includes reconstituted whole blood

Indicators

The six classes of quantitative indicators identified for the 2021 year are:

A. Donors;

B. Donations;

C. Produced blood components;

D. Discarded blood components;

E. Transfused blood components;

for a total of 36 indicators, are presented at national level (Table 13) and regional level (Appendix A).

Table 13. Quantitative indicators for transfusion activities in Italy (2021)

Indicators		Index
A. Donors		
A1	N. of donors/1,000 RP	27.91
A2	M/F ratio: female donors (%)	33.34
A3	N. of donors /1,000 RP in the 18-65 age class	45.08
A4	N. of donors in the 18-65 age class/1,000 RP	3.39
A5	N. of donors in the 18-25 age class /1,000 RP in the 18-65 age class	5.47
A6	N. of donors /1,000 RP	23.39
A7	N. of first-time donors/1,000 RP	5.84
A8	N. of “regular” donors/1,000 RP	9.92
B. Donations		
B1	N. of donations (WB + apheresis)/1,000 RP	51
B2	N. of donations (WB + apheresis)/Total N. of donors (excluding prospective donors)	1.83
B3	N. of donations WB/1,000 RP	43.32
B4	N. of donations WB/N. of WB donors	1.67
B5	N. of donations in apheresis/1,000 RP	7.68
B6	N. of donations in apheresis/N. of apheresis donors	2.11
C. Production of blood components		
C1	N. of RBC units produced/1,000 RP	42.29
C2	N. of plasma units produced from WB and by apheresis/1,000 RP	49.92
C3	N. of plasma units produced from WB/1,000 RP	41.95
C4	N. of plasma units produced by apheresis (monocomponent or multicomponent)/1,000 RP	7.58
C5	Plasma for fractionation (kg)/1,000 RP	13.86
C6	Plasma by apheresis (kg) for fractionation/Total of plasma for fractionation (kg) (%)	28.19
C7	N. of platelet units produced by apheresis (monocomponent + multicomponent)/1,000 RP	1.05
C8	N. of platelet units produced from buffy-coat pools/1,000 RP	3.78
C9	N. of “adult platelet doses”/1,000 RP	4.86
D. Discarded blood components		
D1	N. of discarded RBC units/N. of “usable” RBC units (produced + acquired - released) (%)	2.92
D2	N. of expired RBC units discarded/N. of discarded RBC units (%)	29.09
D3	N. of RBC units discarded for technical reasons/N. of discarded RBC units (%)	30.73
D4	N. of RBC units discarded for health reasons/N. of discarded RBC units (%)	34.76
D5	N. of RBC units discarded for reasons linked to QC/ N. of discarded RBC units (%)	5.42
D6	N. of platelet units by apheresis discarded /N. of platelet units by apheresis produced (%)	10.88
D7	N. of platelet units from buffy-coat pools discarded / N. of platelet units from buffy-coat pools produced (%)	14.80
E. Transfused blood components		
E1	N. of transfused RBC units / 1,000 RP	40.75
E2	N. of transfused plasma units (from WB + by apheresis + IP) / 1,000 RP	3.97
E3	N. of transfused WB plasma units / Total N. of transfused plasma units (from WB + by apheresis + IP) (%)	32.05
E4	N. of transfused apheresis plasma units / N. of transfused plasma units (from WB + by apheresis + IP) (%)	20.29
E5	N. of transfused IP units / Total N. of transfused plasma units (from WB + by apheresis + IP) (%)	47.65
E6	N. of “adult platelet doses”/1,000 RP	3.98

WB: whole blood; RP: resident population; IP: Plasma pooled and treated for virus inactivation: QC: quality control. “Adult platelet dose” ≥ 2x1011 platelets. The “adult platelet dose” from single units of whole blood is conventionally composed of 5 units. Each unit of apheresis platelets is equal to an “adult platelet dose”. Each double platelet from apheresis is equal to 2 “adult platelet doses”. All platelet units produced are expressed as “adult platelet dose”

Conclusions

In 2021, the total number of blood and blood components donors (1.65%), in particular regular donors (2.45%) increased ensuring the achievement of national self-sufficiency.

The data showed an increase in the overall production of blood components. The quantity of red blood cells from apheresis and plasma from multiple apheresis decreased compared with the previous year.

In 2021 there was an increase in the number of transfused units of blood components (2.01%).

Comparing to 2020 the increase of the use of RBCs shows that the Patient Blood Management strategies and techniques, which were included for the first time in the Italian national blood and blood products self-sufficiency programme dating back to 2012 (see the latest Italian self-sufficiency programme 2021 (7)), were not uniformly applied throughout the country.

Although the emergency phase related to COVID-19 appears to be over, it is now clear that health authorities have to cope with new variants of SARS-CoV-2. Therefore, the health care system, including the blood system, will have to continue to take all the necessary preventive measures to contain the disease.

In particular, the measures introduced in 2020 such as blood donation booking for donors respond to the obligation to respect social distance shall be confirmed.

All guidelines elaborated to tackle the pandemic can be used in the future as well.

HAEMOVIGILANCE IN ITALY

Haemovigilance is a set of surveillance procedures covering the monitoring, reporting, investigation and analysis of adverse reactions in recipients, adverse events, adverse reactions in donors as well as the epidemiological surveillance of donors and the surveillance of medical devices used in transfusion activities (Ministry of Health Decree of 2nd November, 2015) (8). Haemovigilance systems are regulated by specific national laws and by European Directives (9, 10), transposed into national laws (11, 12), which state the procedures that must be adopted for the reporting of adverse reactions in recipients during or after transfusion, related to the quality and safety of transfused blood components, including the reporting of every case of transfusion transmitted infection. Haemovigilance also includes adverse reactions in donors defined as any unintended response in donors associated with the collection of blood or blood components that is fatal, life-threatening, disabling, incapacitating, or which results in, or prolongs, hospitalisation or morbidity. The aim of SISTRA is to promote the standardisation and comparability of data at national level through the simplification of their aggregation and processing to produce national reports.

In Italy, BEs are responsible for the collection of haemovigilance data; BEs register and report adverse events occurring in their organisation and must collect data from the related clinical facilities and BCSs. By means of pre-defined forms, the RBCCs are responsible for communicating to the National Competent Authority annual reports concerning adverse reactions in recipients and in donors and adverse events occurred in related BEs. The same flow of information is in place also for the epidemiological surveillance of donors (Figure 1).

In each organisation (BEs, RBCCs and the CNS) there is a person responsible for haemovigilance.

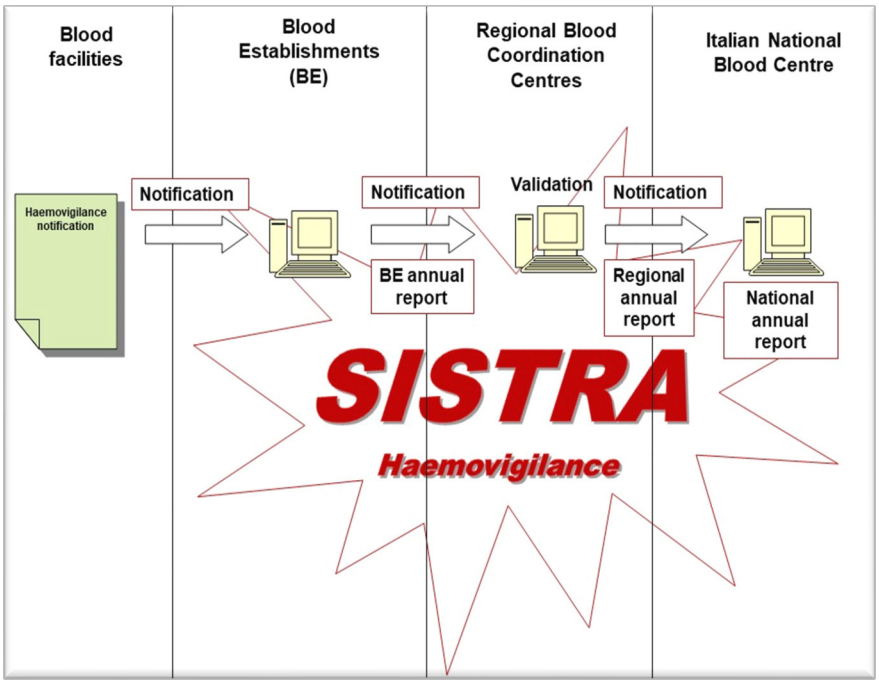


Figure 1. Haemovigilance information flow in SISTRA

The specific section of SISTRA dedicated to the haemovigilance includes:
- adverse reactions in recipients;
- adverse reactions in donors;
- adverse events;
- epidemiological surveillance of donors.

Adverse events and reactions in recipients and in donors

Definitions

For the purpose of this report, also in compliance with the Decree of the Ministry of Health of 2nd November, 2015 (8), donors are classified in:

- *first-time donor*
  People who have never donated either blood or plasma. They can be:
  - first-time pre-qualified donors (newly-registered donors who are screened during their first (pre-donation) visit and who donate during their second visit);
  - first-time not pre-qualified donors (newly-registered donors who are screened and donate during their first visit);
- *regular donor*
  People who routinely donate blood/plasma (i.e., within the last 2 years) in the same BE/BCS.

The levels of severity and imputability of adverse reactions in recipients, adopted in accordance with the European Directives and reported in the Legislative Decree n. 207/2007 (11), are classified as follows:

- *severity level*
  - Level 0 - No symptoms.
  - Level 1 - Mild symptoms (no therapeutic intervention).
  - Level 2 - Symptoms requiring therapeutic intervention.
  - Level 3 - Severe symptoms requiring resuscitation procedures.
  - Level 4 - Death.
- *imputability level*
  - *NA - Not Assessable*
    When there are insufficient data to evaluate the imputability.
  - *Level 0 - Excluded/unlikely*
    When there is conclusive evidence beyond reasonable doubt that the adverse event can be attributed to alternative causes.
  - *Level 1 - Possible*
    When the evidence is not such as to allow the attribution of the adverse event either to the blood/blood component or to alternative causes.
  - *Level 2 - Probable*
    When the available evidence is clearly in favour of attributing the adverse event to the blood or blood component.
  - *Level 3 - Certain*
    When there is conclusive evidence beyond reasonable doubt that the adverse reaction can be attributed to the blood or blood component.

Reporting on 2021

The notified information concerns 2,872,225 transfused blood components and 3,021,143 donations of blood and blood components. The reporting of haemovigilance system, expressed as number of notifications/years, increased constantly up to 2016 and appears to be stable in the period 2017-2021, especially in the number of adverse reactions in recipients (Figure 2). As in the previous year (6), the number of notifications shows a significant regional variability (Figures 3-5).

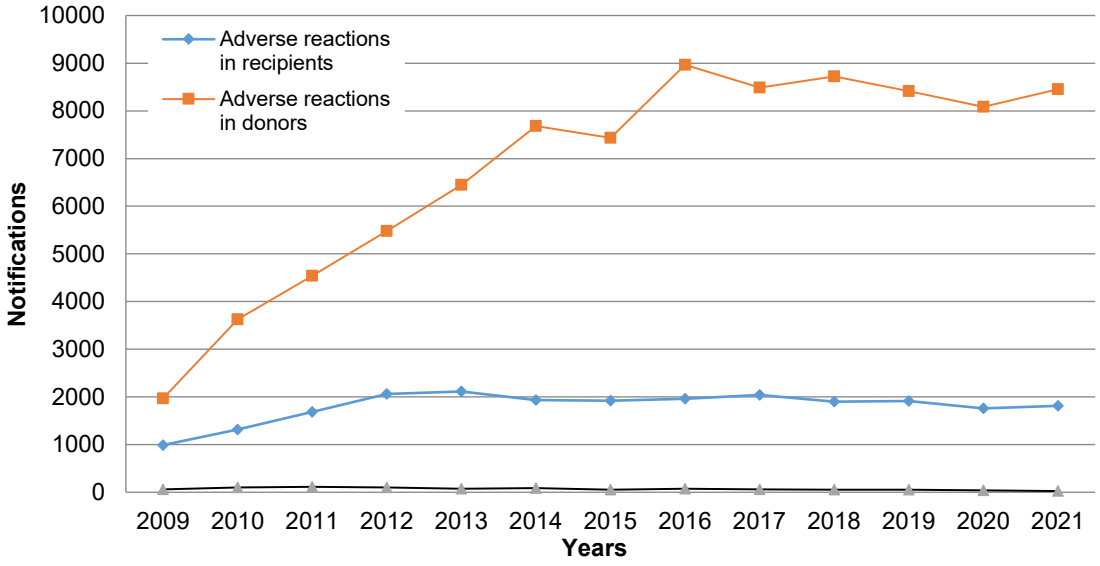


Figure 2. Number of haemovigilance notifications per year (2009-2021)

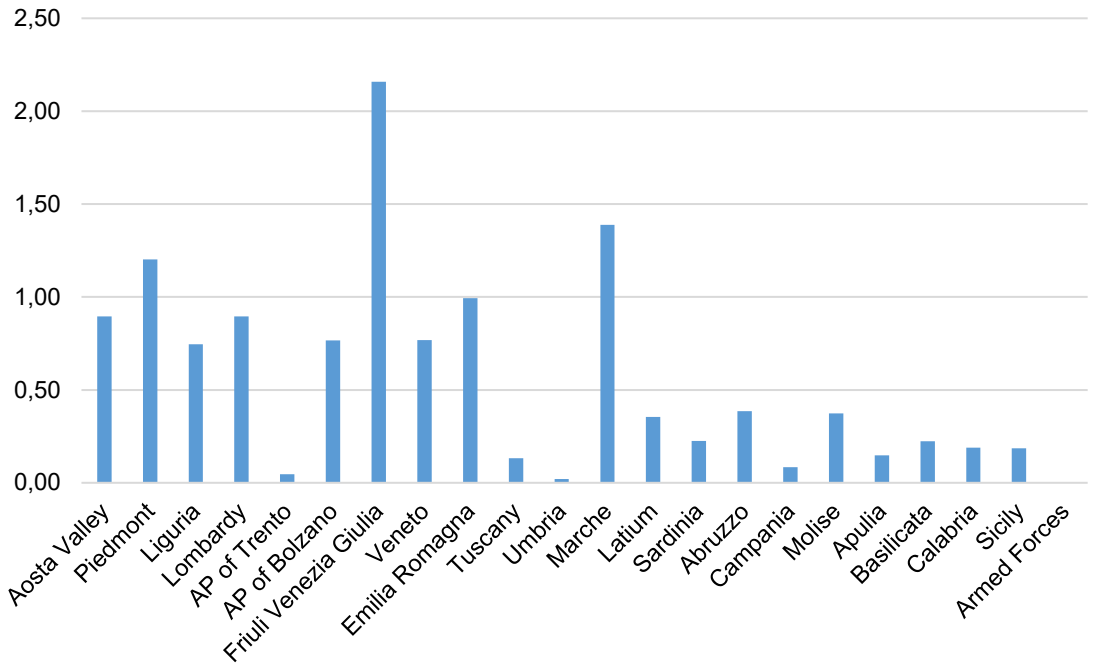


Figure 3. Adverse reactions in recipients notified by region /1,000 transfused components (2021)

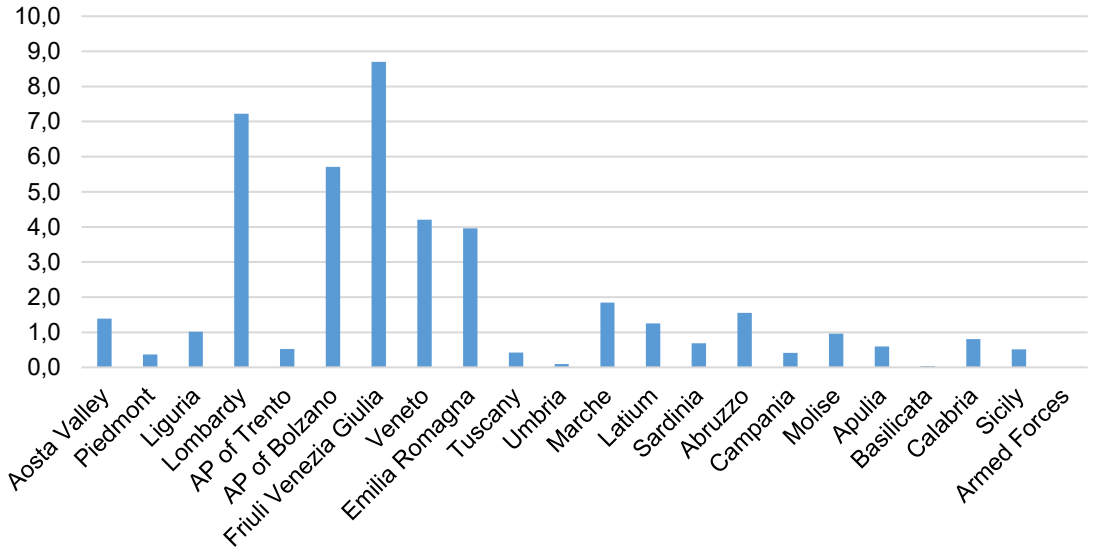


Figure 4. Adverse reactions in donors notified by region /1,000 collection procedures (2021)

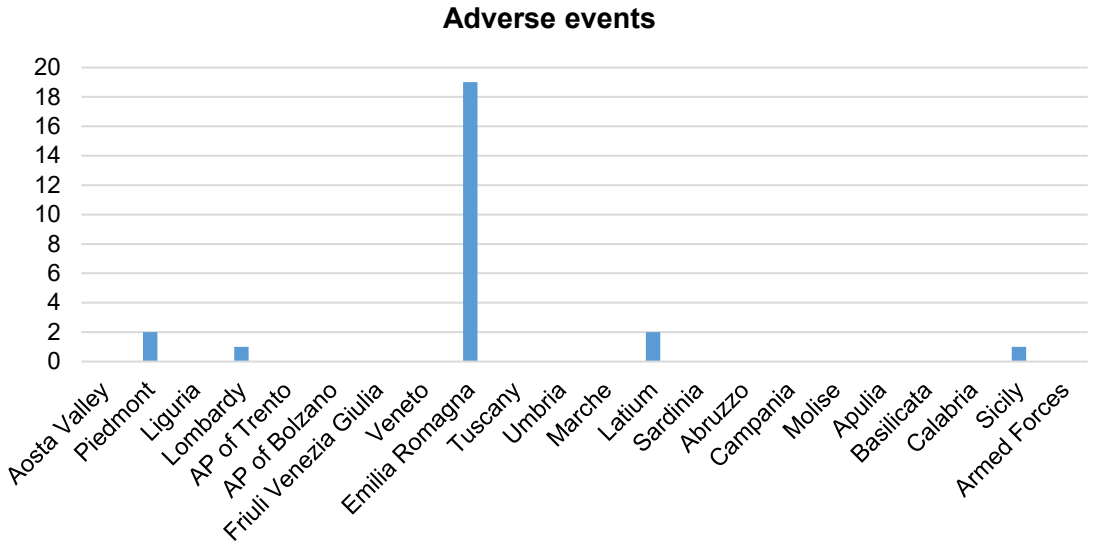


Figure 5. Adverse events notified by region (2021)

Adverse reactions in recipients

From January 1st to December 31st 2021, 1,815 adverse reactions were notified in recipients of blood components (one every 1,582 transfused units) (Table 14).

Adverse reaction related to autologous whole blood transfusion (2 cases) were excluded from the analysis.

Table 15 shows adverse reactions in recipients by absolute number and percentage.

In 2021, the most frequently notified reactions were Febrile Non-Haemolytic Reactions (FNHTR) (40.4%) and allergic manifestations with only mucosal and cutaneous symptoms (28.4%), representing 68.8% of all notified adverse reactions in recipients.

Table 14. Adverse reactions in recipients regardless of severity and imputability levels (2021)

Adverse reaction	n.	%
Transfusion associated dyspnoea (TAD)	67	3.7
Transfusion-related acute lung injury (TRALI)	2	0.1
Transfusion-associated circulatory overload (TACO)	31	1.7
Non-immunological haemolysis - chemical cause	2	0.1
Non-immunological haemolysis - physic cause	1	0.1
Non-immunological haemolysis - mechanic cause	1	0.1
Hypotensive transfusion reaction	38	2.1
Allergic reactions involving the respiratory and/or cardiovascular system	68	3.7
Allergic manifestations with only mucosal and cutaneous symptoms	516	28.4
Post-transfusion purpura	4	0.2
Acute haemolytic reaction due to ABO incompatible transfusion	1	0.1
Haemolytic transfusion reactions due to autoantibodies	9	0.5
Febrile non-haemolytic reaction (FNHTR)	733	40.4
Anaphylactic shock	2	0.1
Transfusion Transmitted HEV	3	0.2
Transfusion Transmitted Bacterial Infections*	2	0.1
Incorrect Blood Component Transfused without reaction	2	0.1
Other	333	18.3
Total	**1,815**	**100.0**

N: number; TAD: Transfusion associated dyspnoea; TRALI: Transfusion related acute lung injury; TACO: Transfusion associated circulatory overload. *Case 1: Transfusion Transmitted Serratia marcescens Infection (Severity: Level 2 - Symptoms requiring therapeutic intervention; Imputability: Level 1 - Possible; Complete resolution within few days). Case 2: Klebsiella pneumoniae multiresistent (Severity: Level 2 - Symptoms requiring therapeutic intervention; Imputability: Level 1 - Possible; Complete resolution within few days)

Adverse reactions to transfusion with an imputability level 2-3 regardless of severity levels

In 2021, among the 1,815 adverse reactions to transfusion 676 were with a high imputability level (imputability level 2-3) (Table 15).

Table 15. Adverse reactions in recipients with an imputability level 2-3 regardless of severity levels (2021)

Adverse reaction	n.	%
Transfusion associated dyspnoea (TAD)	20	3.0
Transfusion-related acute lung injury (TRALI)	1	0.1
Transfusion-associated circulatory overload (TACO)	16	2.4
Non-immunological haemolysis - mechanic cause	1	0.1
Hypotensive transfusion reaction	9	1.3
Allergic reactions involving the respiratory and/or cardiovascular system	36	5.3
Allergic manifestations with only mucosal and cutaneous symptoms	296	43.8
Post-transfusion purpura	1	0.1
Acute haemolytic reaction due to ABO incompatible transfusion	1	0.1
Haemolytic transfusion reactions due to autoantibodies	8	1.2
Febrile non-haemolytic reaction (FNHTR)	230	34.0
Anaphylactic shock	1	0.1
Transfusion Transmitted HEV	3	0.4
Other	53	7.8
Total	**676**	**100.0**

Taking into account only these adverse reactions, the frequency is one every 4,249 transfused units.

Adverse reactions to transfusion classified by transfused blood component with an imputability level 2-3 and a severity level 3-4

Table 16 shows the 7 adverse reactions with an imputability level 2-3 and a severity level 3-4 by transfused blood component. Taking into account only these adverse reactions, the frequency is one every 410,318 transfused units.

Table 16. Adverse reactions to transfusion classified by transfused blood component with an imputability level 2-3 and a severity level 3-4 (2021)

Adverse reactions	RBCs	Platelets	Plasma	Total
Hypotensive transfusion reaction		1	1	2
Transfusion-related acute lung injury (TRALI)	1			1
Transfusion-associated circulatory overload (TACO)			1	1
Transfusion associated dyspnoea (TAD)		1		1
Allergic manifestations with only mucosal and cutaneous symptoms			1	1
Other	1			1
Total	**2**	**2**	**3**	**7**

Severity and imputability levels of adverse reactions

The severity of adverse reactions to transfusion required therapeutic intervention in 75.2% of the cases; no therapeutic intervention was required in 22.5% (Figure 6).

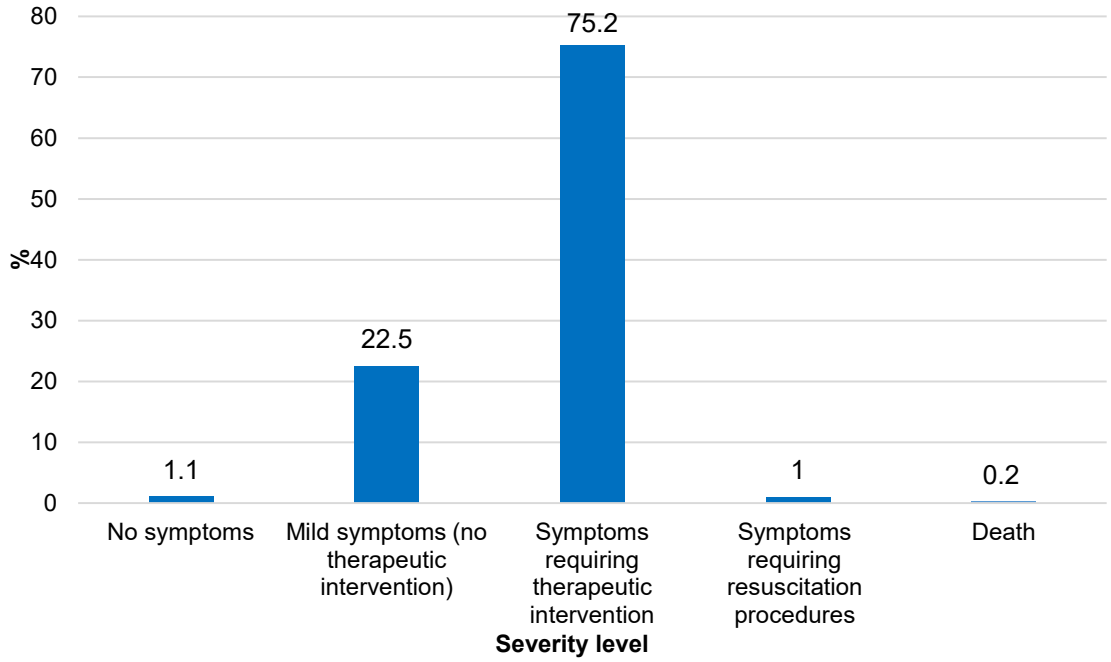


Figure 6. Severity level of adverse reactions in recipients (2021)

In 89.2% of adverse reactions the clinical resolution occurred in a few hours and only in one case a disease persistence within 6 months was observed (Table 17).

Table 17. Adverse reactions in recipients by outcome (2021)

Outcome	n.	%
Resolution within a few hours	1,619	89.2
Resolution within a few days	39	2.1
Complete resolution within 6 months	1	0.1
Not assessable	156	8.6
Total	**1,815**	**100.0**

Concerning the imputability level, data show that 62.7% of adverse reactions in recipients were associated with low levels of imputabilty (Table 18 and Figure 7); 44.7% were possibly imputable, 10.7% were excluded/improbably related to the transfusion, and in 133 cases (7.3%) the imputability was not assessable.

Table 18. Adverse reactions in recipients by imputability level (2021)

Level	Imputability	n.	%
0	Excluded/Improbable	195	10.7
1	Possible	811	44.7
2	Probable	592	32.6
3	Certain	84	4.6
NA	Not Assessable	133	7.3
	Total	**1,815**	**100.0**

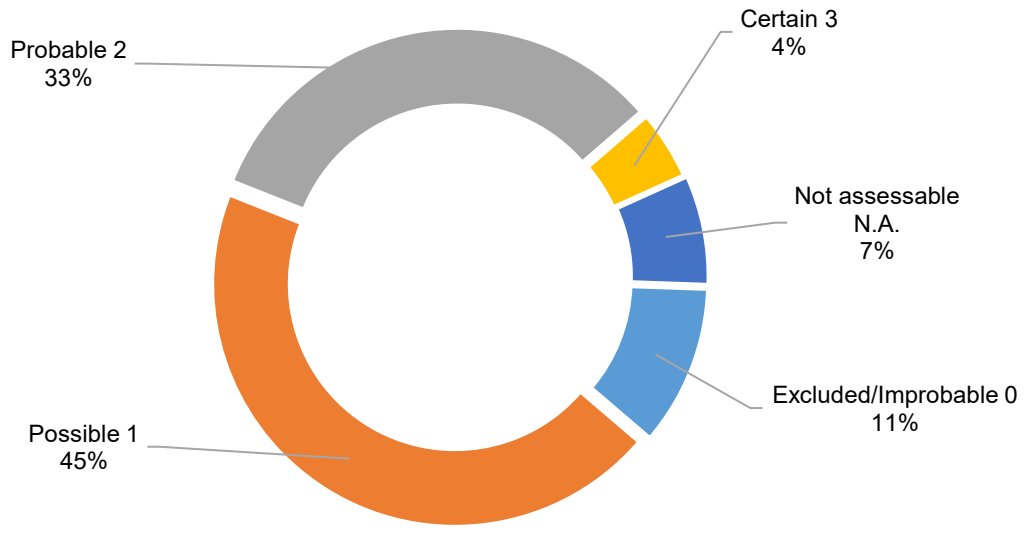


Figure 7. Adverse reactions in recipients linked to the imputability level expressed as a percentage (2021)

Transfusion sites

The majority of adverse reactions occurred in hospital ward (76.6%) or in day-hospital (12.2%) (Table 19 and Figure 8).

Table 19. Transfusion sites notifying adverse reactions (2021)

Transfusion site	n.	%
Hospital ward	1,390	76.6
Day-hospital	224	12.2
Emergency/ICU	110	6.1
Clinic	54	3.0
Operating theatre	23	1.3
Home	14	0.8
Total	**1,815**	**100.0**

ICU: Intensive Care Unit

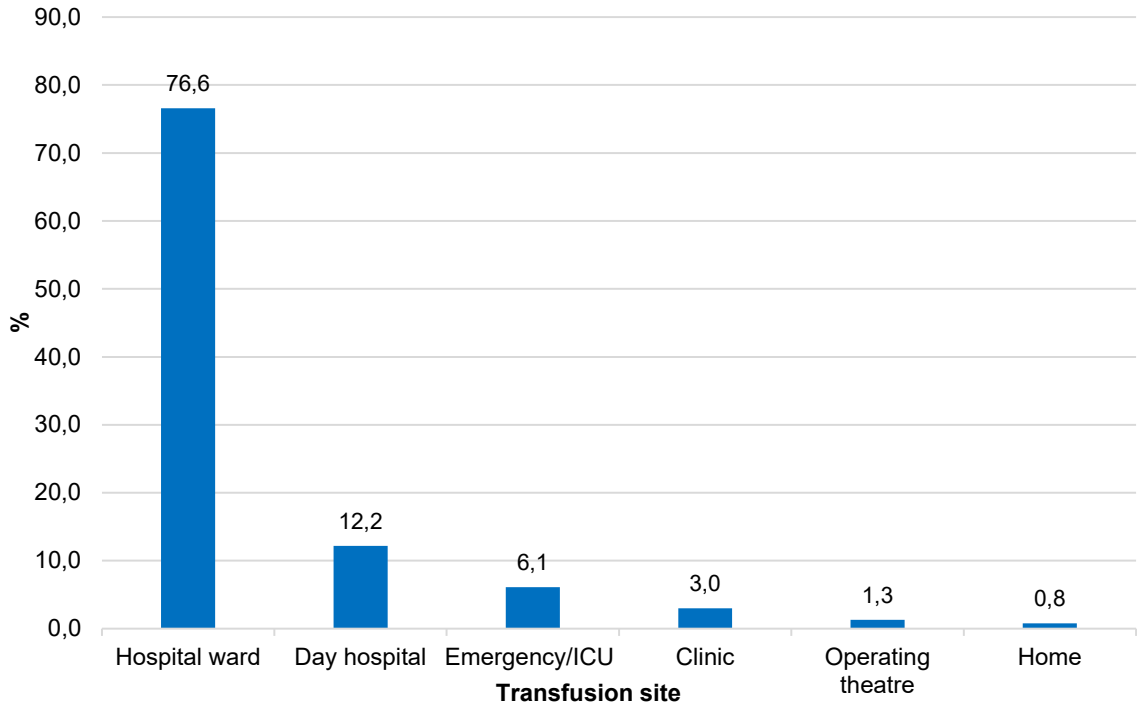


Figure 8. Adverse reactions by transfusion site as a percentage (2021)

Adverse reactions classified by transfused blood component

Among the notified 1,815 adverse reactions in recipients, most were related to RBC transfusion (65.6%).

In 11 cases it was not possible to relate the adverse reaction to a specific blood component because more than one blood component had been transfused (Table 20).

Table 20. Adverse reactions in recipients classified by transfused blood component (2021)

Blood component	n.	%
Red Blood Cells	1,190	65.6
Platelets	410	22.6
Plasma*	201	11.1
More than one blood component transfused**	11	0.6
Haemopoietic Stem Cells	3	0.2
Total	**1,815**	**100.0**

* Includes Plasma pooled and treated for virus inactivation (13 adverse reactions) and COVID-19 Convalescent Plasma (25 adverse reactions).
** Adverse reactions not ascribable to a specific blood component.

Although the absolute number of adverse reactions linked to the transfusion of RBCs was slightly higher than that linked to the transfusion of platelet concentrates and plasma, if expressed in the number of adverse reactions per every 1,000 units of transfused blood components, the highest incidence is found in platelets concentrate transfusions (Table 21).

In addition, 13 adverse reactions resulting from infused pharmaceutical virus-inactivated plasma equal to 0.1 adverse reactions every 1,000 transfused units and 25 adverse reactions resulting from COVID-19 Convalescent Plasma equal to 1.84 adverse reactions every 1,000 transfused units were notified.

Table 21. Adverse reactions/1,000 transfused units grouped by blood component regardless of the imputability and severity levels (2021)

Blood component	Transfused units	Adverse reactions	Adverse reactions/ 1,000 transfused units
Red Blood Cells	2,413,673	1,190	0.49
Plasma*	221,638	200	0.90
Platelets	236,914	411	1.73

* Plasma includes Plasma pooled and treated for virus inactivation (13 adverse reactions to 112,052 transfused units) and COVID-19 Convalescent Plasma (25 adverse reactions to 13,526 transfused units)

ABO incompatible transfusions

In 2021, 3 cases of ABO-incompatible transfusions were notified as follows:

- 1 case as “Acute haemolytic reaction”;
- 2 cases as “ABO incompatible transfusion” (without acute haemolytic reaction) notified also as “Adverse Event”.

Moreover, 2 cases of ABO-compatible transfusions (wrong recipient transfused due to a wrong identification) and 1 case of Rh incompatible transfusion were notified.

Near misses

In 2021, 193 near miss events, as defined by the EDQM Guide (13), were notified.

The majority of them (72 cases equal to 37.3%) were “wrong patient collected” and “wrong information on the tube label” (94 cases equal to 48.7%) (Table 22).

Types of primary error reported in Table 22 are consistent with the International Haemovigilance Network Database (ISTARE) definitions (14).

Table 22. Near misses (2021)

Type of primary error	Near miss	%
Error in pre-transfusion test	5	2.6
Wrong information on the tube label	94	48.7
Wrong patient collected	72	37.3
Wrong/inappropriate blood component type requested	1	0.5
Avoided transfusion wrong blood component type	21	10.9
Total	**193**	**100.0**

Adverse reactions involving the respiratory and/or cardiovascular system

In 2021, 9.3% of all the notifications (168/1,815) were related to the respiratory system; 68 were allergic reactions involving the respiratory and/or cardiovascular system, 67 TAD, 31 TACO and 2 TRALI of which 6 (0.33%) with a severity level 3-4. Only 1.5% of TAD, 12% of TACO, and none of TRALI were certainly imputable.

Viral infections

In 2021, 3 cases of probable HEV transfusion transmitted infections were notified and classified as follows:

- Case 1: (Severity: 0 - No symptoms; Imputability: Level 2 - Probable).
  One unit of pre-storage leukodepleted RBCs was transfused in a male patient with a malignant brain tumour. The patient did not develop any specific symptom related to HEV infection in the month following the transfusion. The patient's pre-transfusion serological status was unknown. The exams carried out three months after the transfusion were Ab anti-HEV IgG/IgM negative, HEV RNA positive. No information about HEV genotyping was provided avoiding the verification of the homology between the donor's and the recipient's virus sequences.
- Case 2: (Severity: 0 - No symptoms; Imputability: Level 2 - Probable).
  A male patient with a haematological disease was transfused with pre-storage leukodepleted inactivated platelet pool. The patient did not develop any specific symptom related to HEV infection. In the month following the transfusion, a transient increase in transaminase was reported. The patient's pre-transfusion serological status was unknown. The exams carried out three months after the transfusion were Ab anti-HEV IgG/IgM positive, HEV RNA positive.
  No information about HEV genotyping was provided avoiding the verification of the homology between the donor's and the recipient's virus sequences.
- Case 3: (Severity: 0 - No symptoms; Imputability: Level 2 - Probable).
  A female patient with a haematological disease was transfused with pre-storage leukodepleted inactivated platelet pool. The patient did not develop any specific symptom related to HEV infection. In the month following the transfusion, a transient increase in transaminase was reported. The patient's pre-transfusion serological status was unknown. The exams carried out three months after the transfusion were Ab anti-HEV IgG/IgM positive, HEV RNA positive.
  No information about HEV genotyping was provided avoiding the verification of the homology between the donor's and the recipient's virus sequences.
  The same donor was implicated in the 3 probable transfusion transmitted infections donating whole blood processed in RBC, platelet and plasma. The single platelet unit

entered in the composition of the platelet pool split in two sub-units and was transfused in two of the three patients. The donor was temporary deferred and tested again one year after the donation showing positive Ab anti-HEV IgG/IgM and negative HEV RNA results.

Bacterial infections

1. *Transfusion Transmitted Serratia marcescens Infection:* (Severity: Level 2 - Symptoms requiring therapeutic intervention; Imputability: Level 1 - Possible; Complete resolution within few days).
   A male patient with a haematological disease was transfused with one unit of pre-storage leukodepleted inactivated with psoralens platelets. During the transfusion, the patient developed chills, cyanosis, fever, hypertension, and tachypnoea with complete resolution after symptomatic therapy. The transfused unit culture turned out to be positive to *Serratia marcescens*.
2. *Klebsiella pneumoniae multiresistent infection*: (Severity: Level 2 - Symptoms requiring therapeutic intervention; Imputability: Level 1 - Possible; Complete resolution within few days).
   A male patient with postoperative anaemia after orthopaedic surgery with positive blood culture for *Ochrobactrum anthropic* and surgical wound swab positive for *Klebsiella pneumonaie* was transfused with one unit of pre-storage leukodepleted RBCs. About 30 minutes after the transfusion, the patient had hyperpyrexia associated with shaking chill. The blood culture reported that the patient was positive to multiresistant *Klebsiella pneumoniae* (different strain from *Klebsiella pneumonaie* previously found in wound swab). No information about exams on the transfused unit was provided.

Deaths

In 2021, 3 cases of death were notified:

– Case 1: the case was excluded/unlikely imputable to the RBCs transfused unit. Cardiovascular arrest occurred in an 82-year-old male cardiopathic patient receiving one unit of pre-storage leukodepleted RBCs for severe anaemia.
– Case 2: the imputability to the transfusion was notified as “not assessable”. Death occurred in a 90-year-old male patient with COVID-19 severe disease. The patient, who was enrolled in an experimental study, received two units of COVID-19 convalescent plasma. Death was related to the progression of COVID-19 disease.
– Case 3: the imputability to the transfusion was notified as “not assessable”. Death occurred in an 86-year-old female patient with COVID-19 severe disease. The patient, who was enrolled in an experimental study, received one unit of COVID-19 convalescent plasma. Death was related to the progression of COVID-19 disease.

Adverse reactions in donors

In 2021, 8,454 adverse reactions to allogeneic donation were notified (1 every 357 donations) (Table 23); 343 of these reactions were severe (1 every 8,808 donations). Autologous donations were excluded from the analysis. Table 23 shows the number of adverse reactions in donors and their related percentage while Table 24 shows them by severity level.

Table 23. Adverse reactions in donors (2021)

Adverse reaction	n.	%
Immediate vasovagal reaction	6,571	77.74
Immediate vasovagal reaction with complications	56	0.66
Delayed vasovagal reaction	744	8.80
Delayed vasovagal reaction with complications	13	0.15
Haematoma	705	8.33
Arterial puncture	47	0.56
Cold/shivers	32	0.38
Thrombophlebitis	2	0.02
Incidents tied to vasovagal syndrome	4	0.05
Nerve injury	6	0.07
Nerve injury due to a haematoma	2	0.02
Citrate reactions	63	0.75
Haemolysis	1	0.01
Systemic allergic reaction	2	0.02
Local allergic reaction	2	0.02
Angina pectoris	1	0.01
Other incidents	42	0.50
Other	161	1.90
Total	**8,454**	**100.00**

In 2021, of all notified reactions, 6,242 (73.8%) were mild, 1,869 (22.1%) moderate and only 343 (4.1%) severe. The most frequent type of notified reaction was the immediate vasovagal reaction (77.7%), of which 2.9% (191/6,571) was severe. The most frequent type of severe notified reaction was immediate vasovagal reaction (55.7%, 191/343), haematoma (17.2%, 59/343), and delayed vasovagal reaction (13.7%, 47/343) (Table 24).

Table 24. Adverse reactions to donations classified per severity level (2021)

Adverse reaction	Mild	%	Moderate	%	Severe	%
Immediate vasovagal reaction	4,916	78.76	1,464	78.33	191	55.69
Immediate vasovagal reaction with complications	25	0.40	22	1.18	9	2.62
Delayed vasovagal reaction	490	7.85	207	11.08	47	13.70
Delayed vasovagal reaction with complications	6	0.10	3	0.16	4	1.17
Haematoma	561	8.99	85	4.55	59	17.20
Arterial puncture	0	0.00	43	2.30	4	1.17
Cold/shivers	27	0.43	0	0.00	5	1.46
Thrombophlebitis	0	0.00	0	0.00	2	0.58
Incidents tied to vasovagal syndrome	0	0.00	0	0.00	4	1.17
Nerve injury	4	0.06	1	0.05	1	0.29
Nerve injury due to a haematoma	2	0.03	0	0.00	0	0.00
Citrate reactions	30	0.48	23	1.23	10	2.92
Haemolysis	0	0.00	0	0.00	1	0.29
Systemic allergic reaction	0	0.00	0	0.00	2	0.58
Local allergic reaction	2	0.03	0	0.00	0	0.00
Angina pectoris	0	0.00	0	0.00	1	0.29
Other incidents	35	0.56	6	0.32	1	0.29
Other	144	2.31	15	0.80	2	0.58
Total (%)	**6,242 (73.8)**	**100.00**	**1,869 (22.1)**	**100.00**	**343 (4.1)**	**100.00**

In 2021, of all notified reactions, 6,252 (74%) were related to whole blood donations and 2,202 (26%) were related to apheresis donations.

The most frequent type of notified reaction related to whole blood donations and to apheresis donations was the immediate vasovagal reaction (81.3% and 67.6% respectively).

If the absolute number of adverse reactions are compared to the total number of donation procedures, there are more adverse reactions related to whole blood donations than to apheresis donations (6,252 against 2,202).

Nevertheless, if expressed in the number of adverse reactions per every 1,000 donation procedures, the highest incidence is linked to apheresis donation (4.8 against 2.4/1,000 donations) (Table 25).

These figures are in line with those of previous years.

Table 25. Adverse reactions to donations classified per donation procedure (2021)

Donation procedure			Adverse reactions			Adverse reactions/ 1,000 donation procedures		
Whole blood	***Apheresis***	***Total***	***Whole blood***	***Apheresis***	***Total***	***Whole blood***	***Apheresis***	***Total***
2,566,235	454,908	3,021,143	6,252	2,202	8,454	2.4	4.8	2.8

Considering only the 343 severe adverse reactions, there were more adverse reactions related to whole blood donations than to apheresis donations (247 against 96).

Nevertheless, if expressed in the number of adverse reactions per every 1,000 donation procedures, the highest incidence was linked to the apheresis donation (0.10 against 0.21/1,000 donations) (Table 26).

Table 26. Severe adverse reactions to donations classified per donation procedure (2021)

Donation procedure			Severe adverse reactions			Severe adverse reactions/ 1,000 donation procedures		
Whole blood	***Apheresis***	***Total***	***Whole blood***	***Apheresis***	***Total***	***Whole blood***	***Apheresis***	***Total***
2,566,235	454,908	3,021,143	247	96	343	0.10	0.21	0.11

Adverse events

In 2021, 25 adverse events were notified; the majority (44%) was due to human error whereas 40% to organisational error, 8% to equipment malfunction and 4% to material defect (Table 27 and Figure 9).

Table 27. Cause of adverse events (2021)

Cause	n.	%
Material defect	1	4
Equipment malfunction	2	8
Human error	11	44
Organisational error	10	40
Other	1	4
Total	**25**	**100**

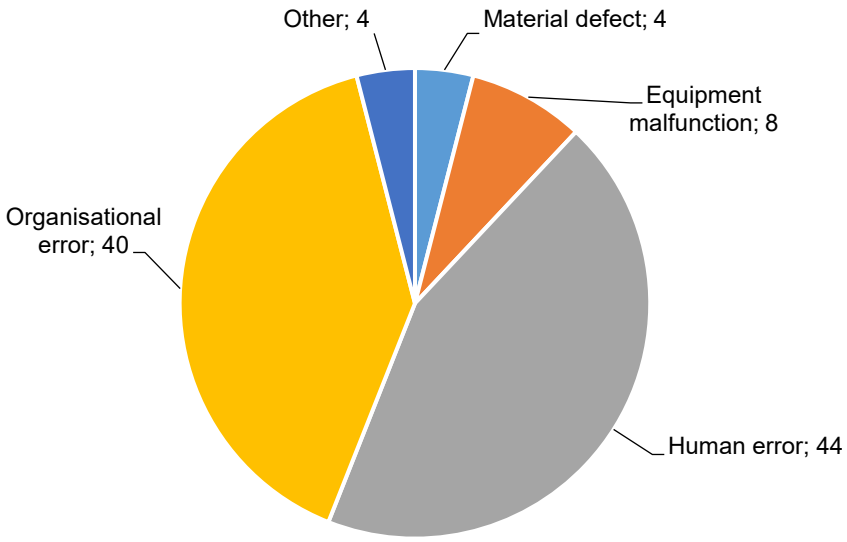


Figure 9. Cause of adverse events (2021)

For the majority of the adverse events (about 56%) the phase was not reported and they were notified as "Other" (Table 28 and Figure 10).

Table 28. Phases in which adverse events occurred (2021)

Phase	n.	%
Collection	2	8
Distribution	9	36
Other	14	56
Total	**25**	**100**

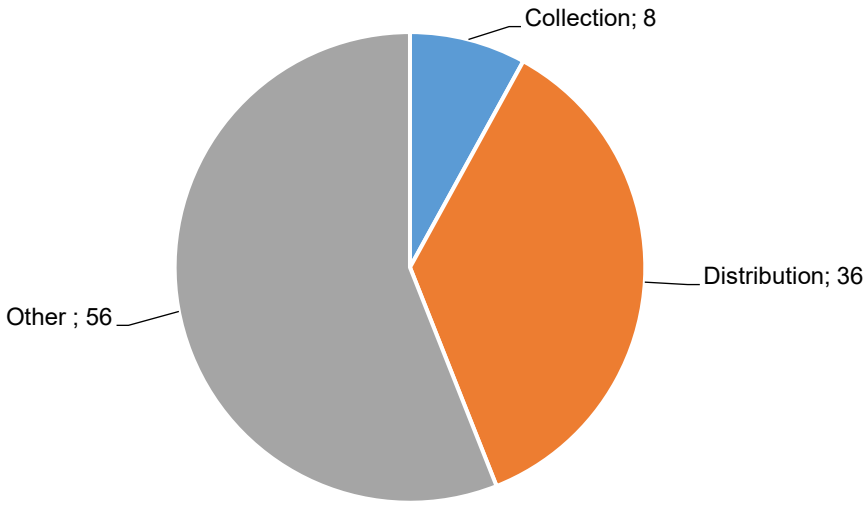


Figure 10. Phases in which adverse events occurred (2021)

In 2021, the majority of the adverse events (56%) occurred in clinical wards and 32% in BEs (Table 29 and Figure 11).

Table 29. Adverse events classified by site of the occurrence (2021)

Site	n.	%
BE	8	32
Clinical ward	14	56
Other	3	12
Total	**25**	**100**

BE: Blood establishment

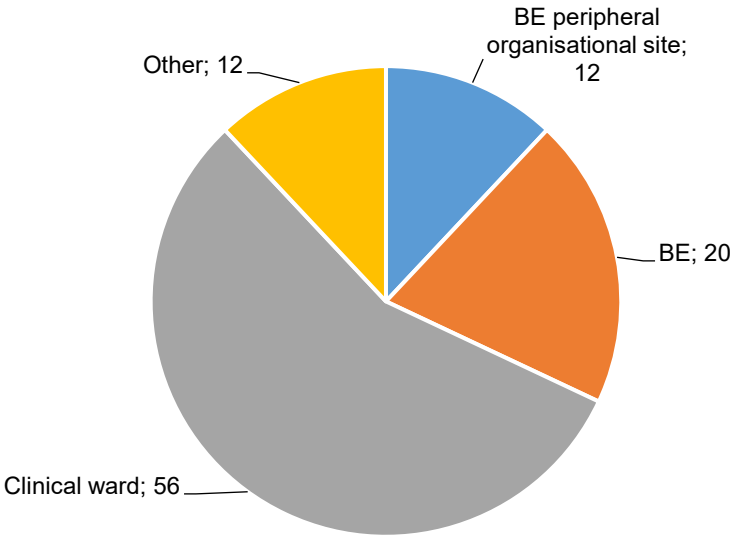


Figure 11. Site in which adverse events occurred (2021).
BE: Blood establishment

Comments and recommendations

The analysis of the 2021 haemovigilance data confirms that, as in the previous year (6) and considering all the imputability and severity levels, the most frequent adverse reactions to transfusion are FNHTR (40.4%) and allergic reactions with only mucosal and cutaneous symptoms (28.4%).

Among the 1,815 adverse reactions to transfusion, 676 were with a high imputability level (imputability level 2-3).

There were 3 cases of ABO-incompatible transfusions, 1 of which was notified as “Acute haemolytic reaction”.

Moreover, 2 cases of ABO-compatible transfusions (wrong recipient transfused due to a wrong identification) and 1 case of Rh incompatible transfusion were notified.

The above-mentioned events were caused by an error or deviation from standard procedures or policies.

Root cause analysis of these events has been carried out to highlight and resolve these system failures. Monitoring and reporting this type of event is important so that suitable preventive measures can be adopted.

In 2021, reactions involving the respiratory system were the 9.3% of all the notifications, of which 68 were allergic reactions involving the respiratory and/or cardiovascular system, 67 TAD, 31 TACO and 2 TRALI.

Although data from scientific literature show variable frequency regarding these adverse reactions associated to several factors (definitions, diagnostic criteria, study population and type of haemovigilance system adopted (active or passive), the unsatisfied quality of TACO and TRALI notifications on SISTRA and of several cases of TAD notified with a low imputability level suggests that, as far as the haemovigilance is concerned, obtaining useful data for a differential diagnosis is often problematical. Further efforts are necessary to minimise the number of incomplete and low grade imputability notifications.

In 2021, 193 near misses were notified. Errors in patient identification (wrong name on tube and wrong patient sample) were commonly reported.

The above-mentioned near misses are errors or deviations from standard procedures or policies or poor practices. Root cause analysis of near miss events should be carried out to highlight and resolve these system failures.

The improvement of near miss reporting is important to support learning from the errors and adopting preventive measures.

In 2021, 8,454 adverse reactions to allogeneic donation were notified. Of all notified reactions, 73.8% were mild, 22.1% moderate, and only 4.1% severe. The most frequent type of notified reactions was immediate vasovagal reaction (77.7%), of which 2.9% (191/6,571) severe.

There were more adverse reactions related to apheresis donation than to whole blood donation.

A final comment concerns the low number of the adverse events notified on SISTRA (overall 25) that, in most cases, were notified without the detail of the specific phase in which the event occurred and notified as “Other”. As in the previous year (6), the number of notifications shows a significant regional variability.

Transfusion transmitted infections in Italy: blood donors’ epidemiological surveillance

The epidemiological surveillance of blood transfusion transmitted infections is the indispensable tool for assessing the safety of donated blood and blood components (11-12).

By means of SISTRA, the CNS monitors the national epidemiological situation of blood donors and the efficiency of analytical systems used in biological qualification activities.

The collected epidemiological data are related to the donor category (*first time and repeat tested*), and to the possible infectious risk factors.

The collected information refers to donors who tested positive to the mandatory tests for the purpose of qualifying blood and blood components (8).

The following serological tests are performed: hepatitis B virus surface antigen (HBsAg), anti-Human Immunodeficiency Virus 1-2 antibodies (HIV1-2 Ab) and the HIV antigen, antibodies against hepatitis C virus (HCV Ab) and anti-*Treponema pallidum* (TP). The Nucleic Acid Test (NAT) make it possible to detect the presence of Hepatitis C virus (HCV) RNA, HIV 1-2 (HIV 1-2 RNA) and Hepatitis B virus (HBV) DNA.

This information is extremely useful for:
- monitoring the epidemiological progress of transfusion transmitted diseases in donors;
- identifying behaviours related to the condition of illness and groups at risk;
- detecting at national and regional level the frequency of transfusion-transmissible infections;
- evaluating the effectiveness over time of intervention programmes and tools to prevent the spread of transfusion-transmissible diseases.

In this section of the report all essential data relative to 2021 are reported.

Materials and methods

SISTRA records the infections detected in blood donors. Notifications are compiled on the information system directly by the BE or the RBCC through the regional information systems.

For better comparability, some data are reported per 1,000 donors (‰) and the incidence and prevalence values are multiplied by a k-factor that corresponds to 100,000 donors.

Definitions

The definitions and indices used for the epidemiological surveillance of blood donors and blood components are both entirely based on what is set forth in the Italian law in force regarding blood transfusion (8) and compliant with the document issued by the European Medicines Agency (EMA) "Guideline on epidemiological data on blood transmissible infections" (15).

The definitions of the principal terms used in the document are:
- *First-time tested donor (FT)*
  Person whose blood/plasma is tested for the first time for infectious disease markers (with or without donation) without evidence of prior testing in a given blood system.
- *Repeat tested donor (RT)*
  Person whose blood/plasma has been tested previously for infectious disease markers in a given blood system. It should be noted that the number of RT and FT donors, reported in this report, and notified on SISTRA by the competent regional authorities, is obtained according to blood donor definitions provided by the national legislation (8).
- *Positive donor*
  A donor (*first-time tested* or *repeat tested donor*) repeatedly reactive in serological and molecular screening tests, as set out in Annex IV to the Ministerial Decree of November 2nd, 2015 and confirmed as positive according to the procedures set out in Annex VIII to the above-mentioned Decree (9).
- *Risk factor*
  Behaviour or condition that exposes the donor to the risk of contracting transfusion-transmissible infections. The risk factors considered here are predefined within SISTRA. For the positive donor, one or more factors considered likely to be the source of infection can be indicated.
- *Screening test*
  Serological or molecular test used for the biological qualification of blood and blood components.
- *Confirmatory test*
  Serological test confirming the repeatedly reactive test used to verify a positive result detected in the screening test.

– *Prevalence*
Measurement of the frequency of infection detected at a specified point in time or over a specified period in a defined population. In the context of donor population studies, the prevalence can be calculated in *first time tested* donors as follows:

$$Prevalence = \frac{N.positive\ FT\ tested\ donors\ in\ a\ specified\ period}{Total\ N.FT\ tested\ donors\ in\ the\ same\ specified\ period} \cdot k$$

where, k is a constant of 10 or a multiple thereof.

– *Incidence*
Rate of new (or newly diagnosed) cases of a disease. It is generally reported as the number of new cases occurring within a period of time (e.g., per month, per year). It is more meaningful when the incidence rate is reported as a fraction of the population at risk of developing the disease (e.g., per 100,000 or per 1,000,000 population).
In the context of donor population studies, the incidence can be calculated in *repeat tested* donors as follows:

$$Incidence = \frac{N.of\ positive\ RT\ donors\ in\ a\ calendar\ year}{Total\ N.of\ RT\ donors\ in\ the\ same\ calendar\ year} \cdot k$$

where, k is a constant of 10 or a multiple thereof.

General data

The data come from the information flows starting in the Italian BEs. The BEs notify the infections detected in blood donors to the RBCCs that in turn draft their annual regional report. From January 1st to December 31st 2021, out of a total of 1,863,050 blood donors, 1,213 were tested and turned out to be positive for the currently mandatory infectious disease markers.

Table 30 shows the total number of positive donors by Italian Region, and the number of positive donors per 1,000 tested donors (‰).

The Region with the highest number of positive donors detected was Campania (2.40‰), followed by Apulia (1.76‰) and Latium (1.02‰).

The data shown in Table 30 (positive donors per 1,000 tested donors (‰)) were the same as those shown in Figure 12.

The analysis of the distribution of positive donors by age class shows that positive blood donors are more frequent in the central age classes (36-45, 45-55) (highlighted in grey) (Table 31, column 5).

The data on the incidence of infections by age classes (Table 31, column 6) shows highly significant differences between the observed values ($\chi 2$ value for 5 degrees of freedom = 54.8123, P = 0.000).

Table 32 shows the distribution by age class and gender of the 1,213 positive donors; the number of male positive donors appears to be on average 3 times higher than the number of female positive donors (Figure 13).

Considering the number of infections detected in the total number of donors (‰ tested donors) for each age class, the biggest difference in the number of infections between males and females was found in the 18-25, 26-35, 56-65 and over 65 age classes, while it was reduced in the 36-45 and 46-55 age class (Figure 14).

Table 30. Tested donors and positive donors to infectious markers at national and regional level (2021)

Region/AP (Autonomous Province)	Tested donors	Positive donors	
	n.	n.	‰
Aosta Valley	3,794	0	0.00
Piedmont	123,202	59	0.48
Liguria	49,010	37	0.75
Lombardy	298,825	103	0.34
AP of Trento	21,436	11	0.51
AP of Bolzano	18,027	1	0.06
Friuli Venezia Giulia	47,639	1	0.02
Veneto	176,955	33	0.19
Emilia Romagna	164,969	66	0.40
Tuscany	138,833	49	0.35
Umbria	27,619	10	0.36
Marche	54,157	21	0.39
Latium	142,120	145	1.02
Sardinia	56,469	24	0.43
Abruzzo	39,764	4	0.10
Campania	134,895	324	2.40
Molise	9,177	0	0.00
Apulia	122,844	216	1.76
Basilicata	20,095	4	0.20
Calabria	47,837	27	0.56
Sicily	164,028	78	0.48
Armed Forces	1,355	0	0.00
Italy	**1,863,050**	**1,213**	**0.65**

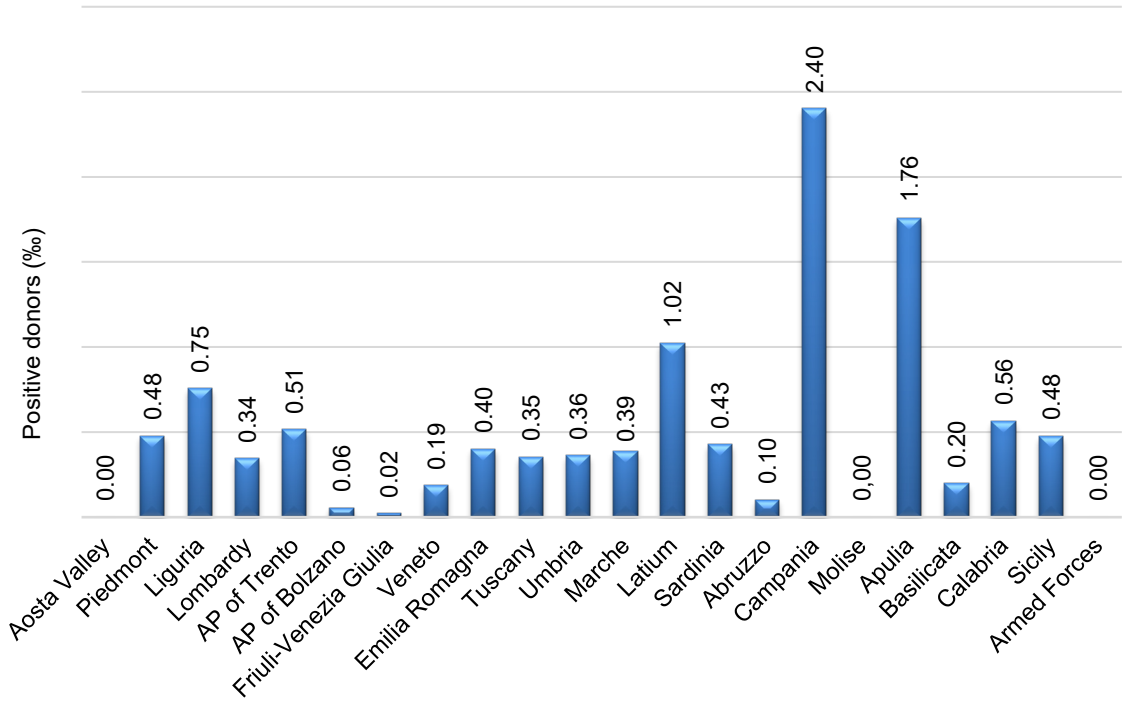


Figure 12. Positive donors per 1,000 tested donors (‰) by Italian Regions (2021)

Table 31. Positive donor by age class (2021)

Age class	Total donors		Positive donors		
	n.	%	n.	%	‰
18-25	259,113	13.9	95	7.8	0.37
26-35	343,546	18.4	190	15.7	0.55
36-45	419,925	22.5	307	25.3	0.73
46-55	525,844	28.2	374	30.8	0.71
56-65	291,746	15.7	234	19.3	0.80
over 65	22,876	1.2	13	1.1	0.57
Total	**1,863,050**	**100**	**1,213**	**100**	**0.65**

The blood donor age classes with the highest frequency of positivity (36-45, 45-55) are highlighted in gray

Table 32. Positive donors by age class and gender (2021)

Age class	Male				Female			
	donors		positive donors		donors		positive donors	
	n.	%	n.	%	n.	%	n.	%
18-25	134,224	11.1	73	8.1	124,889	19.3	22	7.0
26-35	212,090	17.5	149	16.6	131,456	20.3	41	13.1
36-45	284,512	23.4	221	24.6	135,413	20.9	86	27.4
46-55	360,473	29.7	263	29.3	165,371	25.5	111	35.4
56-65	205,621	16.9	182	20.2	86,125	13.3	52	16.6
over 65	17,457	1.4	11	1.2	5,419	0.8	2	0.6
Total	**1,214,377**	**100.0**	**899 (74%)**	**100.0**	**648,673**	**100.0**	**314 (26%)**	**100.0**

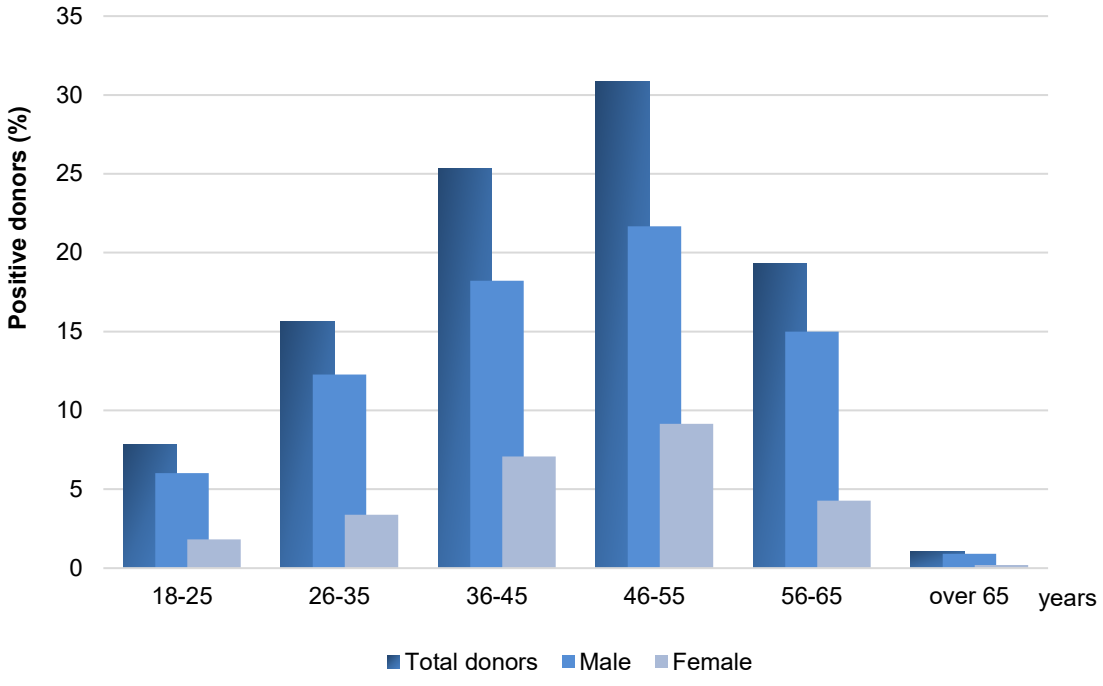


Figure 13. Positive donors (total, male and female donors) by age class (%) (2021)

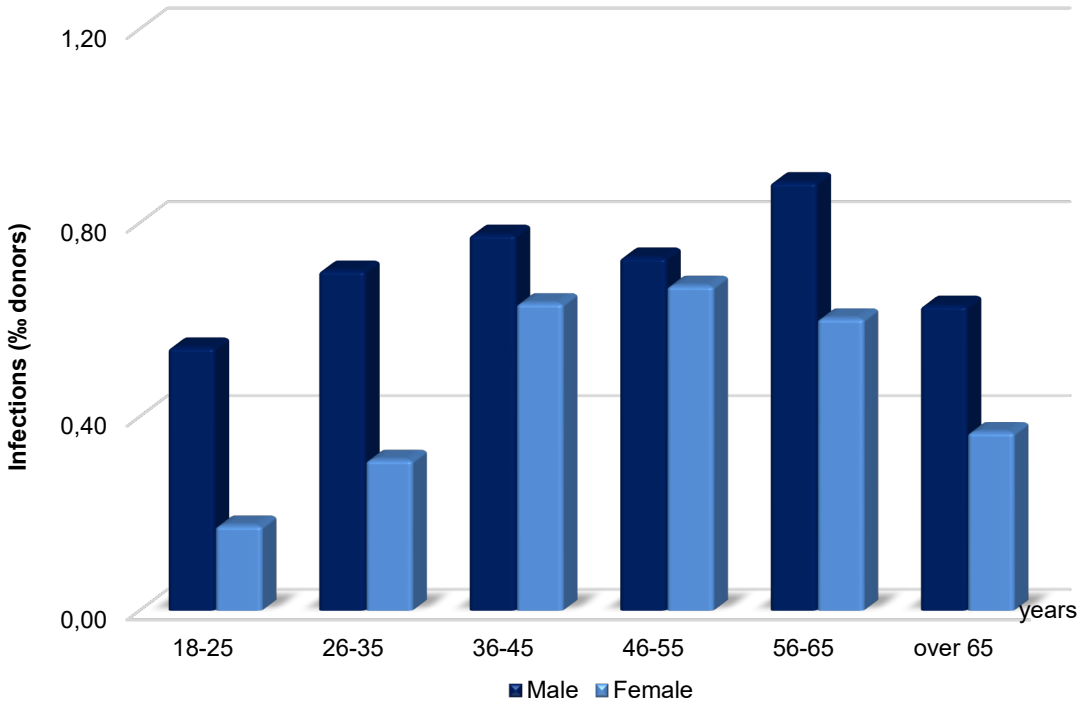


Figure 14. Positive donors by age class and gender (‰ total donors) (2021)

Figure 15 shows the percentages of infections observed for each single marker (HIV, HBV, HCV and TP) with the percentage distribution of all donors tested, distributed by age class.

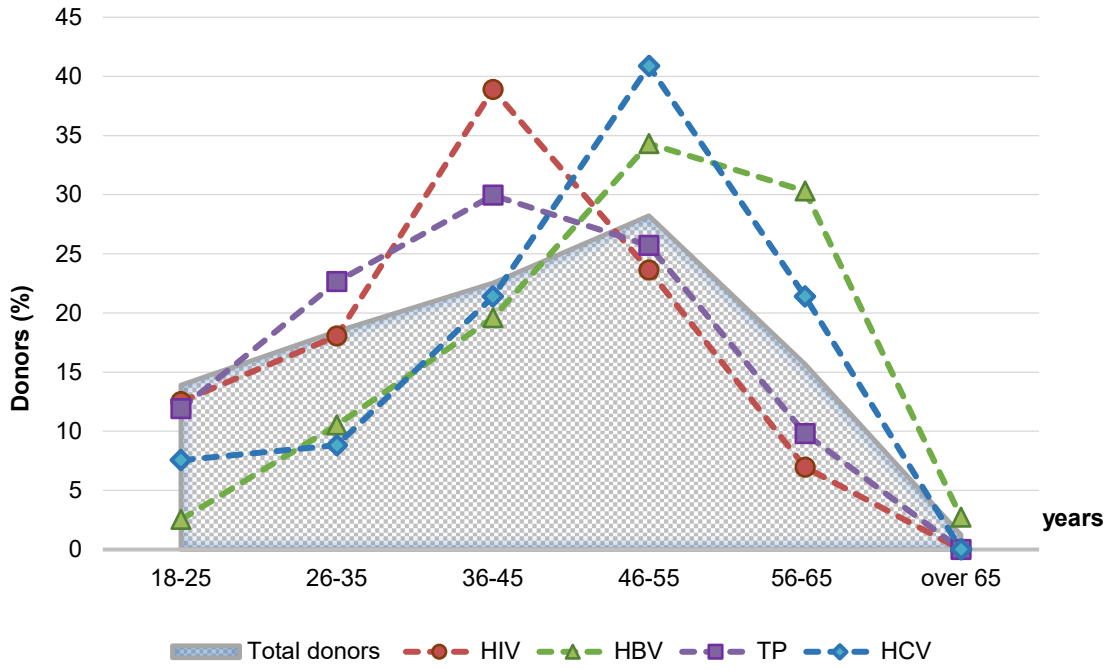


Figure 15. Total donors and HIV, HBV, HCV and TP positive donors by age class (2021)

The results show significant variations in the values between the trend of distribution of tested donors and that of the positive donors for each marker of HIV, TP and HCV infections.

HIV and TP infection are more frequent in the 26-35, 36-45 and 46-55 age classes, with a peak at 36-45; on the contrary, HBV and HCV infections are more frequent respectively in the 36-45, 46-55 and 56-65 age classes, and in the 46-55 and 56-65 age classes, both with a peak at 46-55.

The number of positive donors changed significantly also in relationship with the category (Table 33). In fact, it emerged that 2.2‰ of FT donors were positive to one of the infectious markers compared to 0.2‰ of RT donors (Table 34).

Figure 16 shows the same data reported in Table 34.

Table 33. Positive donors by category (2021)

Donor category	Donors	Positive donors	
	n.	n.	%
First-time tested donors	**400,808**	**865**	**71.31**
Prospective donors (first screening without donation)	178,334	265	21.85
First-time not pre-qualified donors	222,474	600	49.46
Repeat tested donors	**1,462,242**	**348**	**26.69**
First-time pre-qualified donors	123,241	12	0.99
Regular donors	1,339,001	336	27.70
Total donors	**1,863,050**	**1,213**	**100.00**

Table 34. Positive donors per 1,000 (‰) tested donors: distribution by category (2021)

Donor category	Donors	Positive donors	
	n.	n.	‰
First-time tested donors	**400,808**	**865**	**2.16**
Prospective donors (first screening without donation)	178,334	265	1.49
First-time not pre-qualified donors	222,474	600	2.70
Repeat tested donors	**1,462,242**	**348**	**0.24**
First-time pre-qualified donors	123,241	12	0.10
Regular donors	1,339,001	336	0.25
Total donors	**1,863,050**	**1,213**	**0.65**

Table 35 shows the number of FT and RT positive donors in Italy divided by region.

The regions with the highest number of FT and RT positive donors are respectively Campania (4.43‰) and Apulia (1.03‰).

Figure 17 shows the percentage of positive donors by category (FT/RT). On a distribution of 100% positivity for each region, with 50% as the cut-off value (red line in Figure 17), the percentages of FT with respect to RT were evaluated.

In general, with the exception of the Sicily and Friuli-Venezia Giulia regions, for all regions more than 50% of positive donors were FT. The male/female ratio for FT and RT positive donors was about 2:1 (Figure 18).

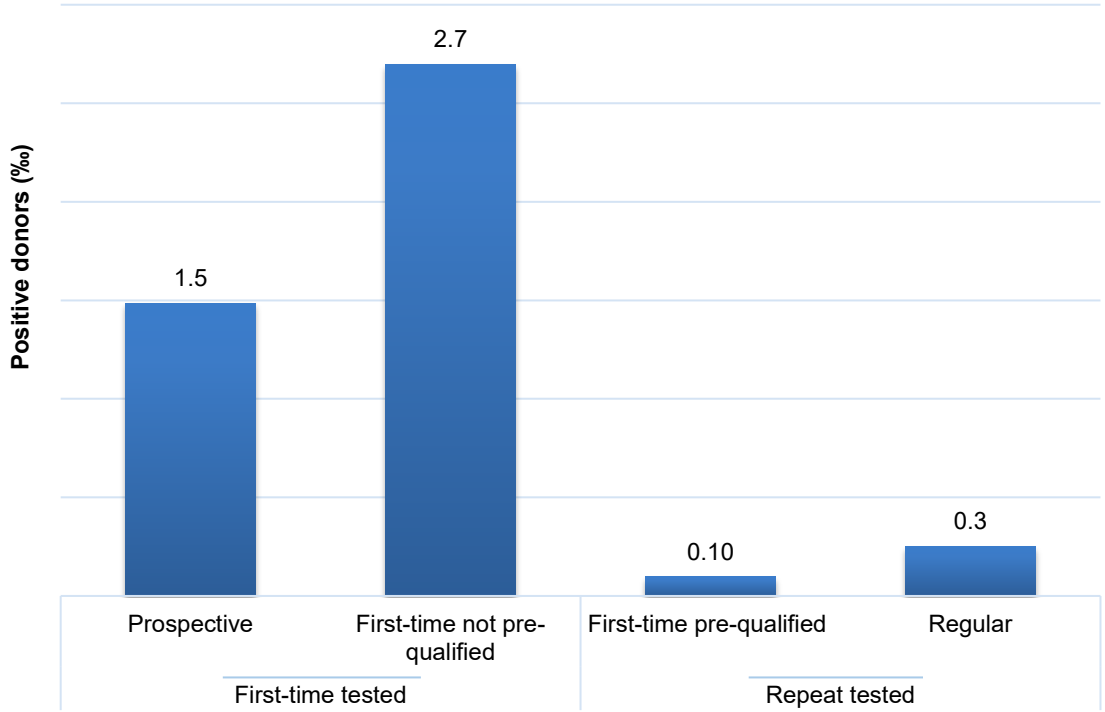


Figure 16. Categories of positive donors (2021)

Table 35. FT and RT positive donors (total and per 1,000 (‰) tested donors) in Italy (2021)

Region/AP	Total of donors		Positive donors			
	FT	RT	FT	RT	FT (‰ FT)	RT (‰ RT)
Aosta Valley	613	3,181	0	0	0.00	0.00
Piedmont	17,042	106,160	37	22	2.17	0.21
Liguria	11,188	37,822	26	11	2.32	0.29
Lombardy	50,404	248,421	56	47	1.11	0.19
AP of Trento	3,210	18,226	9	2	2.80	0.11
AP of Bolzano	1,841	16,186	1	0	0.54	0.00
Friuli Venezia Giulia	10,297	37,342	0	1	0.00	0.03
Veneto	26,720	150,235	24	9	0.90	0.06
Emilia Romagna	23,803	141,166	48	18	2.02	0.13
Tuscany	25,921	112,912	39	10	1.50	0.09
Umbria	6,047	21,572	6	4	0.99	0.19
Marche	8,138	46,019	16	5	1.97	0.11
Latium	49,948	92,172	121	24	2.42	0.26
Sardinia	18,084	38,385	14	10	0.77	0.26
Abruzzo	6,325	33,439	3	1	0.47	0.03
Campania	64,329	70,566	285	39	4.43	0.55
Molise	1,887	7,290	0	0	0.00	0.00
Apulia	28,478	94,366	119	97	4.18	1.03
Basilicata	5,883	14,212	4	0	0.68	0.00
Calabria	7,984	39,853	23	4	2.88	0.10
Sicily	31,899	132,129	34	44	1.07	0.33
Armed Forces	767	588	0	0	0.00	0.00
Italy	**400,808**	**1,462,242**	**865**	**348**	**2.16**	**0.24**

AP Autonomous Province

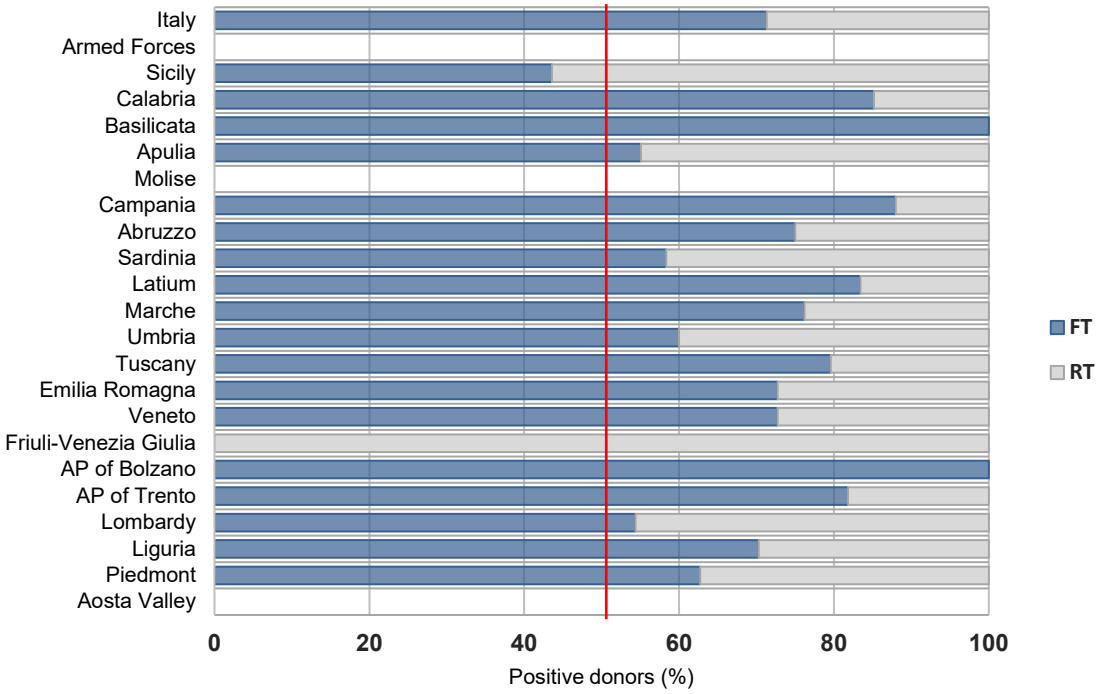


Figure 17. Positive donors by FT and RT category (%) at national and regional level (2021)

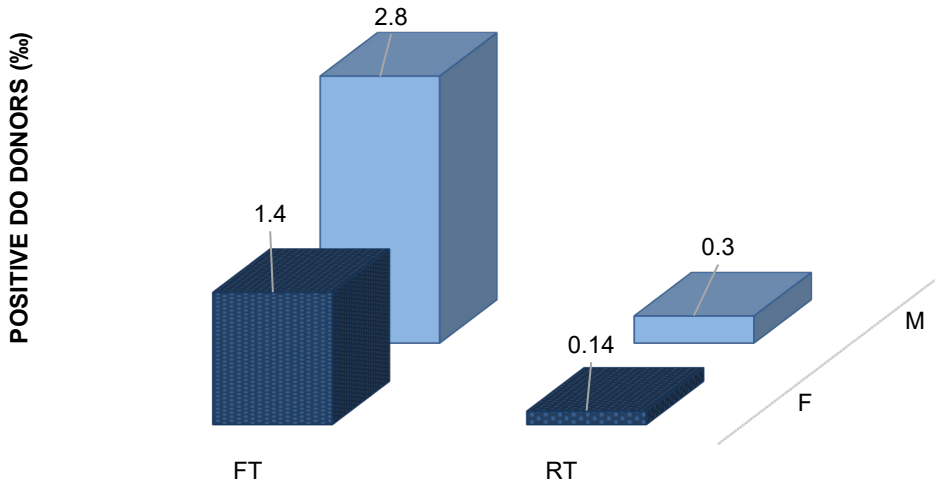


Figure 18. Positive donors by FT and RT category (‰ total male and female donors) and gender (2021)

Figure 19 shows the positive donor distribution at national and regional level for each infectious marker per 100,000 tested donors. The Region with the highest number of all infections was Campania (HIV: 10.4/100,000, HBV: 101.6/100,000, HCV: 33.4/100,000, and TP: 97.1/100,000 tested donors).

These values were from 3 (HIV) to 4 times (HBV) higher compared to the national data.

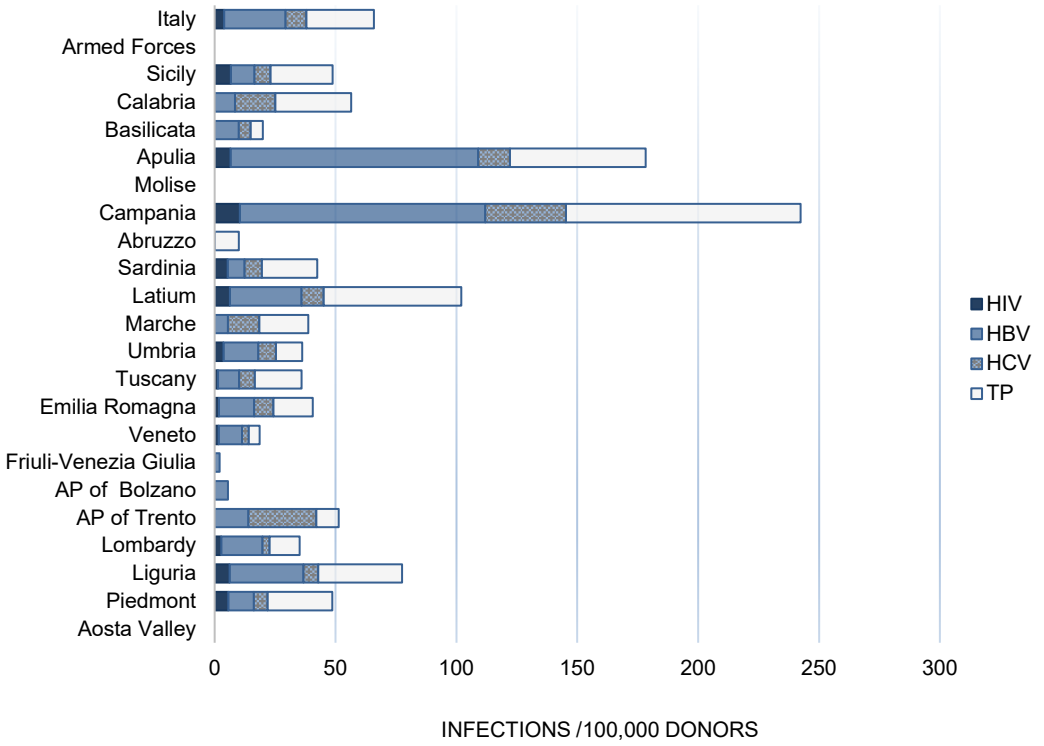
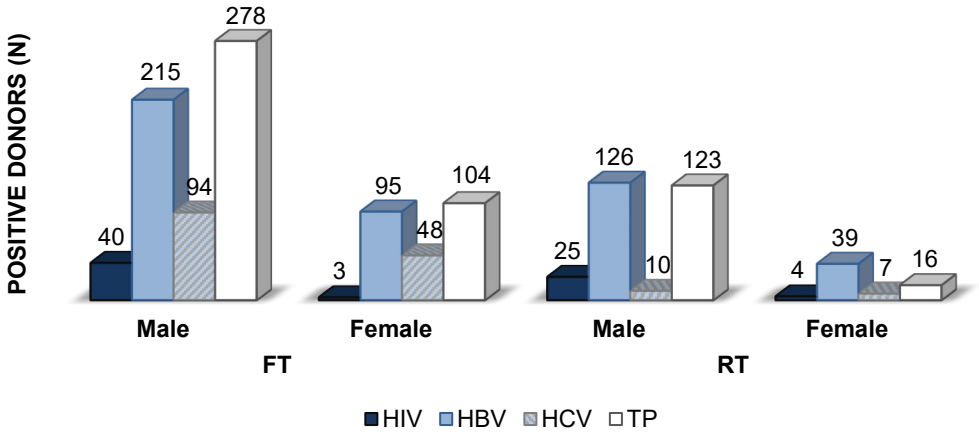


Figure 19. Number of positive donor distribution at national and regional level for each infectious marker per 100,000 donors (2021)

Figure 20 shows the distribution of infections by category (FT/RT), gender and infectious marker. HBV, HCV and TP in FT donors were higher compared to RT both for male and female donors. HIV in FT donors were higher compared to RT for male. The ratio of infections between FT and RT ranges from about 2:1 (HIV) to about 9:1 (HCV).



FT First time tested donors; RT Repeat tested donors

Figure 20. Infections by donor category (FT/RT), gender and infectious marker (2021)

In Tables 36 and 37 data on HIV, HBV, HCV and TP prevalence and incidence at national and regional level are reported.

Table 36. Prevalence by infectious marker/100,000 FT donors (2021)

Region/AP	HIV	HBV	HCV	TP
Aosta Valley	0.0	0.0	0.0	0.0
Piedmont	11.7	64.6	35.2	111.5
Liguria	26.8	89.4	17.9	107.3
Lombardy	7.9	45.6	17.9	43.7
AP of Trento	0.0	62.3	155.8	62.3
AP of Bolzano	0.0	54.3	0.0	0.0
Friuli Venezia Giulia	0.0	0.0	0.0	0.0
Veneto	7.5	44.9	11.2	26.2
Emilia Romagna	4.2	67.2	50.4	84.0
Tuscany	7.7	38.6	30.9	77.2
Umbria	16.5	33.1	16.5	33.1
Marche	0.0	24.6	86.0	86.0
Latium	14.0	70.1	24.0	134.1
Sardinia	5.5	22.1	22.1	27.7
Abruzzo	0.0	0.0	0.0	47.4
Campania	17.1	186.5	66.8	175.7
Molise	0.0	0.0	0.0	0.0
Apulia	10.5	186.1	52.7	175.6
Basilicata	0.0	34.0	17.0	17.0
Calabria	0.0	37.6	100.2	150.3
Sicily	18.8	12.5	18.8	62.7
Armed Forces	0.0	0.0	0.0	0.0
Italy	**10.7**	**77.3**	**35.4**	**95.3**

AP Autonomous Province

Table 37. Incidence by infectious marker/100,000 RT donors (2021)

Region/AP	HIV	HBV	HCV	TP
Aosta Valley	0.0	0.0	0.0	0.0
Piedmont	4.7	1.9	0.9	13.2
Liguria	0.0	13.2	2.6	13.2
Lombardy	1.6	11.3	0.0	6.0
AP of Trento	0.0	5.5	5.5	0.0
AP of Bolzano	0.0	0.0	0.0	0.0
Friuli Venezia Giulia	0.0	2.7	0.0	0.0
Veneto	0.7	3.3	1.3	0.7
Emilia Romagna	1.4	5.7	0.7	5.0
Tuscany	0.0	1.8	0.9	6.2
Umbria	0.0	9.3	4.6	4.6
Marche	0.0	2.2	0.0	8.7
Latium	2.2	7.6	1.1	15.2
Sardinia	5.2	0.0	0.0	20.8
Abruzzo	0.0	0.0	0.0	3.0
Campania	4.3	24.1	2.8	25.5
Molise	0.0	0.0	0.0	0.0
Apulia	5.3	77.4	1.1	20.1
Basilicata	0.0	0.0	0.0	0.0
Calabria	0.0	2.5	0.0	7.5
Sicily	3.8	9.1	3.8	16.7
Armed Forces	0.0	0.0	0.0	0.0
Italy	**2.0**	**11.3**	**1.2**	**9.5**

AP Autonomous Province

The highest incidence value was for HBV (11.3/100,000 RT donors) and TP (9.5/100,000 RT donors) infections (Table 37).

At national level, the highest prevalence value was for TP (95.3/100,000 FT donors), followed by HBV (77.3/100,000 FT donors) (Table 36).

Moreover, it is important to note that in 53% of cases no information on causes of missed deferral of positive donors was reported in SISTRA.

When the cause of missed deferral was reported (47%), in most cases the donor "denied the risk factor" (Figure 21).

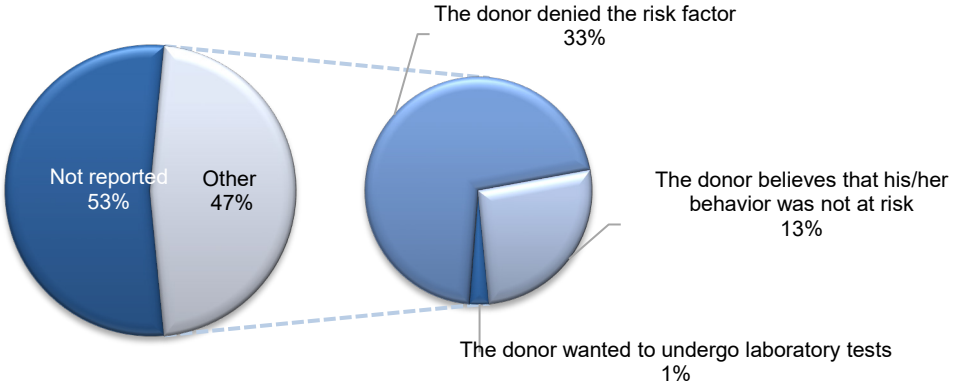


Figure 21. Causes of missed deferral of donor positive to infectious markers (2021)

Table 38 shows the number of donors positive to infectious markers by nationality and category.

Table 38. Positive donors to infectious markers by nationality and category (FT/RT) (2021)

Nationality	Positive donors		FT		RT	
	n.	%	n.	%	n.	%
Italians	952	78.5	621	71.8	331	95.1
Foreigners	261	21.5	244	28.2	17	4.9
Total	**1,213**	**100**	**865**	**100**	**348**	**100.0**

Table 39 shows the distribution of positive donors to infectious markers by geographical area of birth and category (FT/RT). The data shown in Table 38 and Table 39 were the same as those shown in Figure 22.

Table 39. Positive donors to infectious markers by category (FT/RT) and by geographical area of birth (2021)

Geographical area of birth	FT	RT	Total
Africa	50	4	54
America	23	2	25
Asia	21	0	21
Europe	150	11	161
Italy	621	331	952
Total	**865**	**348**	**1,213**

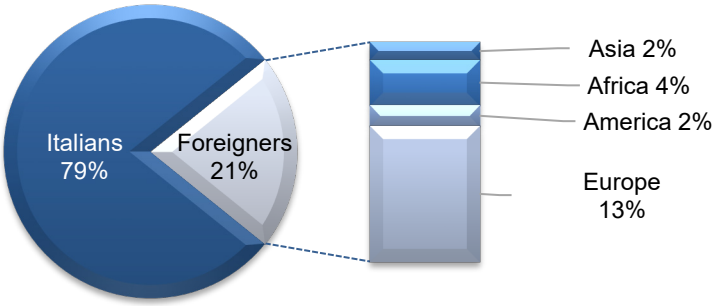


Figure 22. Positive donors to infectious markers by nationality (%) (2021)

HIV surveillance data

Table 40 reports the number of HIV positive donors and the incidence and prevalence by Italian Region and in Italy. In Italy, in 2021, 72 HIV infections were reported, with a prevalence of 10.7 per 100,000 FT donors and an incidence of 2.0 per 100,000 RT donors. The highest number of HIV infections was found in the Campania Region (14 cases). The Region with the highest prevalence was Liguria (26.8) while the Region with the highest incidence was Apulia (5.3).

Table 40. Number, prevalence and incidence of HIV infections per 100,000 donors at national and regional level (2021)

Region/AP	HIV infections		
	n.	prevalence	incidence
Aosta Valley	0	0.0	0.0
Piedmont	7	11.7	4.7
Liguria	3	26.8	0.0
Lombardy	8	7.9	1.6
AP of Trento	0	0.0	0.0
AP of Bolzano	0	0.0	0.0
Friuli-Venezia Giulia	0	0.0	0.0
Veneto	3	7.5	0.7
Emilia Romagna	3	4.2	1.4
Tuscany	2	7.7	0.0
Umbria	1	16.5	0.0
Marche	0	0.0	0.0
Latium	9	14.0	2.2
Sardinia	3	5.5	5.2
Abruzzo	0	0.0	0.0
Campania	14	17.1	4.3
Molise	0	0.0	0.0
Apulia	8	10.5	5.3
Basilicata	0	0.0	0.0
Calabria	0	0.0	0.0
Sicily	11	18.8	3.8
Armed Forces	0	0.0	0.0
Italy	**72**	**10.7**	**2.0**

AP Autonomous Province

Figure 23 shows the distribution, expressed as a percentage, of HIV positive donors by nationality; 11% of all positive donors were foreigners. Table 41 shows the distribution of HIV

positive donors by geographical area of birth. In about 36% of the HIV positive donors (26/72) it was not possible to identify the risk factor; in the remaining 64%, who denied the risk factor or who believed that their behaviour was not at risk or wanted to be tested, the most frequently identified risk factor was occasional exposure (Figure 24).

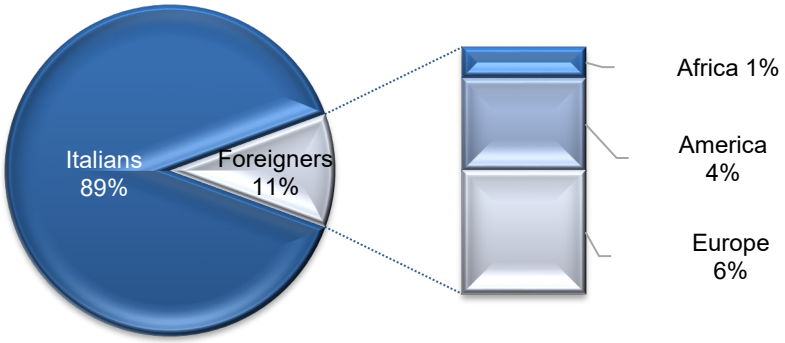


Figure 23. Distribution of HIV positive donors by nationality (%) (2021)

Table 41. HIV infections by geographical area of birth (2021)

Geographical area of birth	n. of infections
Africa	1
America	3
Europe	4
Italy	64
Total	**72**

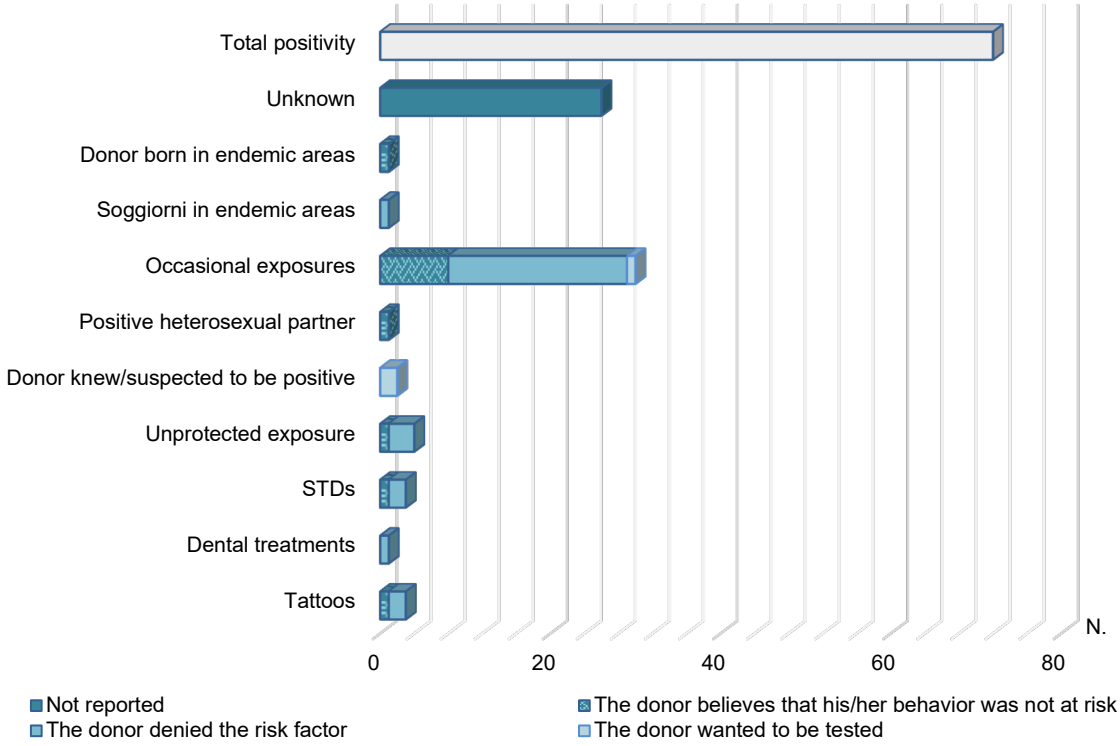


Figure 24. Causes of failed deferral and risk factors detected in HIV positive donors (2021)

Table 42. HIV infections obtained from the different combinations of the results of the individual molecular and serological tests (2021)

Combinations of results			n. of infections
NAT	**SER**	**CONF**	
+	**+**	**+**	61
+	**+**	**-**	3
+	**-**	**-**	1
-	**+**	**+**	2
ND*	**+**	**+**	5
Total			**72**

*NAT unavailable because prospective donors only underwent serological screening tests

Moreover, in most cases (61/72) the molecular (NAT) serological and confirmatory tests were positive; in 2 cases the molecular test was negative with positive serological and confirmatory tests (Table 42).

HCV surveillance data

Table 43 reports the number of HCV positive donors and the incidence and prevalence by Italian Region and in Italy. In Italy, in 2021, 159 HCV infections were reported, with a prevalence of 35.4 infections per 100,000 FT donors and an incidence of 1.2 infections per 100,000 RT donors. The highest number of HCV infections was found in the Campania Region (45). The AP of Trento has the highest HCV prevalence (155.8) and incidence (5.5).

Table 43. Number, prevalence and incidence of HCV infections per 100,000 donors at national and regional level (2021)

Region/AP	HCV nfections		
	n.	**prevalence**	**incidence**
Aosta Valley	0	0,0	0,0
Piedmont	7	35,2	0,9
Liguria	3	17,9	2,6
Lombardy	9	17,9	0,0
AP of Trento	6	155,8	5,5
AP of Bolzano	0	0,0	0,0
Friuli Venezia Giulia	0	0,0	0,0
Veneto	5	11,2	1,3
Emilia Romagna	13	50,4	0,7
Tuscany	9	30,9	0,9
Umbria	2	16,5	4,6
Marche	7	86,0	0,0
Latium	13	24,0	1,1
Sardinia	4	22,1	0,0
Abruzzo	0	0,0	0,0
Campania	45	66,8	2,8
Molise	0	0,0	0,0
Apulia	16	52,7	1,1
Basilicata	1	17,0	0,0
Calabria	8	100,2	0,0
Sicily	11	18,8	3,8
Armed Forces	0	0,0	0,0
Italy	**159**	**35.4**	**1.2**

AP Autonomous Province

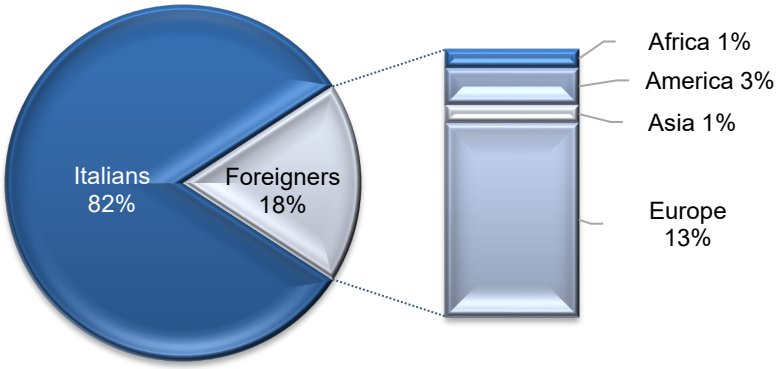


Figure 25. HCV positive donors by nationality (%) (2021)

Table 44. HCV infections by geographical area of birth (2021)

Geographical area of birth	N. of infections
Africa	2
America	4
Asia	2
Europe	21
Italy	130
Total	**159**

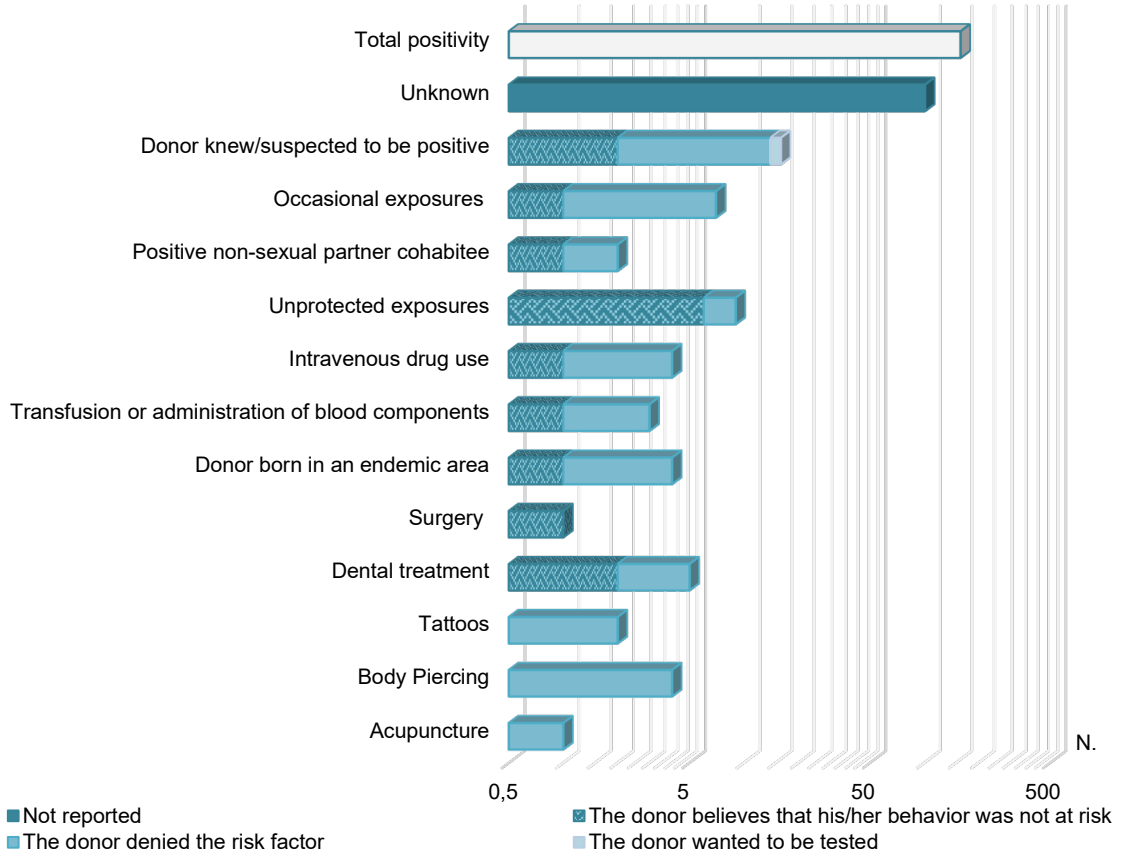


Figure 26. Causes of failed deferral and risk factors detected in HCV positive donors (values reported on a logarithmic scale) (2021)

Figure 25 shows the distribution, expressed as a percentage, of HCV positive donors by nationality; 18% of all positive donors were foreigners. Table 44 shows the distribution of HIV positive donors by geographical area of birth. In about 64% of HCV positive donors (101/159) it was not possible to identify the risk factor. in the remaining 36%, who denied the risk factor or who believed that their behaviour was not at risk or wanted to be tested, the most frequently identified risk factor was donor knew/suspected to be positive (Figure 26). In most cases (64/159), the molecular (NAT), serological and confirmatory tests were positive; in 67 cases the molecular test was negative with a positive serological screening and confirmatory tests. In 25 cases the infection was detected exclusively by means of the serological test (Table 45).

Table 45. HCV infections obtained from the different combinations of the results of the individual molecular and serological tests (2021)

Combinations of results			N. of infections
NAT	**SER**	**CONF**	
+	**+**	**+**	64
-	**+**	**+**	67
+	**+**	**-**	3
ND*	**+**	**+**	25
Total			**159**

* NAT unavailable because prospective donors only underwent serological screening tests

HBV surveillance data

Table 46 reports the number of HBV positive donors and the incidence and prevalence by Italian Region and in Italy.

Table 46. Number, prevalence and incidence of HBV infections per 100,000 donors at national and regional level (2021)

Region/AP	HBV infections		
	n.	**prevalence**	**incidence**
Aosta Valley	0	0.0	0.0
Piedmont	13	64.6	1.9
Liguria	15	89.4	13.2
Lombardy	51	45.6	11.3
AP of Trento	3	62.3	5.5
AP of Bolzano	1	54.3	0.0
Friuli Venezia Giulia	1	0.0	2.7
Veneto	17	44.9	3.3
Emilia Romagna	24	67.2	5.7
Tuscany	12	38.6	1.8
Umbria	4	33.1	9.3
Marche	3	24.6	2.2
Latium	42	70.1	7.6
Sardinia	4	22.1	0.0
Abruzzo	0	0.0	0.0
Campania	137	186.5	24.1
Molise	0	0.0	0.0
Apulia	126	186.1	77.4
Basilicata	2	34.0	0.0
Calabria	4	37.6	2.5
Sicily	16	12.5	9.1
Armed Forces	0	0.0	0.0
Italy	**475**	**77.3**	**11.3**

In Italy, in 2021, 475 HBV infections were reported, with a prevalence of 77.3 infections per 100,000 FT donors and an incidence of 11.3 infections per 100,000 RT donors.

The highest number of HBV infections was found in the Campania Region (137).

The Region with the highest prevalence (186.5) was Campania.

The Region with the highest incidence (77.4) was Apulia. Figure 27 shows the distribution, expressed as a percentage, of HBV positive donors by nationality; 30% of all positive donors were foreigners.

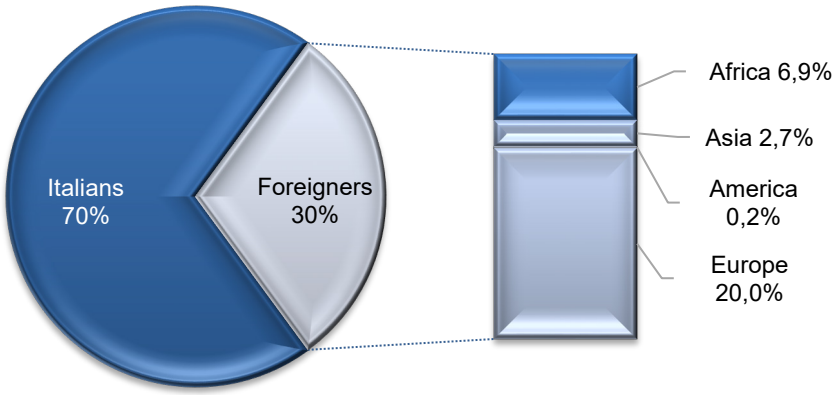


Figure 27. HBV positive donors by nationality (%) (2021)

Table 47 shows the distribution of HIV positive donors by geographical area of birth.

In about 64% of the HBV positive donors (302/475) it was not possible to identify the risk factor.

Table 47. HBV infections by geographical area of birth (2021)

Geographical area of birth	N. of infections
Africa	33
America	1
Asia	13
Europe	95
Italy	333
Total	**475**

In the remaining 36%, who denied the risk factor or who believed that their behaviour was not at risk or wanted to be tested, the most frequently identified risk factors were donor born in an endemic area and unprotected exposure (Figure 28).

Moreover, in most cases (240/475), both the molecular test (NAT) and the serological tests were positive; in 189 cases the infection was detected exclusively by means of the NAT test (NAT only); in 38 cases the infection was detected exclusively by means of the serological and confirmatory tests (Table 48).

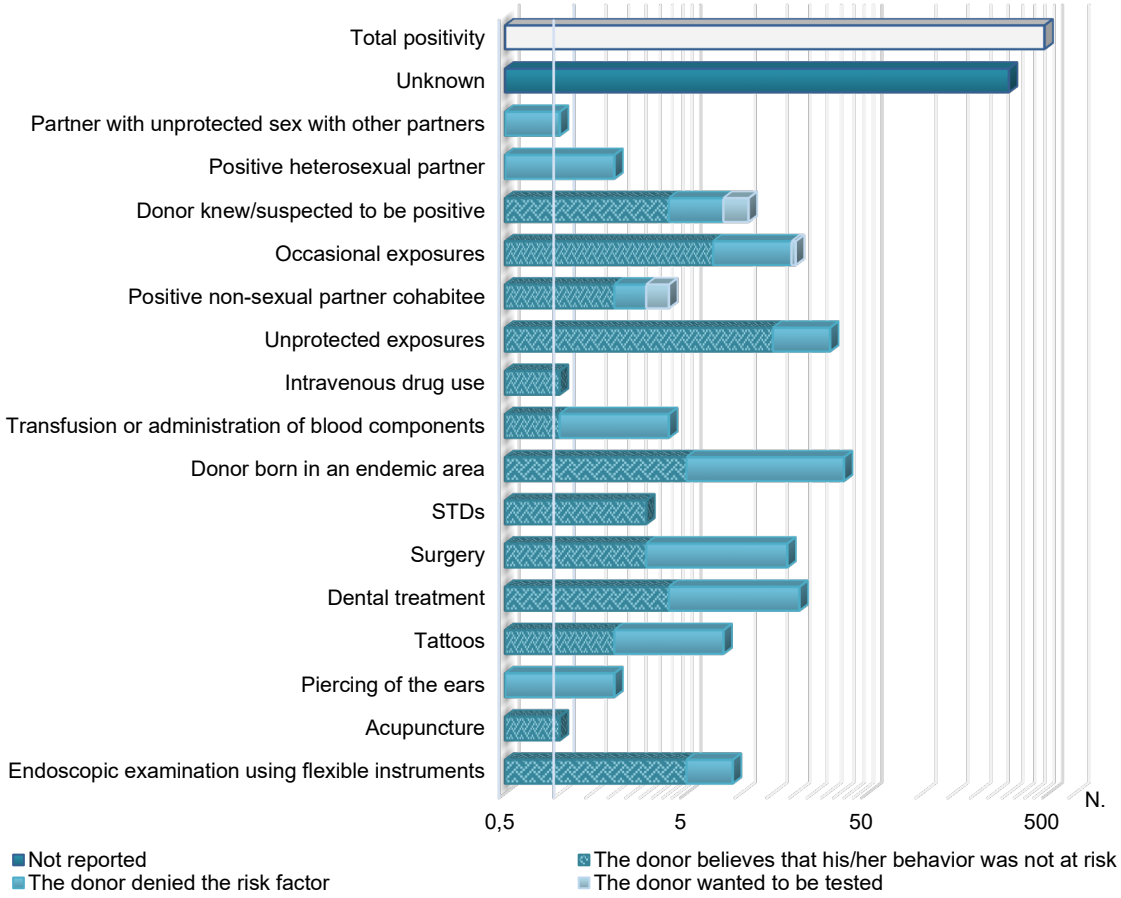


Figure 28. Causes of failed deferral and risk factors detected in HBV positive donors (values reported on a logarithmic scale) (2021)

Table 48. Number of HBV infections obtained from different combinations of the results of individual molecular and serological tests (2021)

Combinations of results			n. of infections
NAT	**SER**	**CONF**	
+	+	+	240
+	+	-	3
+	-	-	189
+	-	+	5
-	+	+	17
ND*	+	+	21
	Total		**475**

*NAT unavailable because prospective donors only underwent serological screening tests

TP surveillance data

Table 49 reports the number of TP positive donors and the incidence and prevalence by Italian Region and in Italy. In Italy, in 2021, 521 TP infections were reported, with a prevalence of 95.3 infections per 100,000 FT donors and an incidence of 9.5 infections per 100,000 RT donors.

Table 49. Number, prevalence and incidence of TP infections per 100,000 donors at national and regional level (2021)

Region/AP	TP infections		
	n.	prevalence	incidence
Aosta Valley	0	0.0	0.0
Piedmont	33	111.5	13.2
Liguria	17	107.3	13.2
Lombardy	37	43.7	6.0
AP of Trento	2	62.3	0.0
AP of Bolzano	0	0.0	0.0
Friuli Venezia Giulia	0	0.0	0.0
Veneto	8	26.2	0.7
Emilia Romagna	27	84.0	5.0
Tuscany	27	77.2	6.2
Umbria	3	33.1	4.6
Marche	11	86.0	8.7
Latium	81	134.1	15.2
Sardinia	13	27.7	20.8
Abruzzo	4	47.4	3.0
Campania	131	175.7	25.5
Molise	0	0.0	0.0
Apulia	69	175.6	20.1
Basilicata	1	17.0	0.0
Calabria	15	150.3	7.5
Sicily	42	62.7	16.7
Armed Forces	0	0.0	0.0
Italy	**521**	**95.3**	**9.5**

Autonomous Provinces

The highest number of TP infections was found in the Campania Region (131).

The Region with the highest prevalence (175.7) and incidence (25.5) was Campania. Figure 29 shows the distribution, expressed as a percentage, of the TP positive donors by nationality; 17% of all positive donors were foreigners.

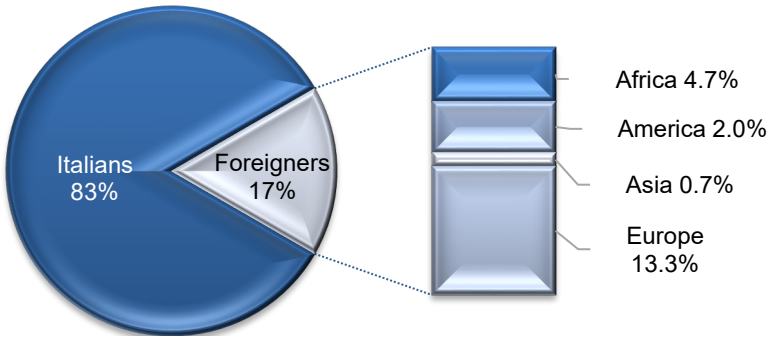


Figure 29. Distribution of TP positive donors by nationality (%) (2021)

Table 50 shows the distribution of TP positive donors by geographical area of birth.

In about 55% of the TP positive donors (286/521) it was not possible to identify the risk factor. In the remaining 45%, who denied the risk factor or who believed that their behaviour was not at risk or wanted to be tested, the most frequently identified risk factors were occasional exposures and unprotected exposure (Figure 30).

Table 50. Number of TP infections by geographical area of birth (2021)

Geographical area of birth	N. of infections
Africa	19
America	18
Asia	5
Europe	45
Italy	434
Total	**521**

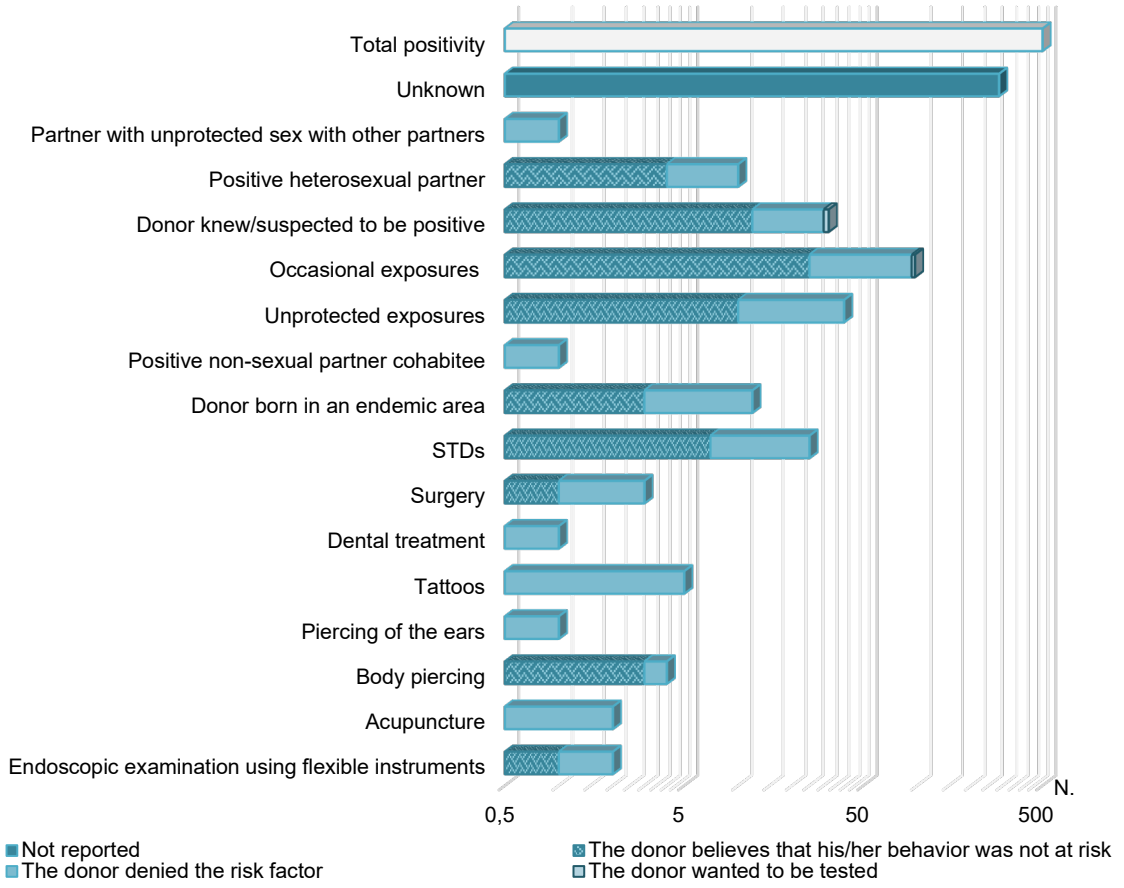


Figure 30. Causes of failed deferral and risk factors detected in TP positive donors (values reported on a logarithmic scale) (2021)

Except for one case (indeterminate screening test and positive confirmatory test), both the serological tests (screening and confirmatory) were positive (Table 51).

Table 51. Number of TP infections obtained from individual serological test (2021)

Results		N. of infections
SER	CONF	
+	+	520
+/-	+	1
Total		521

Coinfections

In this chapter, the authors want to provide more accurate epidemiological data on coinfection notifications regarding blood donors for the year 2021.

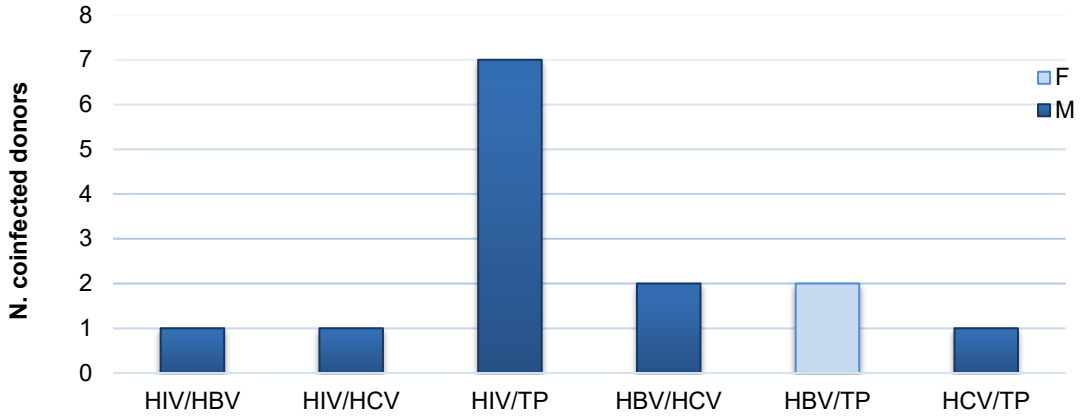


Figure 31. Number of coinfected donors by type of coinfection and by gender (2021)

Figure 31 shows the number of coinfected donors by gender and type of coinfection diagnosed; of the 14 coinfections notified, 10 included TP.

The majority of coinfected donors were males. In particular, in about 1/3 of cases the coinfection was diagnosed in male donors in the 26-35 age class (Figure 32).

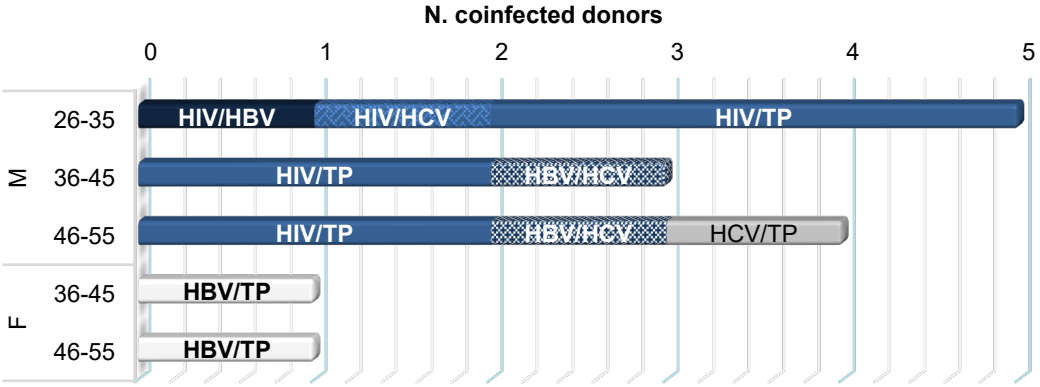


Figure 32. Number of coinfected donors by type of coinfection, age class and sex (2021)

For the majority of coinfected donors (HIV/HBV, HIV/TP, HBV/HCV, HBV/TP and HCV/TP) it was not possible to trace the reasons for missed deferral and the risk factors are not known.

For 5 cases of coinfection the risk factors were identified and were generally due to high-risk sexual behaviours; in the remaining 3 cases the risk factors were identified and were transfusion or administration of blood components, donor knew to be positive and positive non-sexual partner cohabitee (Figure 33).

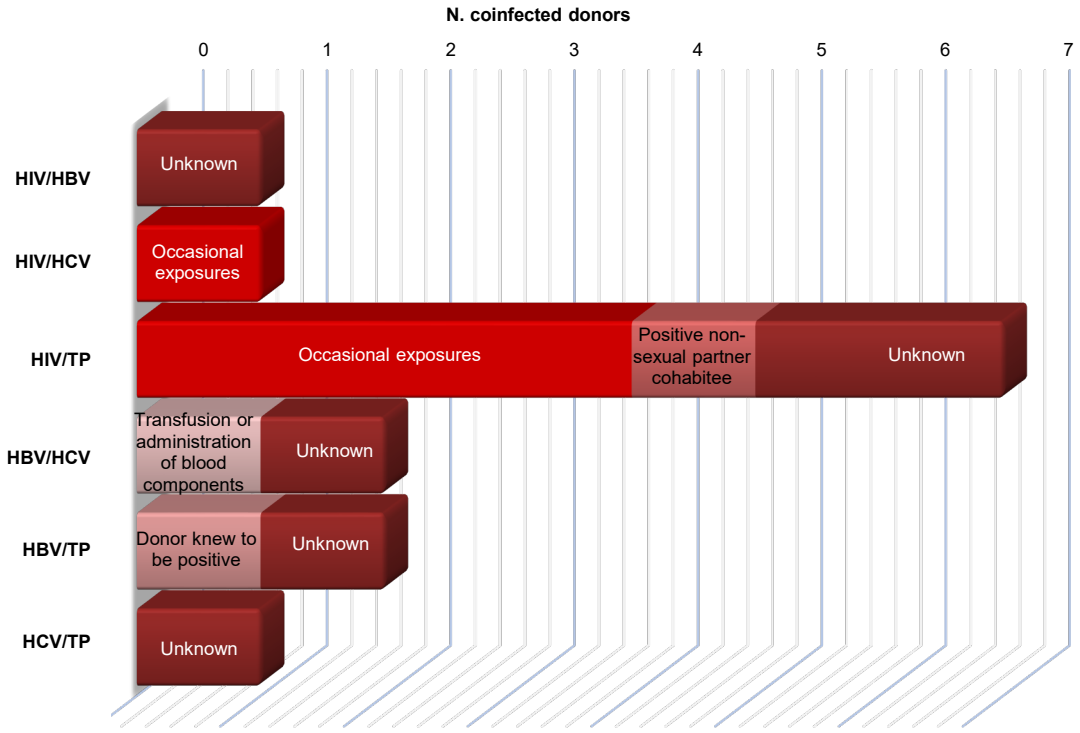


Figure 33. Number of coinfected donors by type of coinfection and risk factor (2021)

Discussion

The detection, through SISTRA, of positive blood donors, allows to calculate the incidence and prevalence of transmissible infections on an annual basis as well as to monitor the trends and to assess the risk with the aim to guarantee the blood donation safety.

As in the previous years, a considerable regional variability in the total number of positive donors is still present in 2021, with the highest numbers in Campania and Apulia Regions.

The majority of donors who turned out to be positive to infectious markers were males (74%) and FT (71%), with a statistically significant variability of the incidence in the different age classes.

About 79% of the positive donors were Italian, while the remaining 21% were foreigners. Most foreign donors belonged to the FT category and came from other European countries. However, it is not possible to make further epidemiological assessments, as the total number of foreign donors donating in the year is not known.

National data show the highest values of HBV incidence and TP prevalence in the blood donor population.

Regarding hepatitis viruses (HBV and HCV), chronic infections are more frequent in blood donors compared to those detected in the general population by the national epidemiological system, which mainly reports acute infections.

Acute HBV infections in general population occur mainly in the regions of Central-Northern Italy (Lombardy, Emilia-Romagna, Tuscany and Lazio). While, the highest number of acute HCVs was reported in the Lazio, Tuscany and Apulia regions. For HBV and HCV infections, a slight decrease in the incidence trend has been observed in recent years, and the most affected

subjects are mainly males over the age of 35 (16). This downward trend is certainly justified by the introduction, in the 90s, of the mandatory HBV vaccination to all subjects born since 1979, and by the introduction, for the treatment of HCV, of new direct-acting anti-viral therapies.

Compared to general population, blood donors' population recorded, in 2021, higher rates of HBV incidence and prevalence in the Southern Italian Regions (respectively Apulia and Campania), with almost half of NAT-only infections. On the other hand, HCV new infections are more frequent in Campania Region, and the highest prevalence has been recorded in Apulia Region.

According to national data, HBV and HCV infections in blood donors are more frequent in over 36-year age classes, with a peak at 46-55. In addition, for both infections, the stated risk factors were risky sexual behaviours.

In contrast to HBV and HCV, the distribution of HIV and TP positivity in blood donors is higher in younger age classes (36-45). The most commonly reported risk factors were sexual risk behaviours. These data correspond to the findings in the general population: the highest incidence of HIV infection has been observed in 25-29 and 30-39 age classes; subjects affected by syphilis I-II report a median age of 36 years (IQR, 29-45 years) while subjects with latent syphilis report a median age of 39 years (IQR, 30-50 years). In both cases the stated risk factors reported sexual risk behaviours (17-18).

The HIV geographical distribution in the general population showed in 2020 the highest incidence in Central-Northern Italy (Valle d'Aosta, Liguria, Autonomous Province of Trento and Lazio) compared to the South and Islands (17). The blood donor population shows, in 2021, a higher incidence in the regions of Southern Italy (Apulia Region, followed by Piedmont and Campania Regions).

The analysis of coinfections showed that the majority of coinfected donors were TP positive.

As in the previous years, many coinfected and monoinfected donors did not declare any risk factor. This phenomenon indicates a probable criticality in the collection of post-donation information. In order to optimise and standardise the collection of post-donation information, homogeneous counselling techniques across the country are recommended to make communication with donors more effective.

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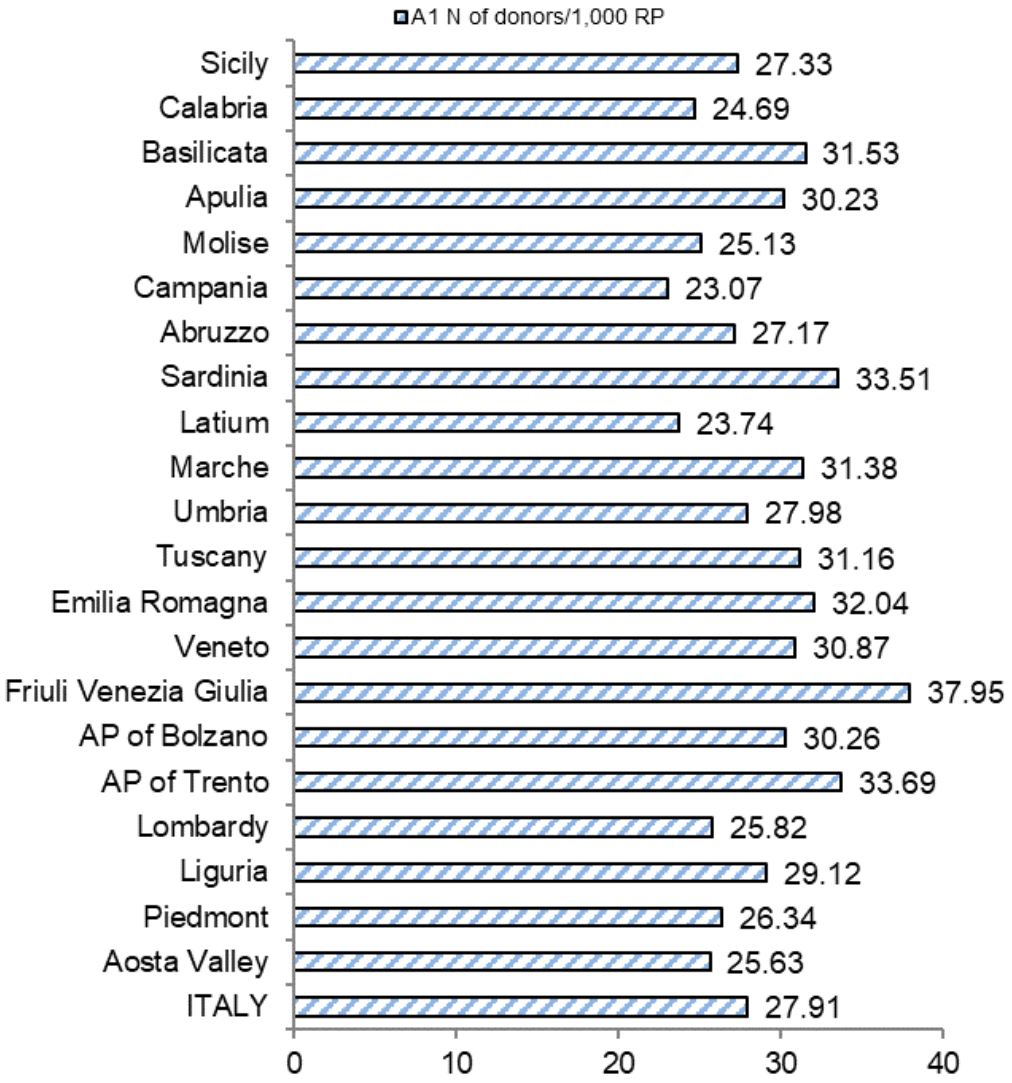
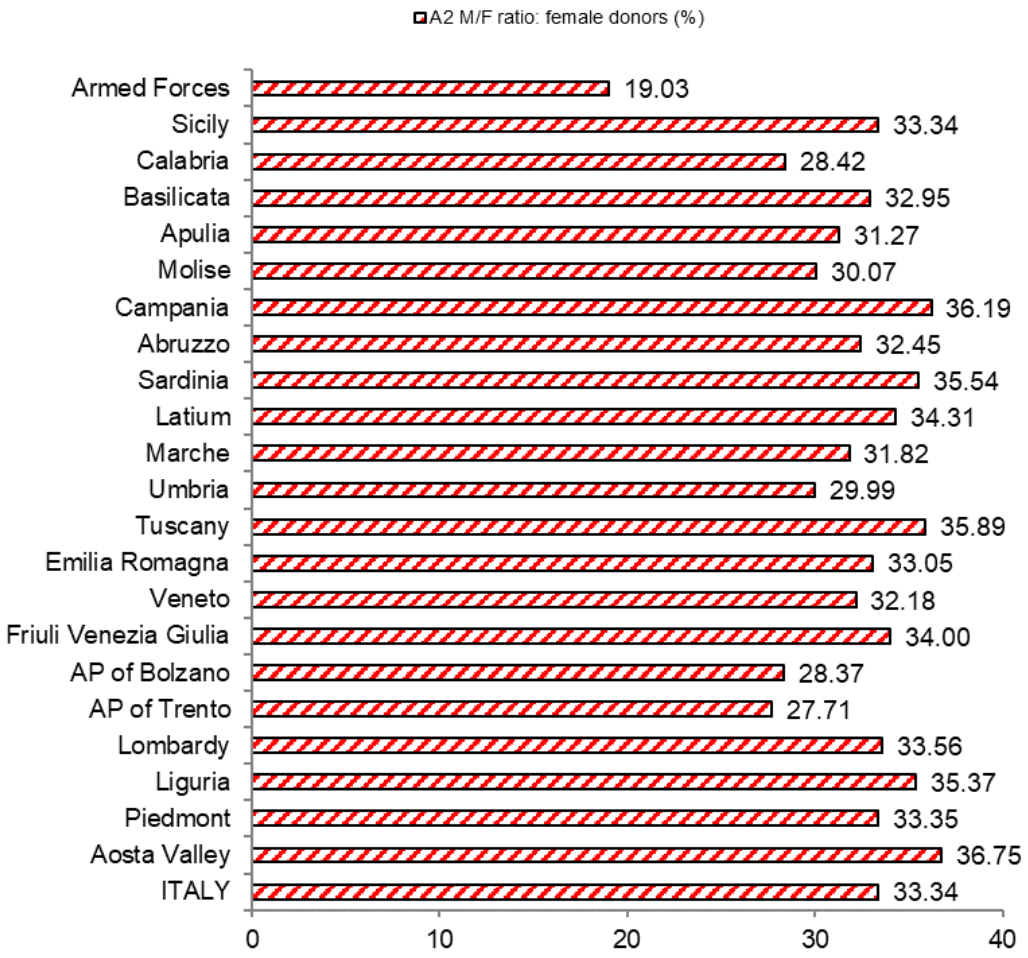
APPENDIX A
Regional and national indicators 2021



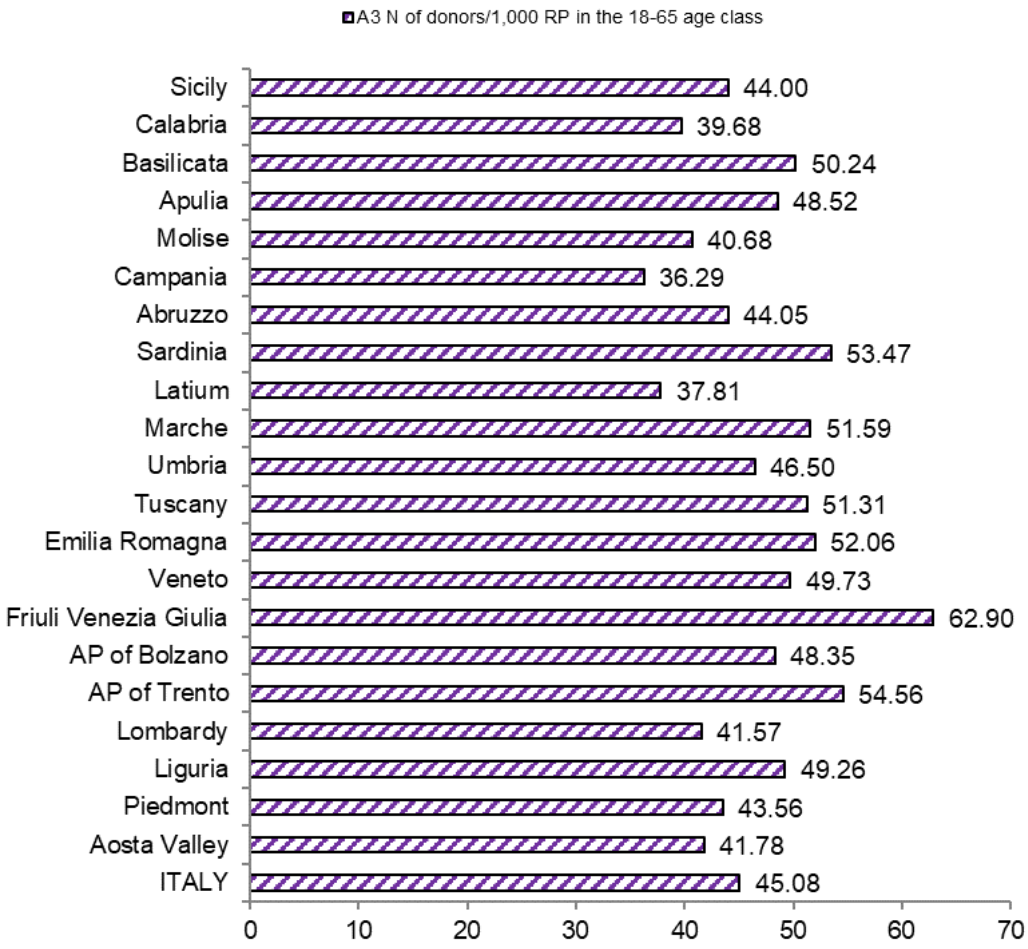
N. number; RP resident population; AP Autonomous Province

Figure A1. INDICATOR A1: Regional blood donors distribution/1,000 resident population (2021)



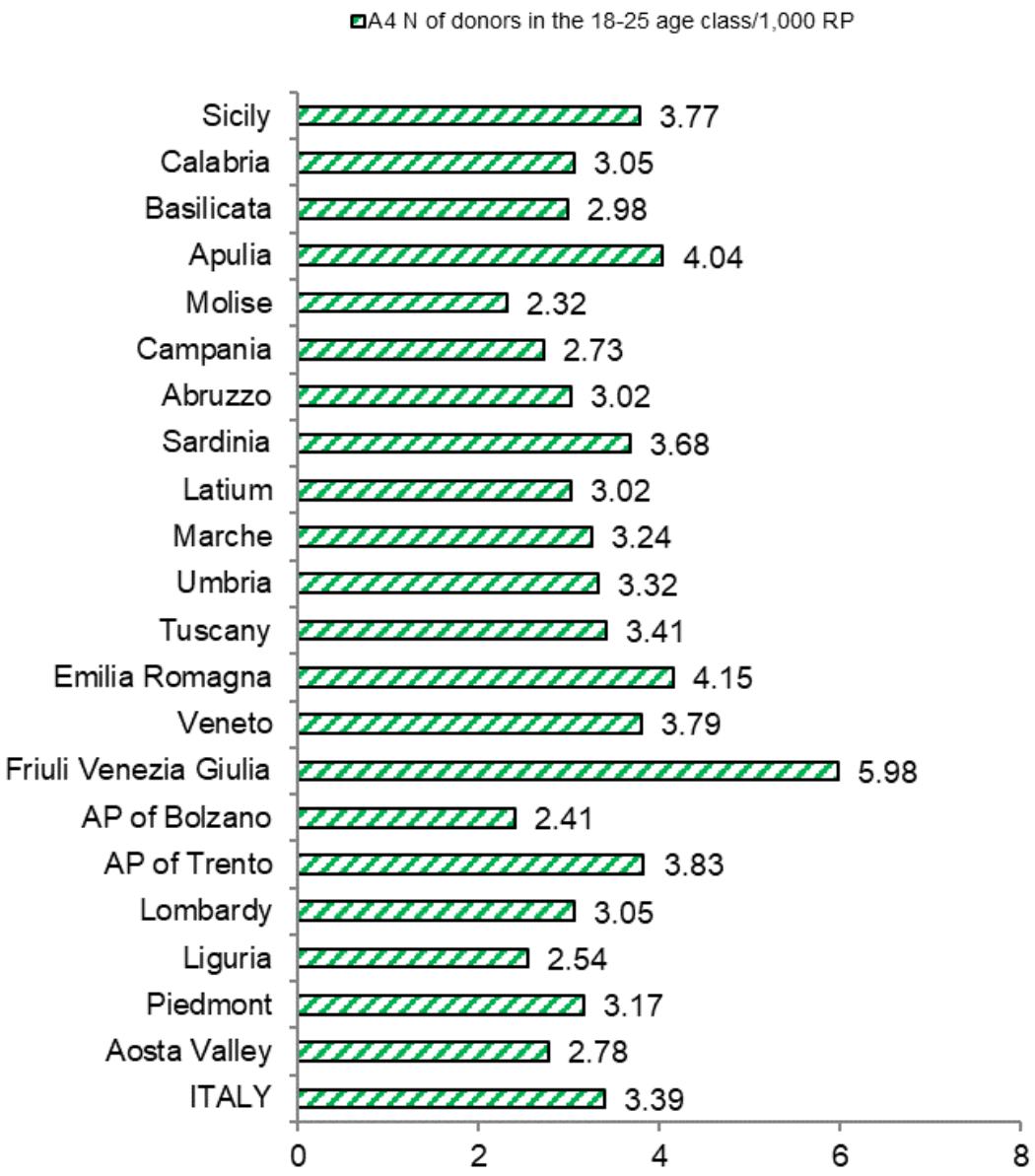
AP Autonomous Province; M male; F Female

Figure A2. INDICATOR A2: M/F ratio, female donors percentage (2021)



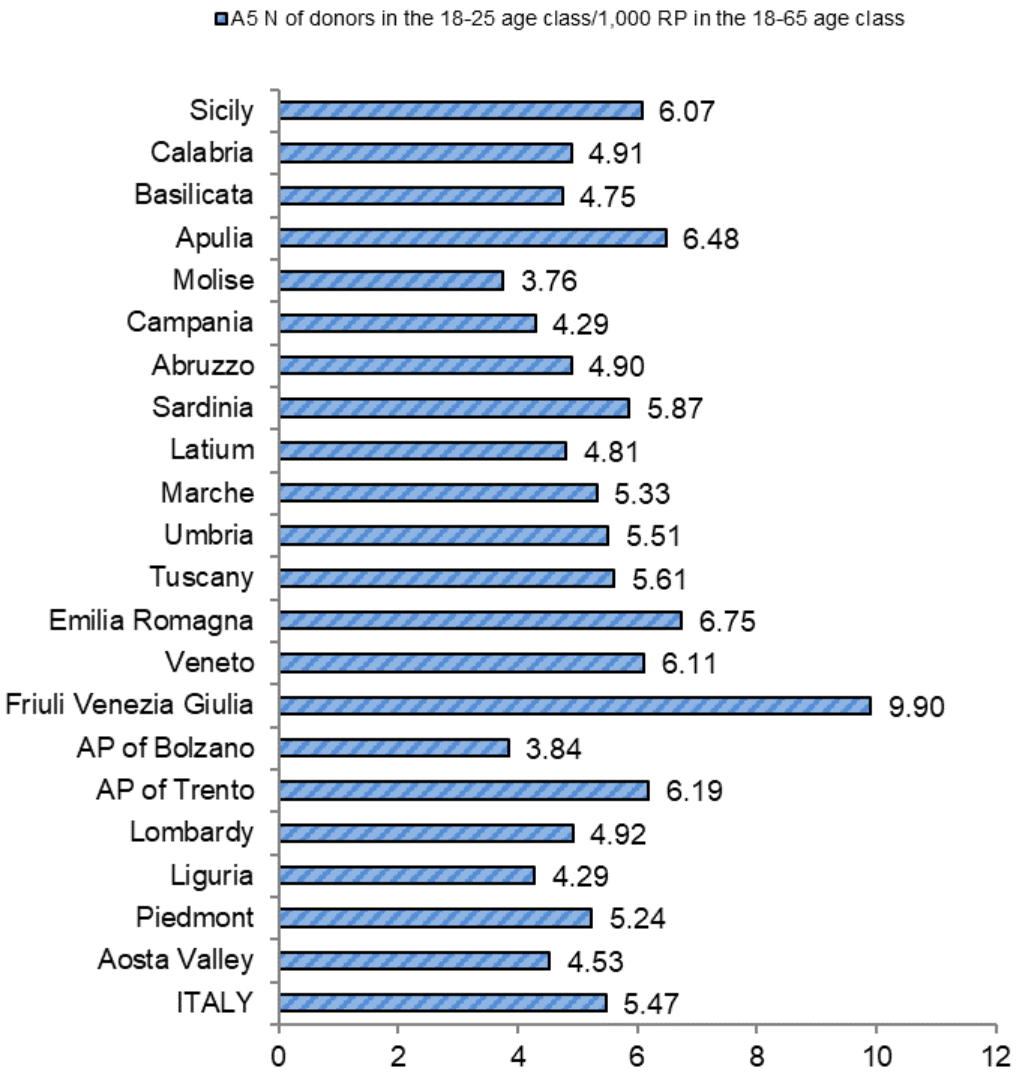
N. number; RP resident population; AP Autonomous Province

Figure A3. INDICATOR A3: N. of donors/1,000 resident population in the 18-65 age class (2021)



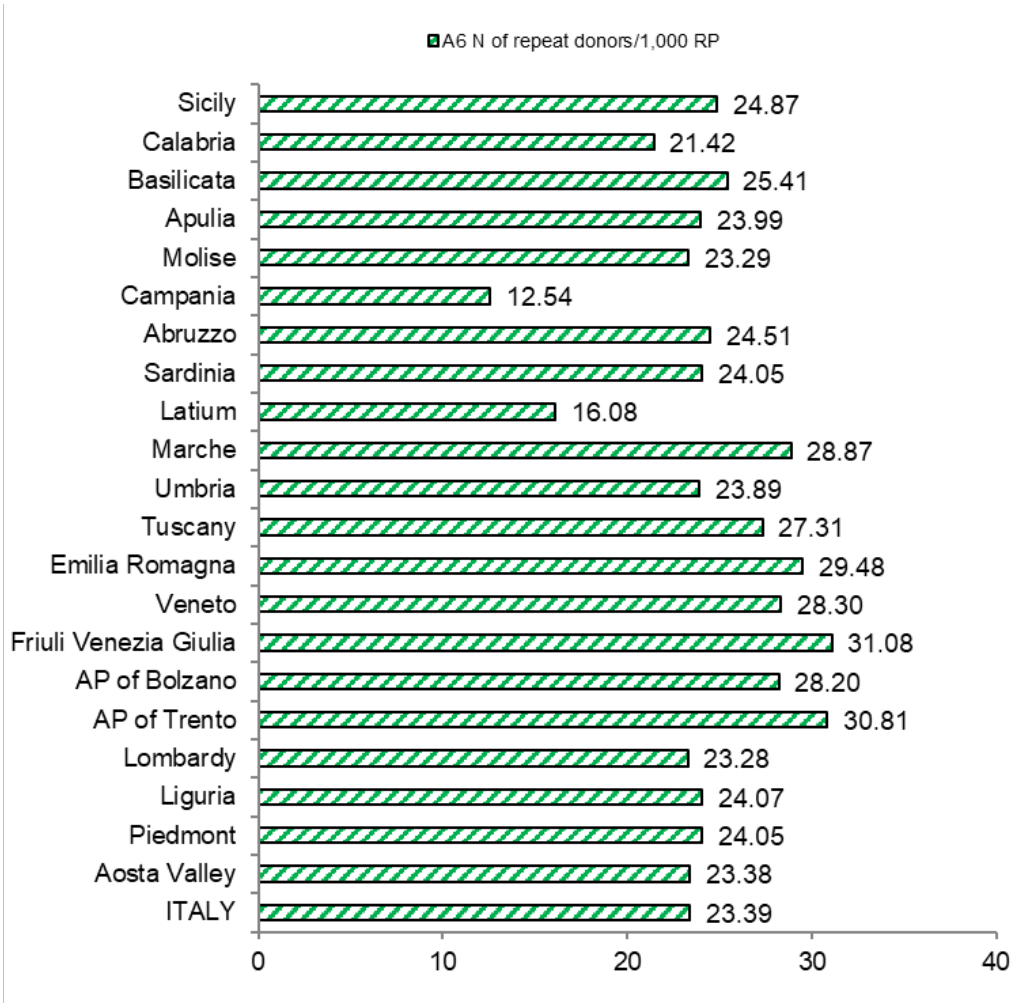
N. number; RP resident population; AP Autonomous Province

Figure A4. INDICATOR A4: N. of donors in the 18-25 age class/1,000 resident population (2021)



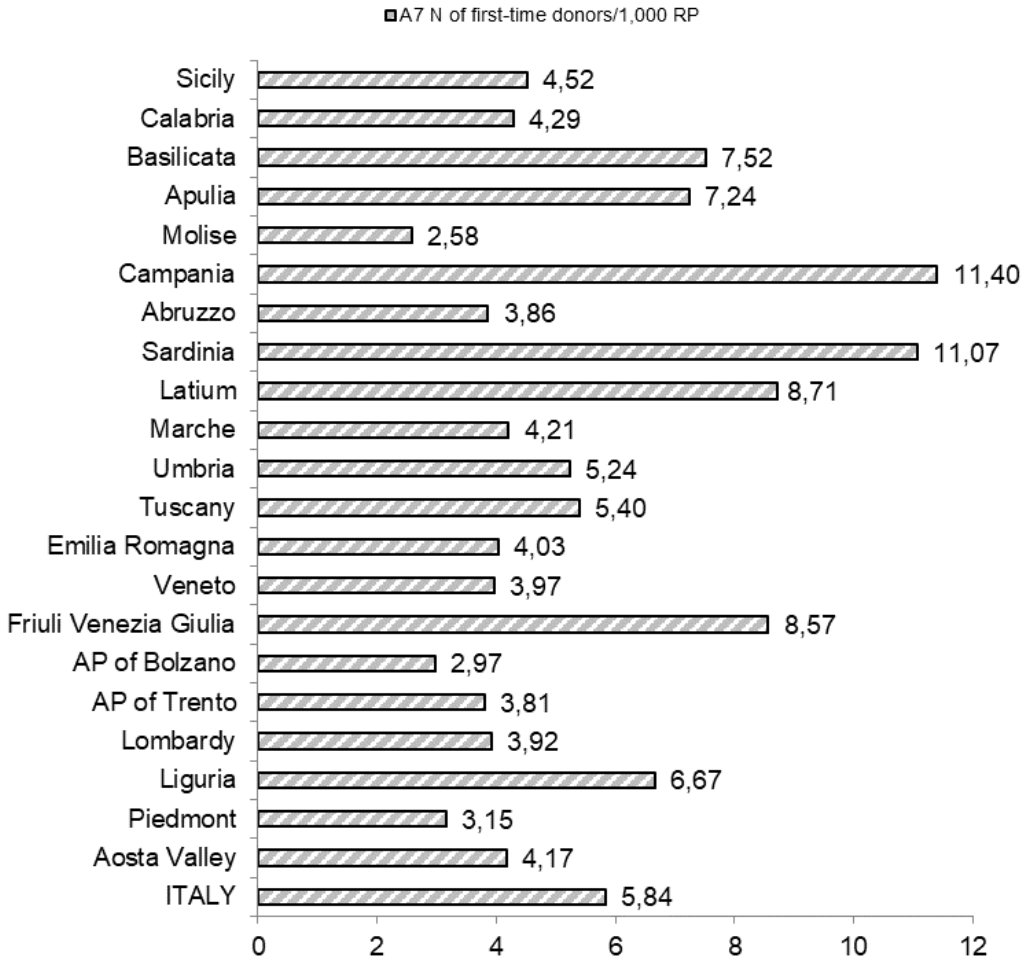
N. number; RP resident population; AP Autonomous Province

Figure A5. INDICATOR A5: N. of donors in the 18-25 age class/1,000 resident population in the 18-65 age class (2021)



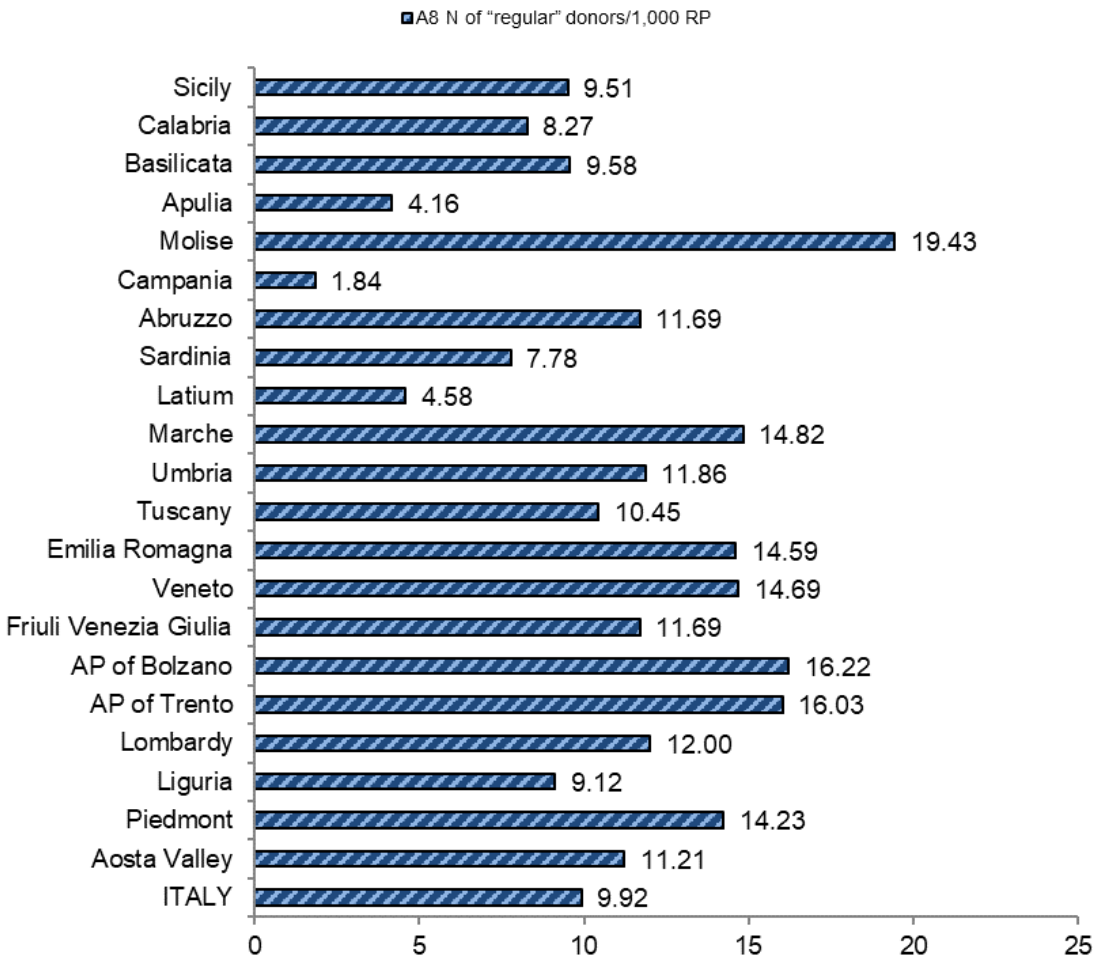
N. number; RP resident population; AP Autonomous Province

Figure A6. INDICATOR A6: N. of repeat donors/1,000 resident population (2021)



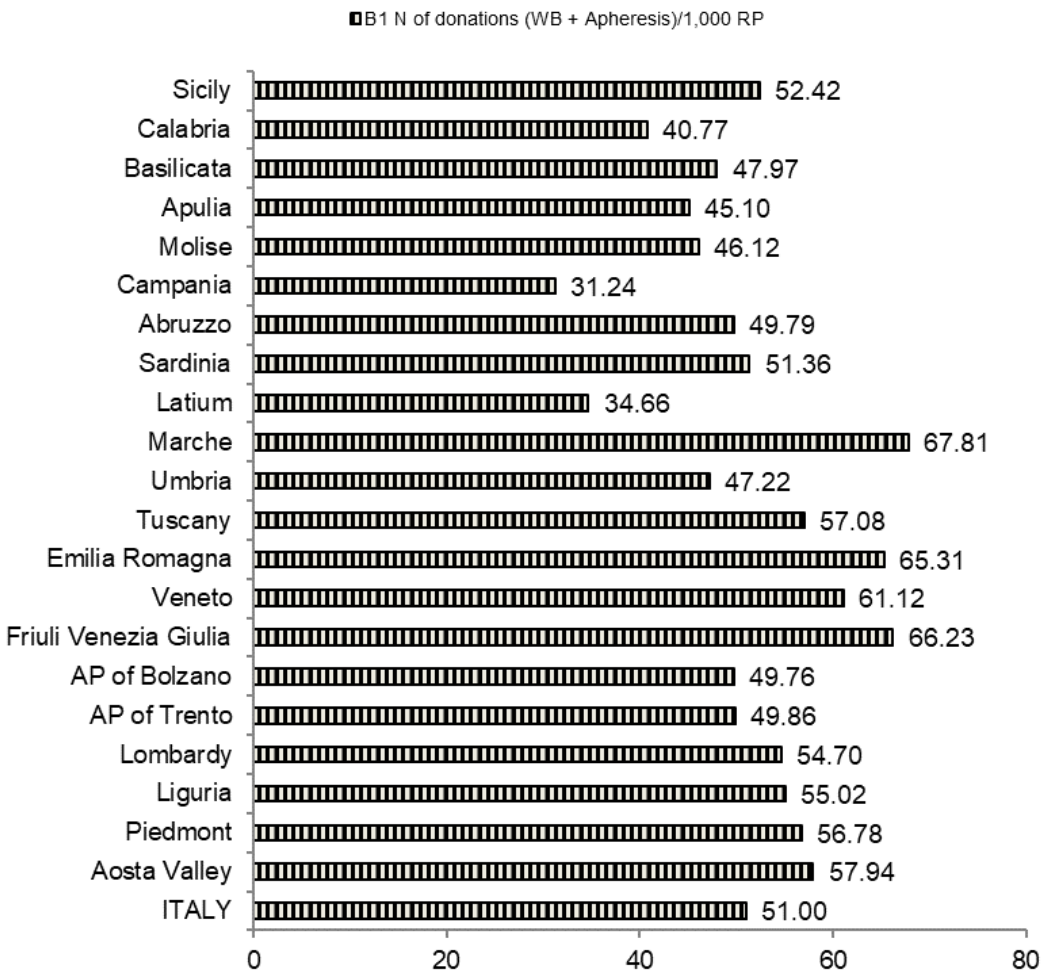
N. number; RP resident population; AP Autonomous Province

Figure A7. INDICATOR A7: N. of first-time donors/1,000 resident population (2021)



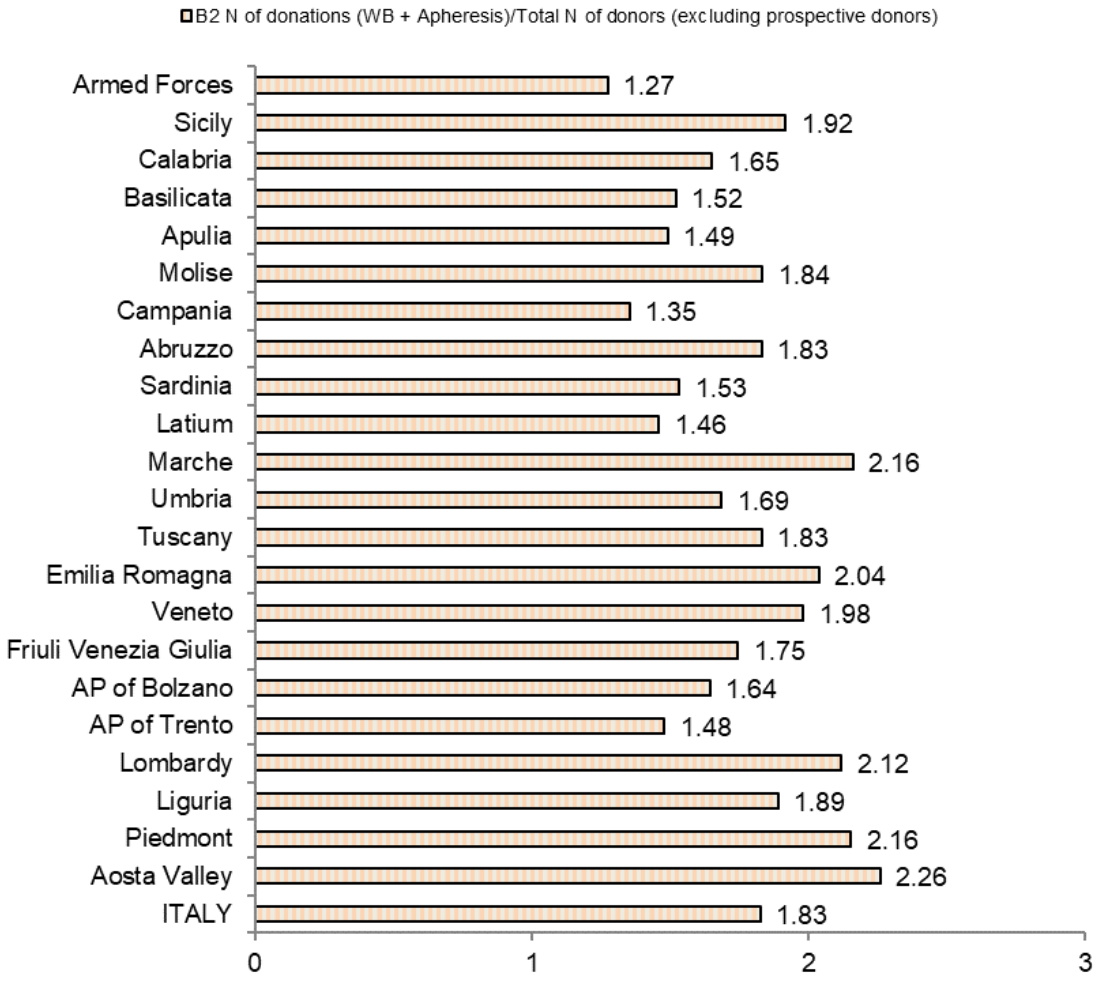
N. number; RP resident population; AP Autonomous Province

Figure A8. INDICATOR A8: N. of "regular" donors/1,000 resident population (2020)



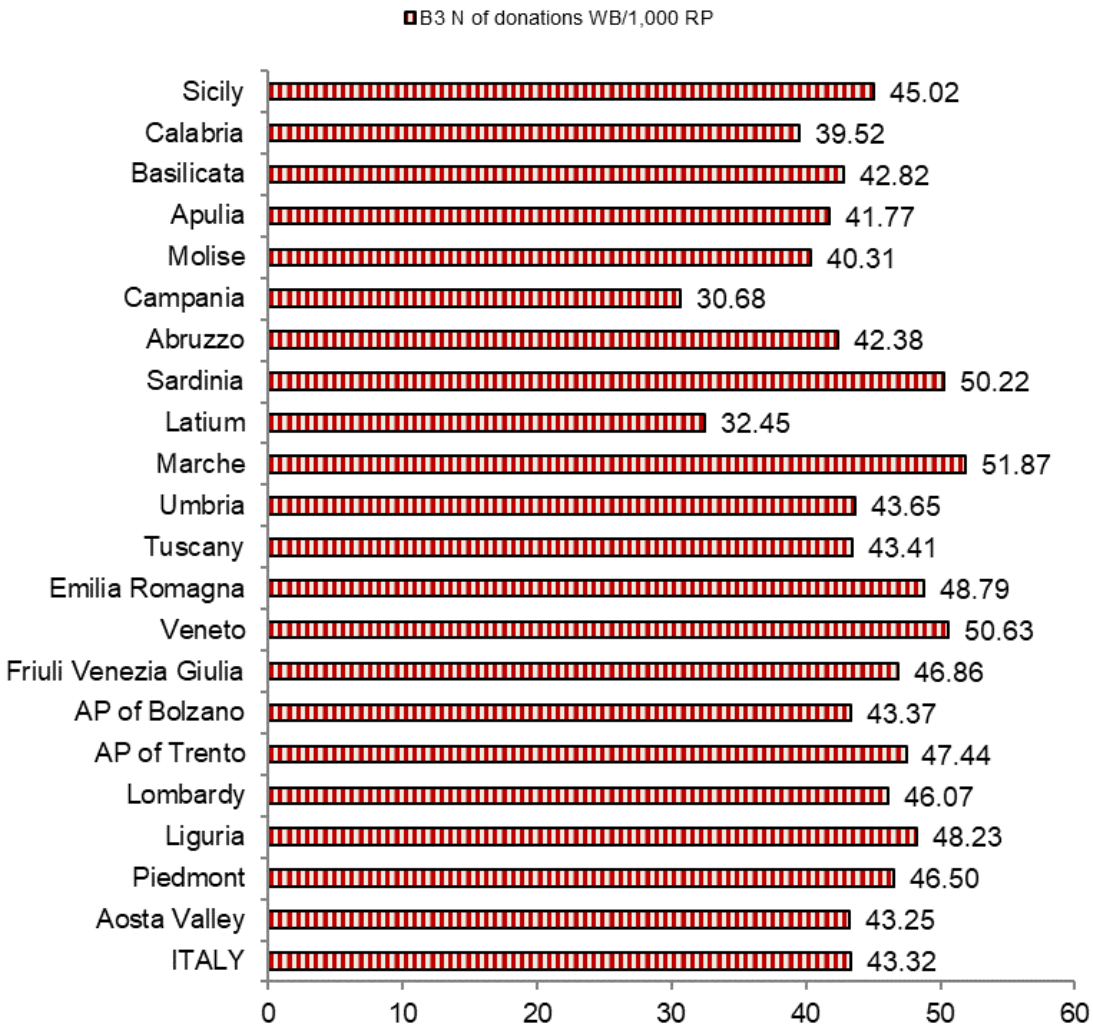
N. number; RP resident population; AP Autonomous Province; WB whole blood

Figure A9. INDICATOR B1: N. of whole blood and apheresis donations/1,000 resident population (2021)



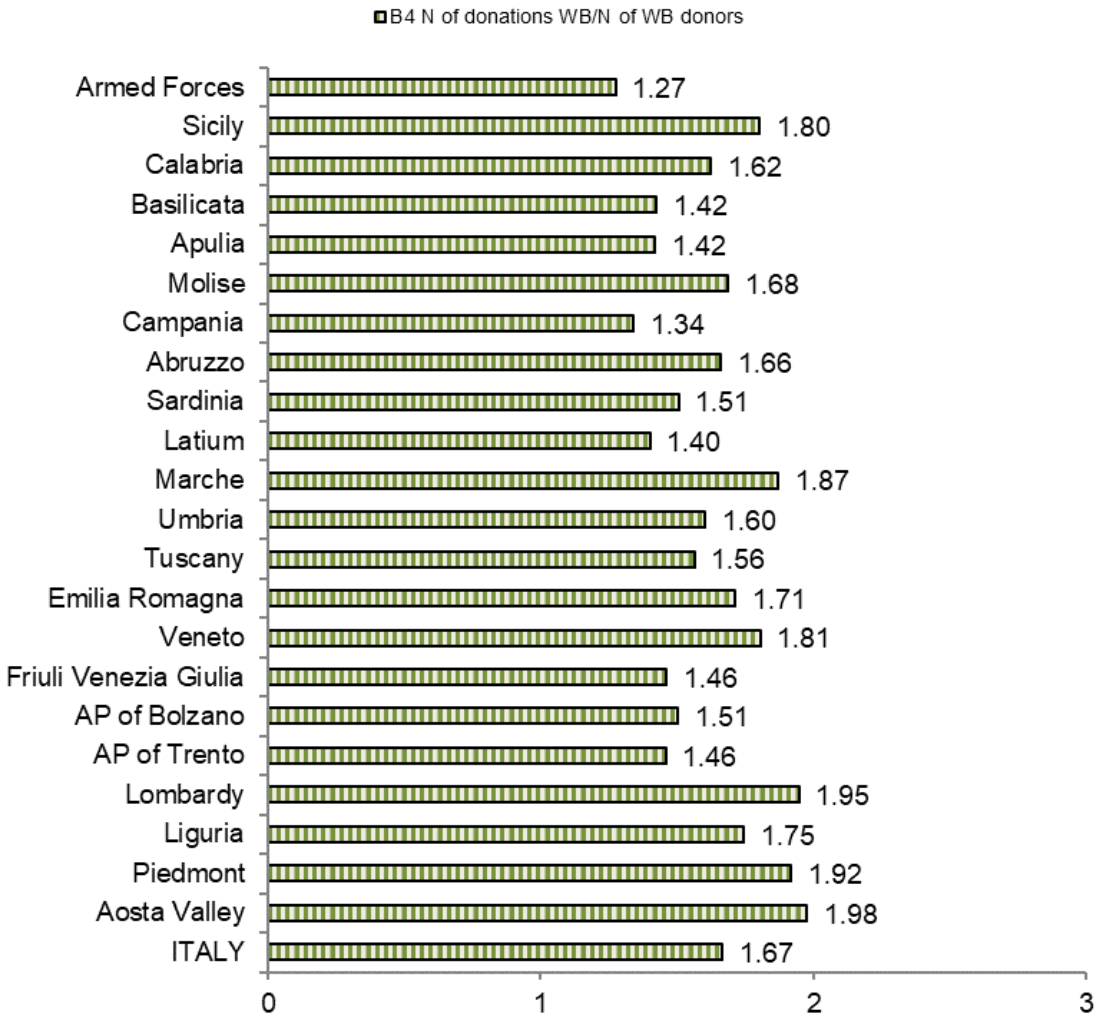
N. number; AP Autonomous Province; WB whole blood

Figure A10. INDICATOR B2: N. of whole blood and apheresis donations/Total N. of donors (excluding prospective donors) (2021)



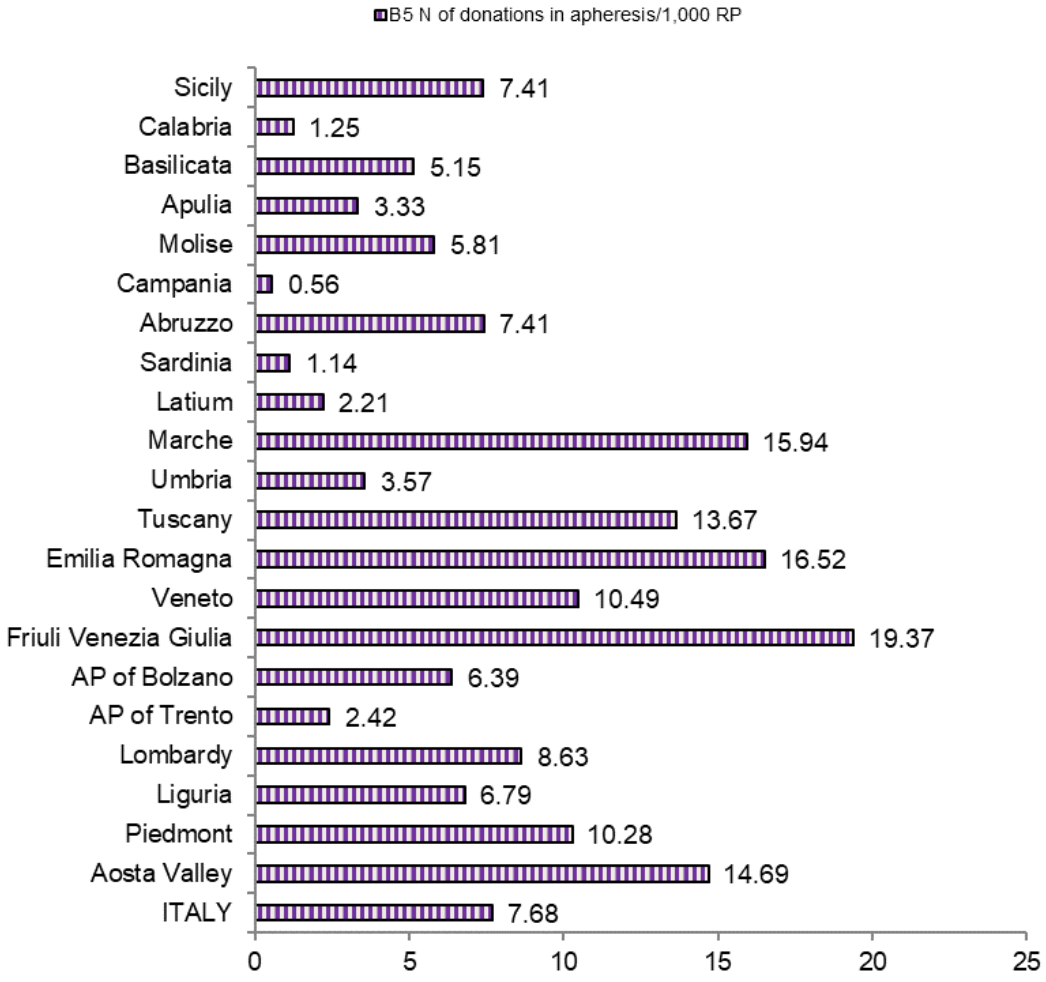
N. number; RP resident population; AP Autonomous Province; WB whole blood

Figure A11. INDICATOR B3: N. of whole blood donations/1,000 resident population (2021)



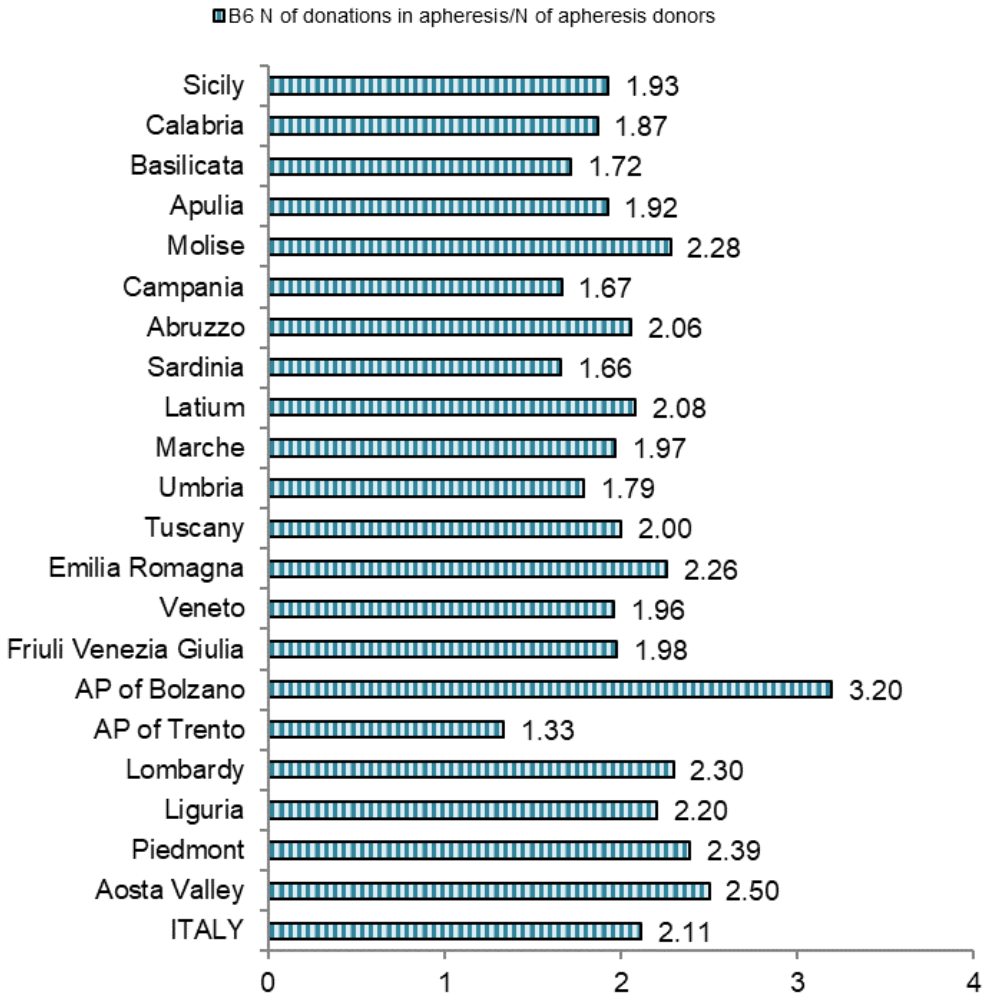
N. number; AP Autonomous Province; WB whole blood

Figure A12. INDICATOR B4: N. of whole blood donations/N. of whole blood donors (2021)



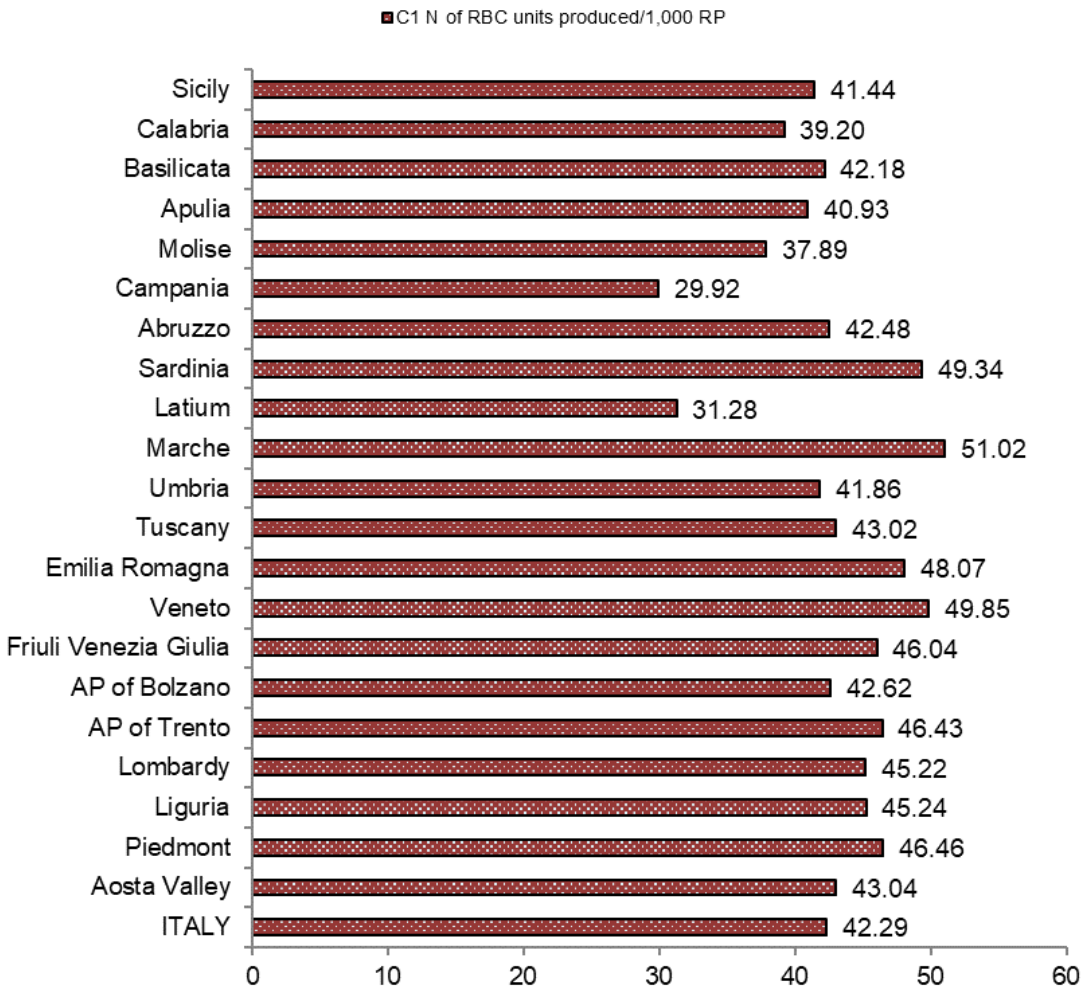
N. number; RP resident population; AP Autonomous Province

Figure A13. INDICATOR B5: N. of donations in apheresis/1,000 resident population (2021)



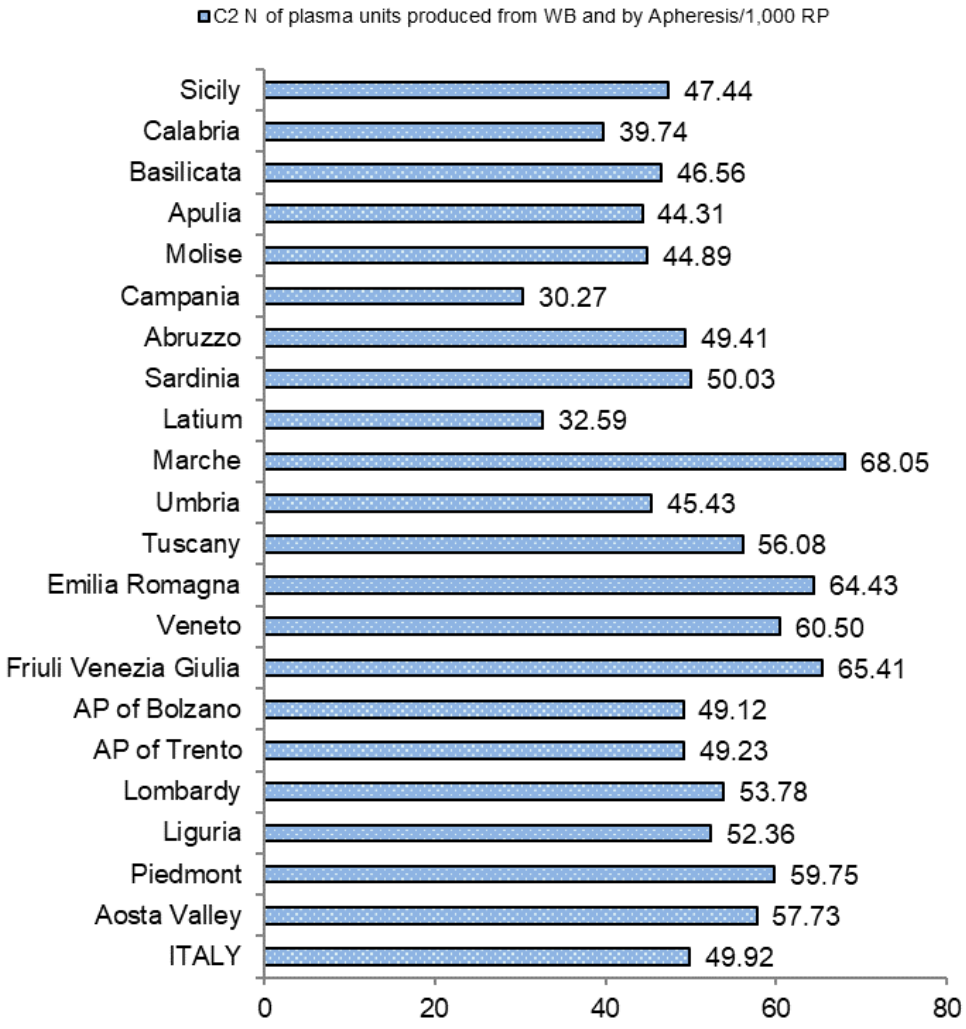
N. number; AP Autonomous Province

Figure A14. INDICATOR B6: N. of donations in apheresis/N. of apheresis donors (2021)



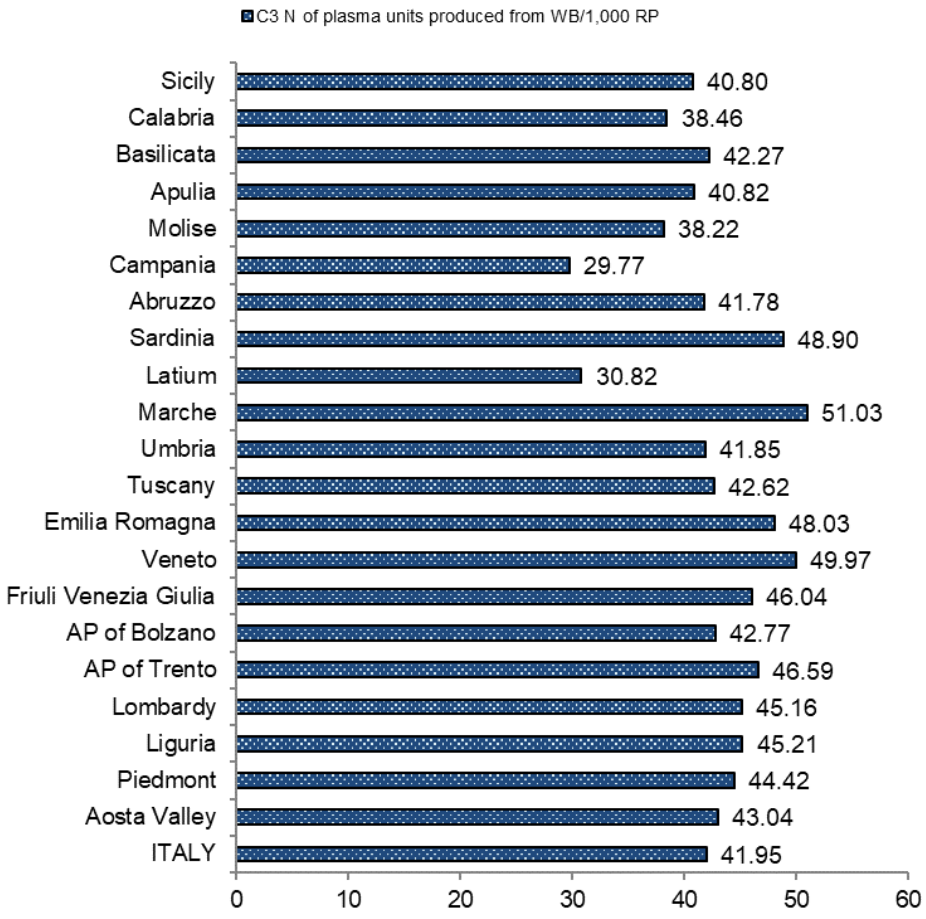
N. number; RP resident population; AP Autonomous Province

Figure A15. INDICATOR C1: RBC units produced/1,000 resident population (2021)



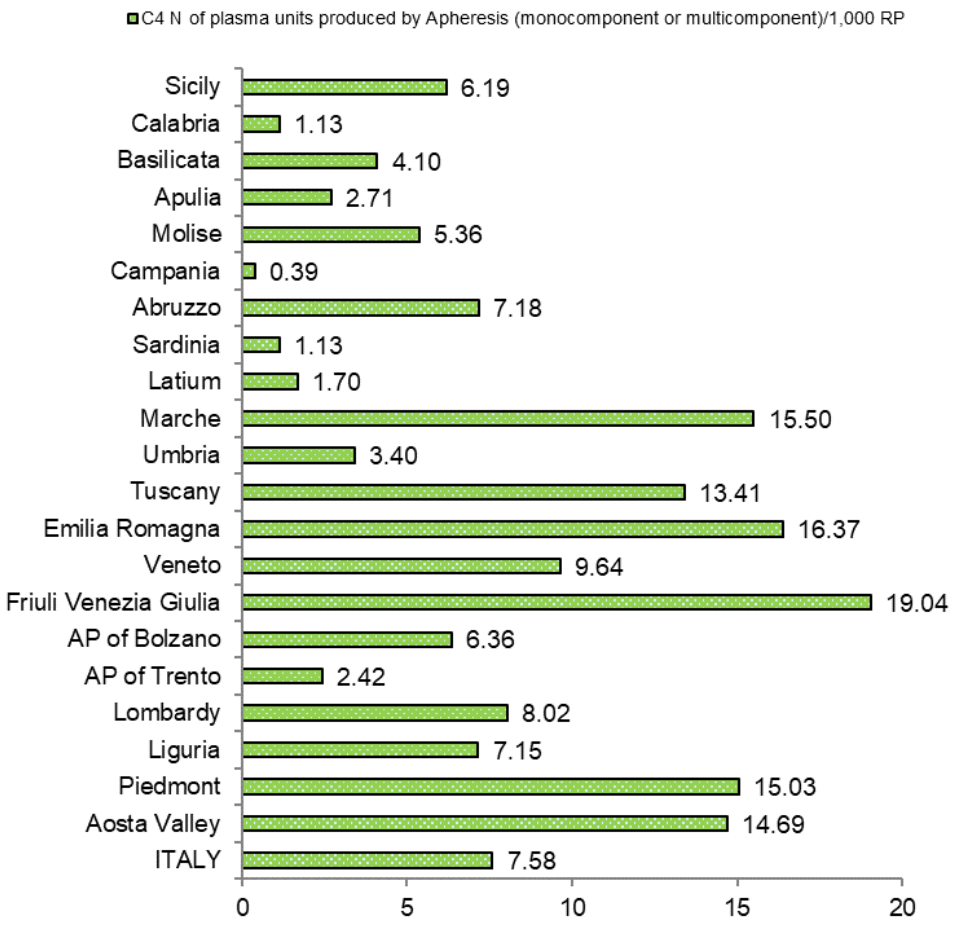
N. number; RP resident population; AP Autonomous Province; WB whole blood

Figure A16. INDICATOR C2: N. of plasma units produced from whole blood and by apheresis/1,000 resident population (2021)



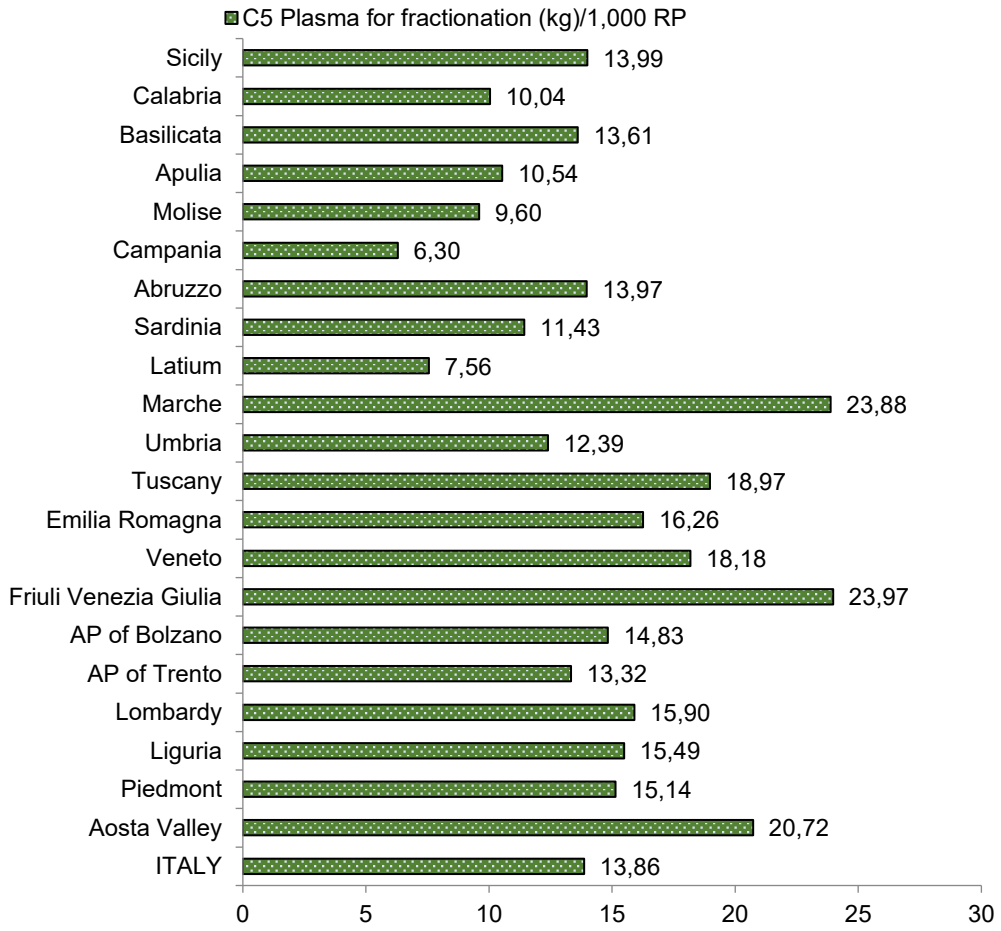
N. number; RP resident population; AP Autonomous Province; WB whole blood

Figure A17. INDICATOR C3: N. of plasma units produced from whole blood/1,000 resident population (2021)



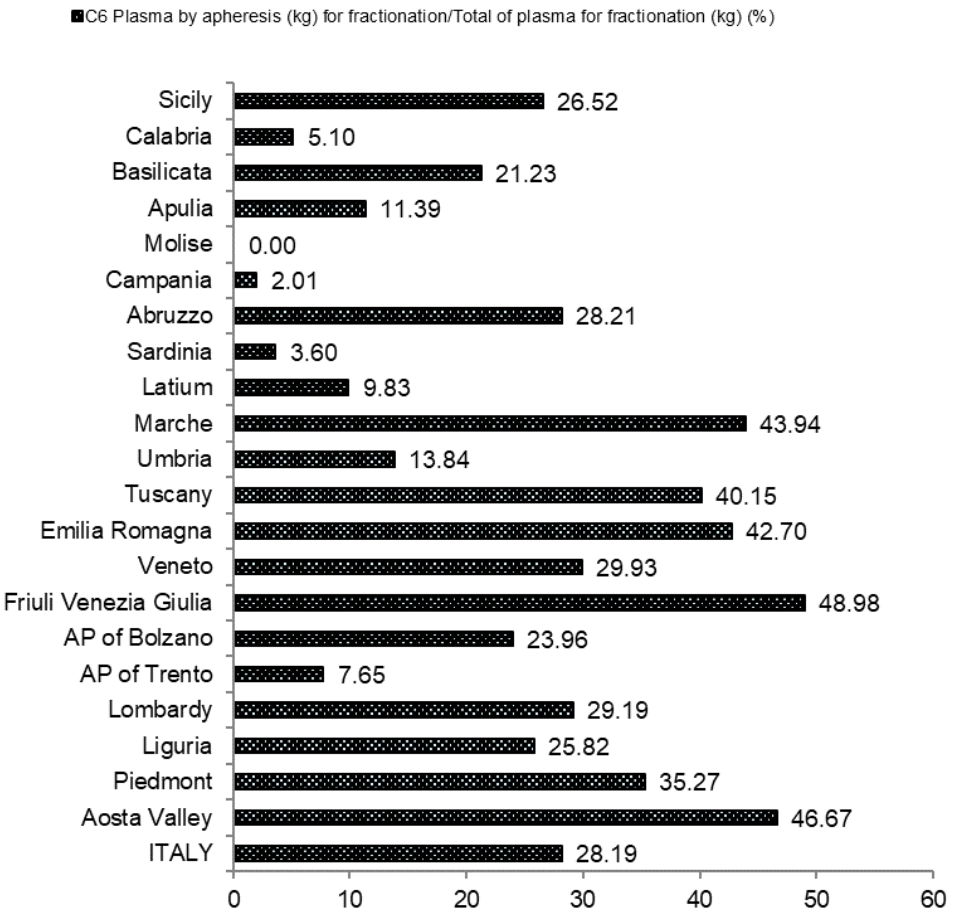
N. number; RP resident population; AP Autonomous Province

Figure A18. INDICATOR C4: N. of plasma units produced from apheresis (monocomponent + multicomponent)/1,000 resident population (2021)



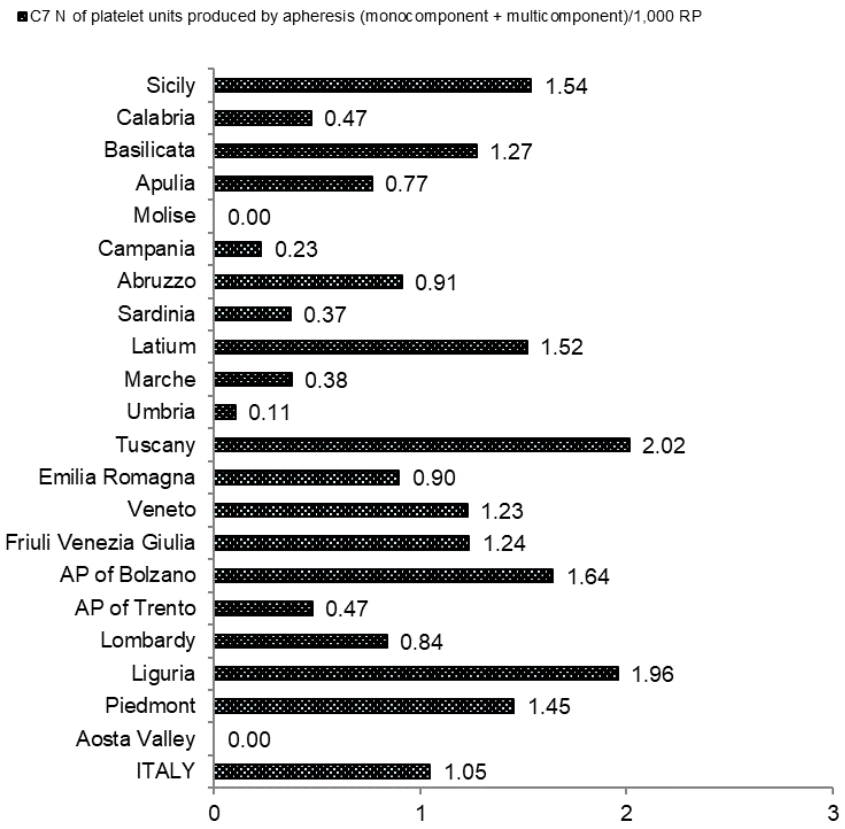
kg kilograms; RP resident population; AP Autonomous Province

Figure A19. INDICATOR C5: plasma (kg) for fractionation/1,000 resident population (from SISTRA) (2021)



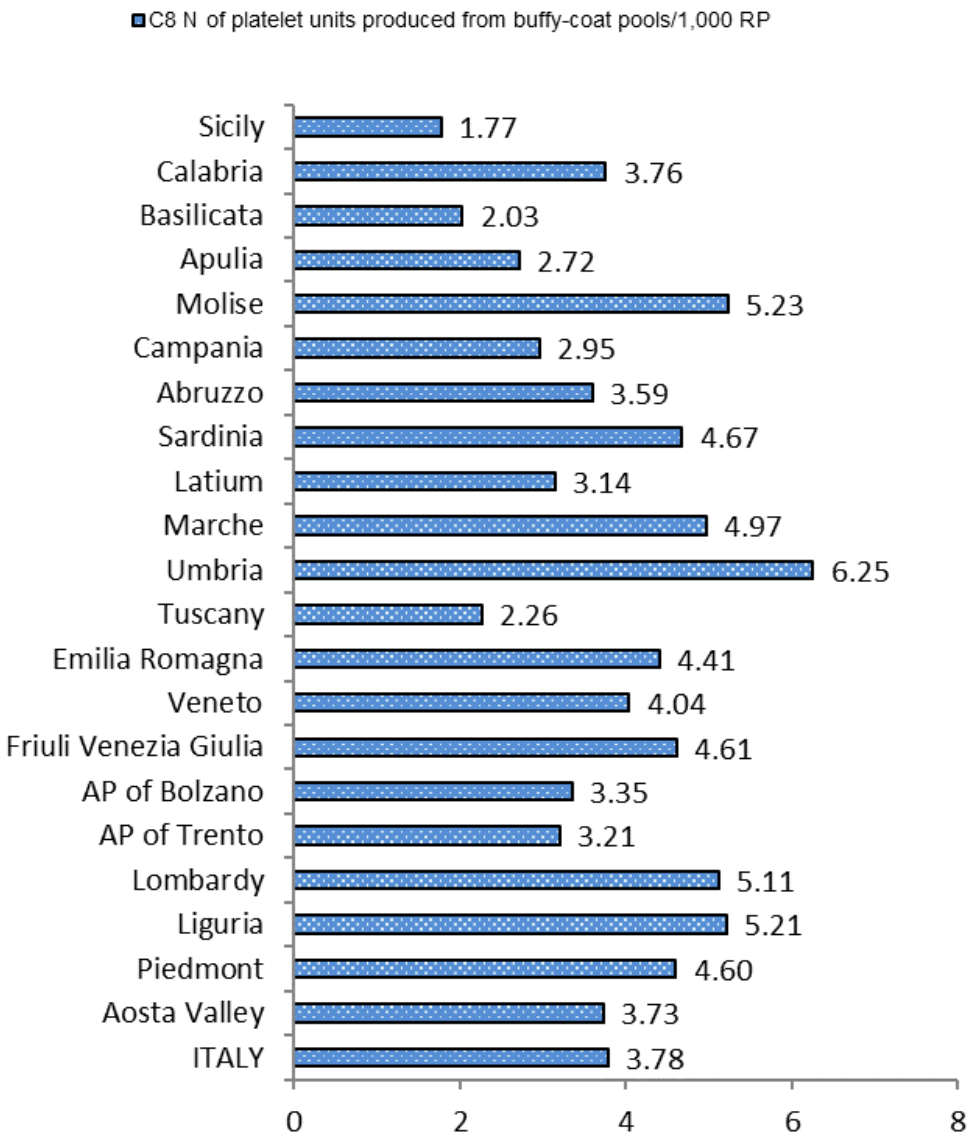
kg kilograms; AP Autonomous Province

Figure A20. INDICATOR C6: plasma by apheresis (kg) for fractionation/Total of plasma for fractionation (kg) (%) (2021)



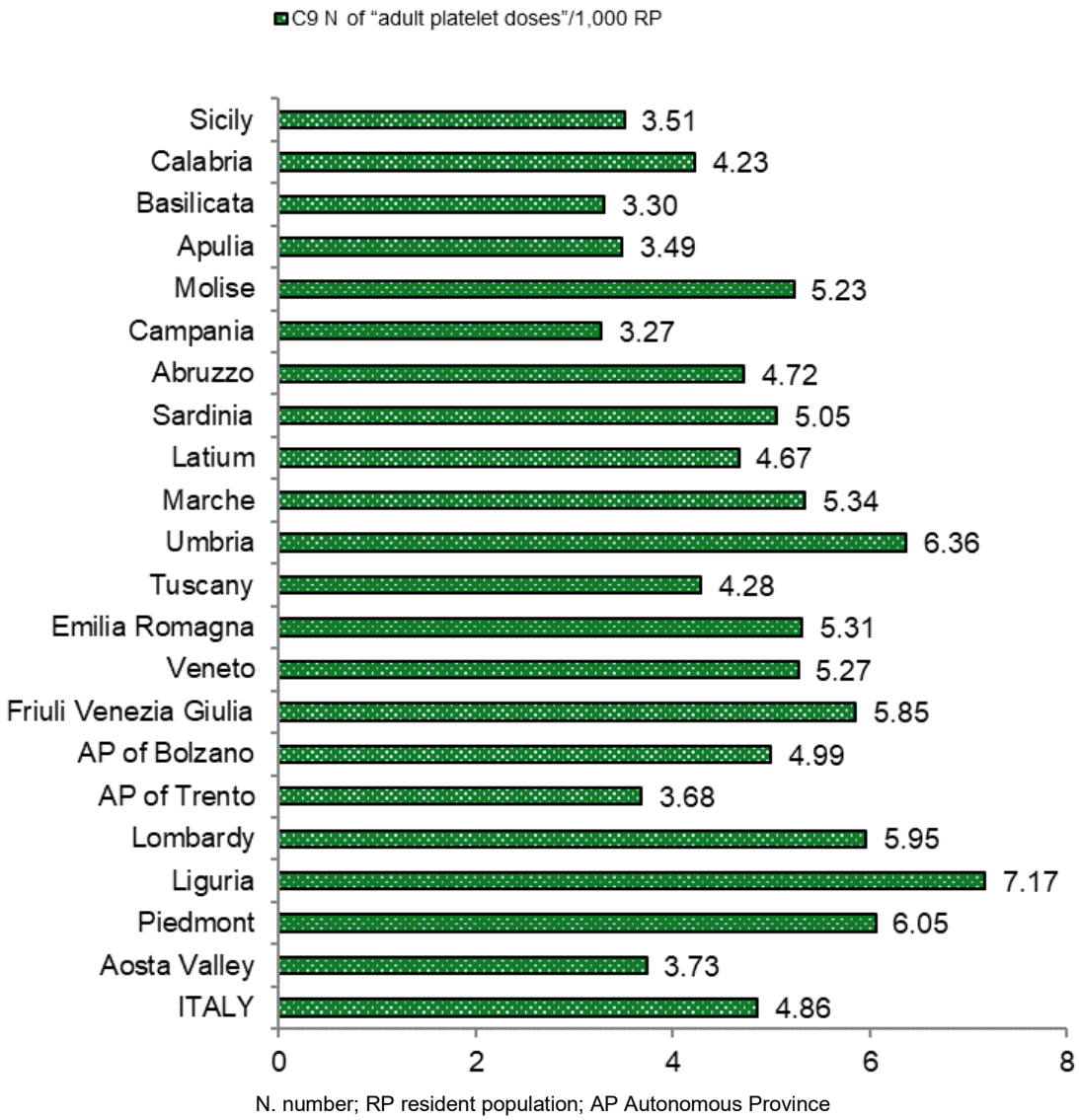
N. number; RP resident population; AP Autonomous Province

Figure A21. INDICATOR C7: N. of platelet units produced by apheresis (monocomponent + multicomponents)/1,000 resident population (2021)



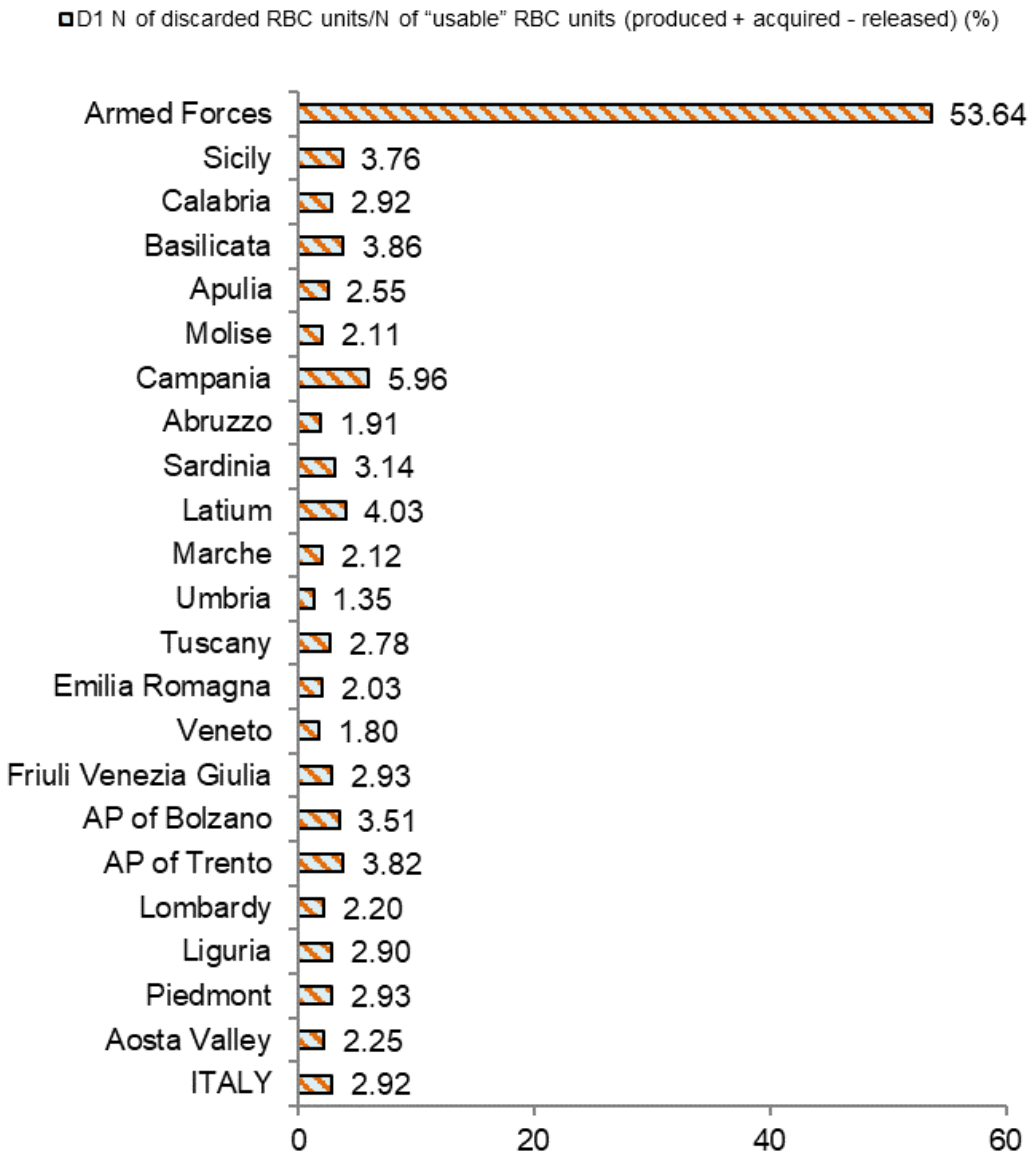
N. number; RP resident population; AP Autonomous Province

Figure A22. INDICATOR C8: N. of platelet units produced from buffy-coat pools/1,000 resident population (2021)



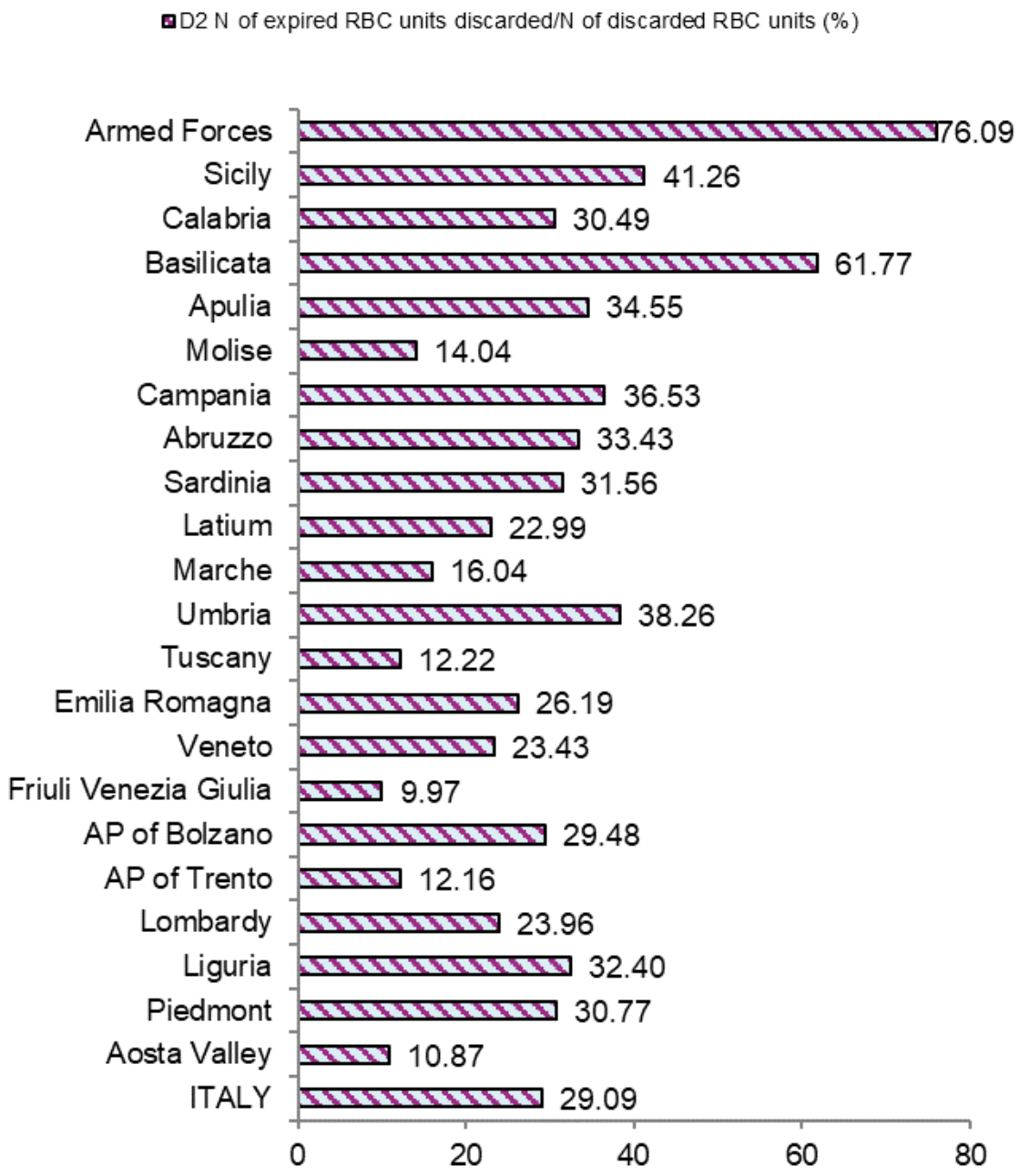
N. number; RP resident population; AP Autonomous Province

Figure A23. INDICATOR C9: N. of "adult platelet doses"/1,000 resident population (2021)



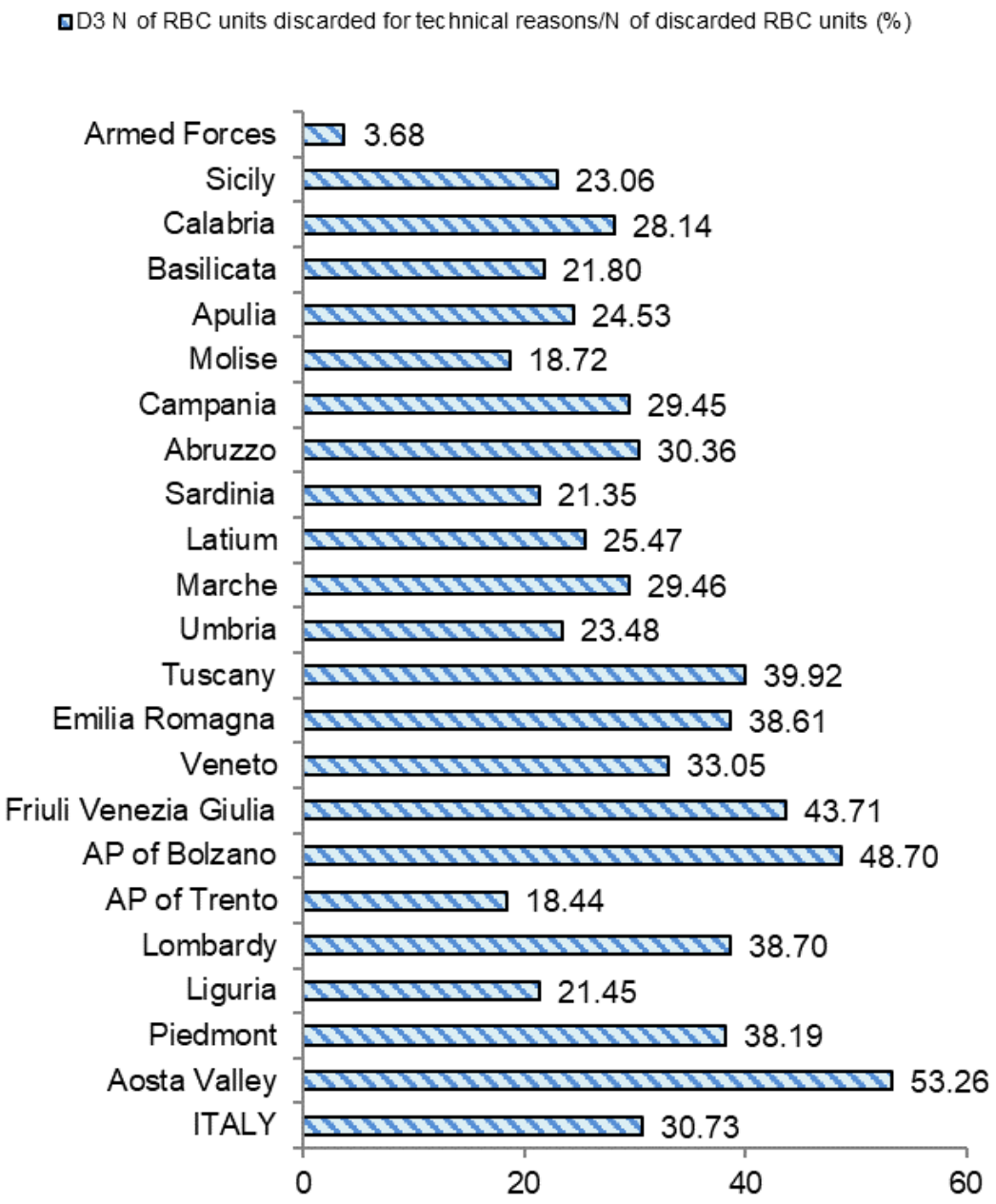
N. number; RBC Red Blood Cells; AP Autonomous Province

Figure A24. INDICATOR D1: N. of discarded RBC units/N. of "usable" RBC units (produced + acquired- released) (%) (2021)



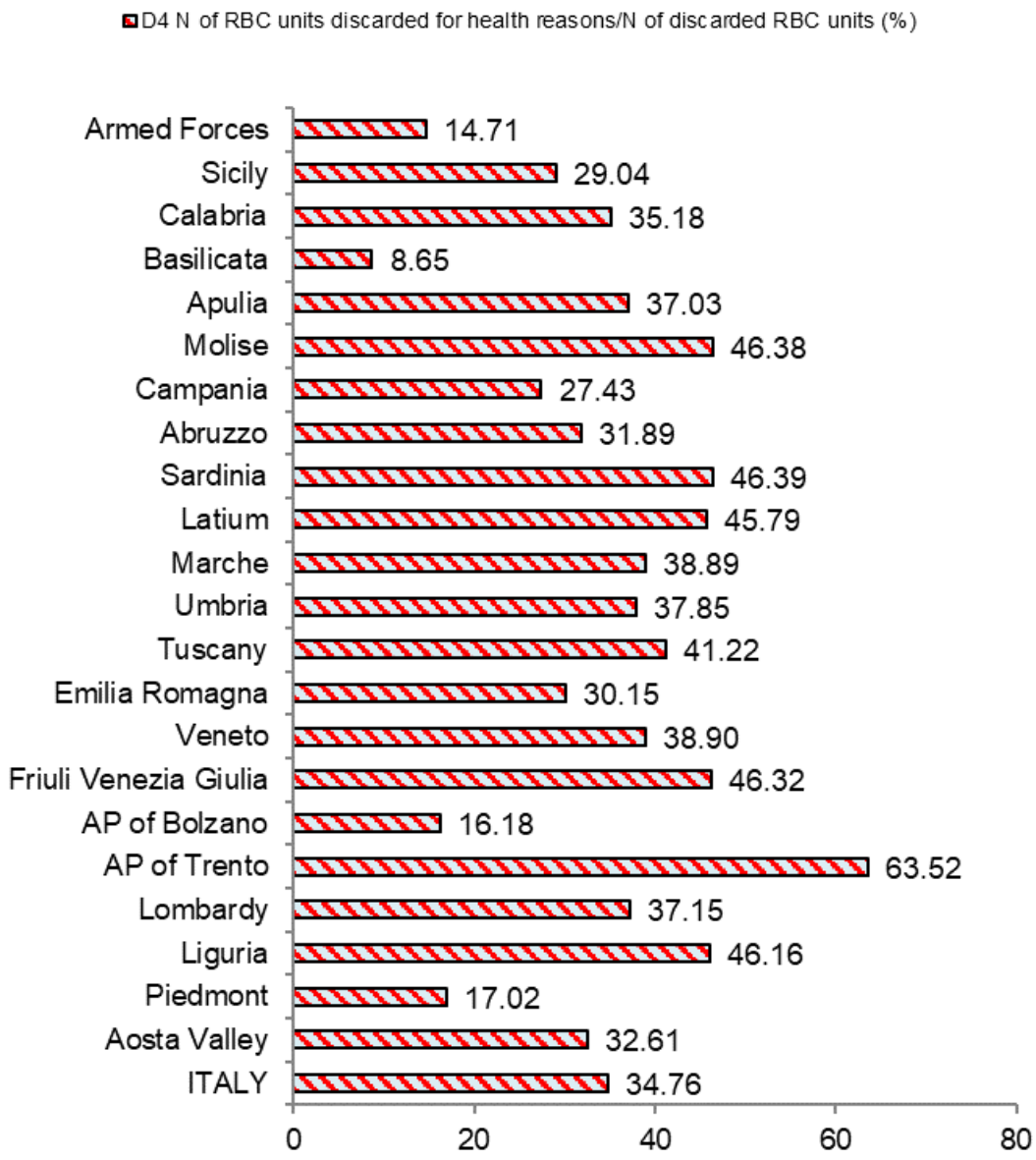
N. number; RBC Red Blood Cells; AP Autonomous Province

Figure A25. INDICATOR D2: N. of expired RBC units discarded/N. of discarded RBC units (%) (2021)



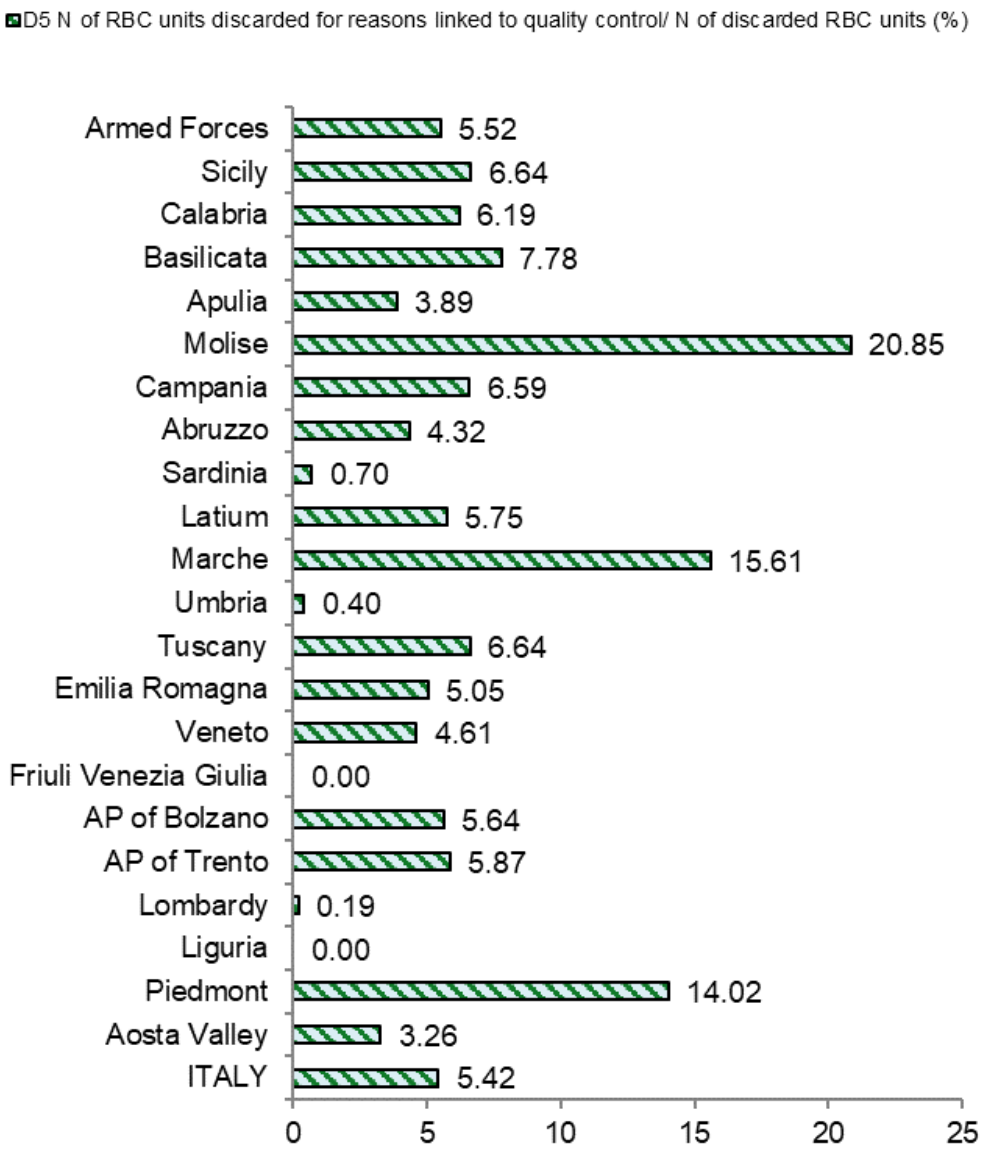
N. number; RBC Red Blood Cells; AP Autonomous Province

Figure A26. INDICATOR D3: N. of RBC units discarded for technical reasons/N. of discarded RBC units (%) (2021)



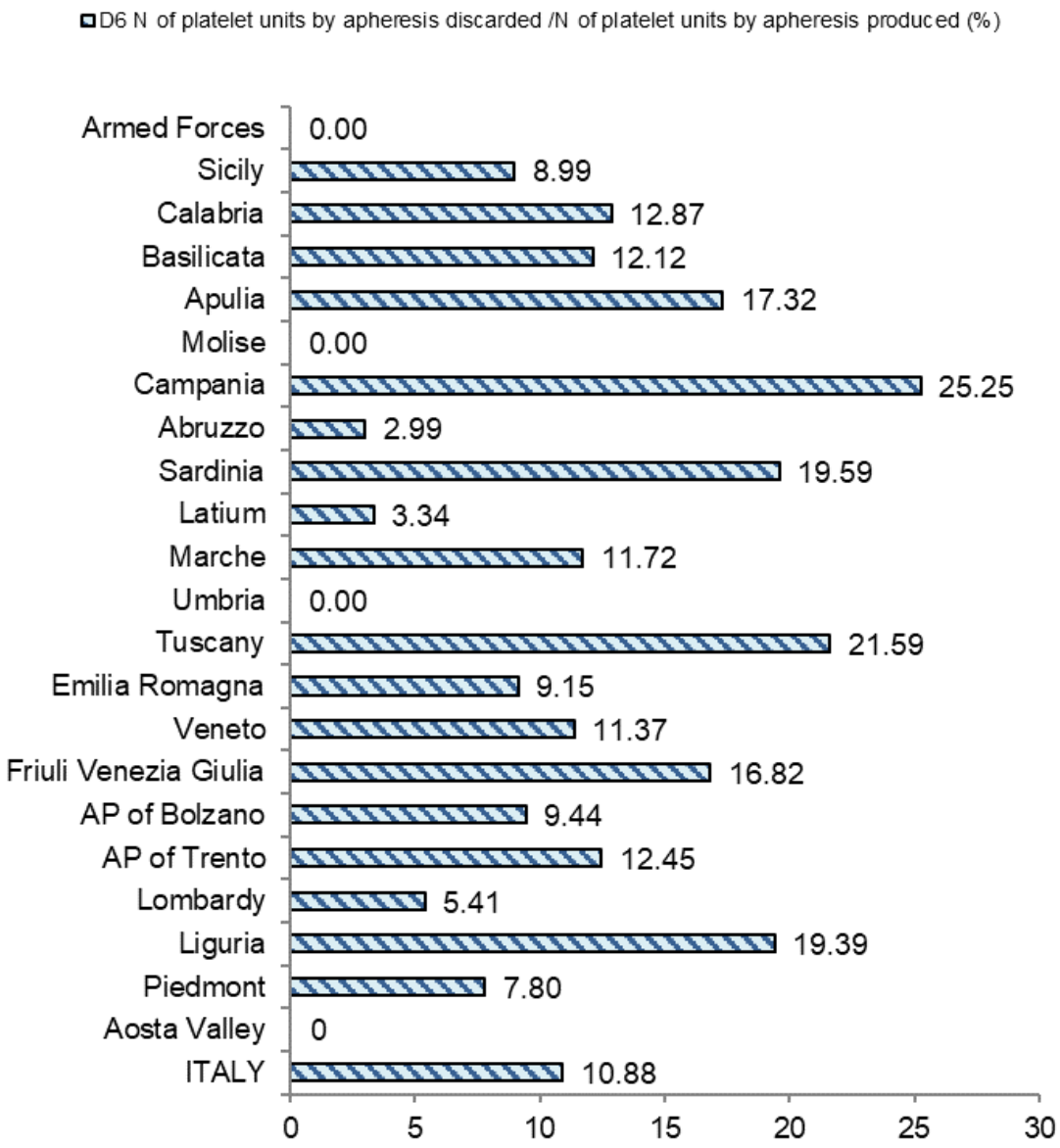
N. number; RBC Red Blood Cells; AP Autonomous Province

Figure A27. INDICATOR D4: N. of RBC units discarded for health reasons/N. of discarded RBC units (%) (2021)



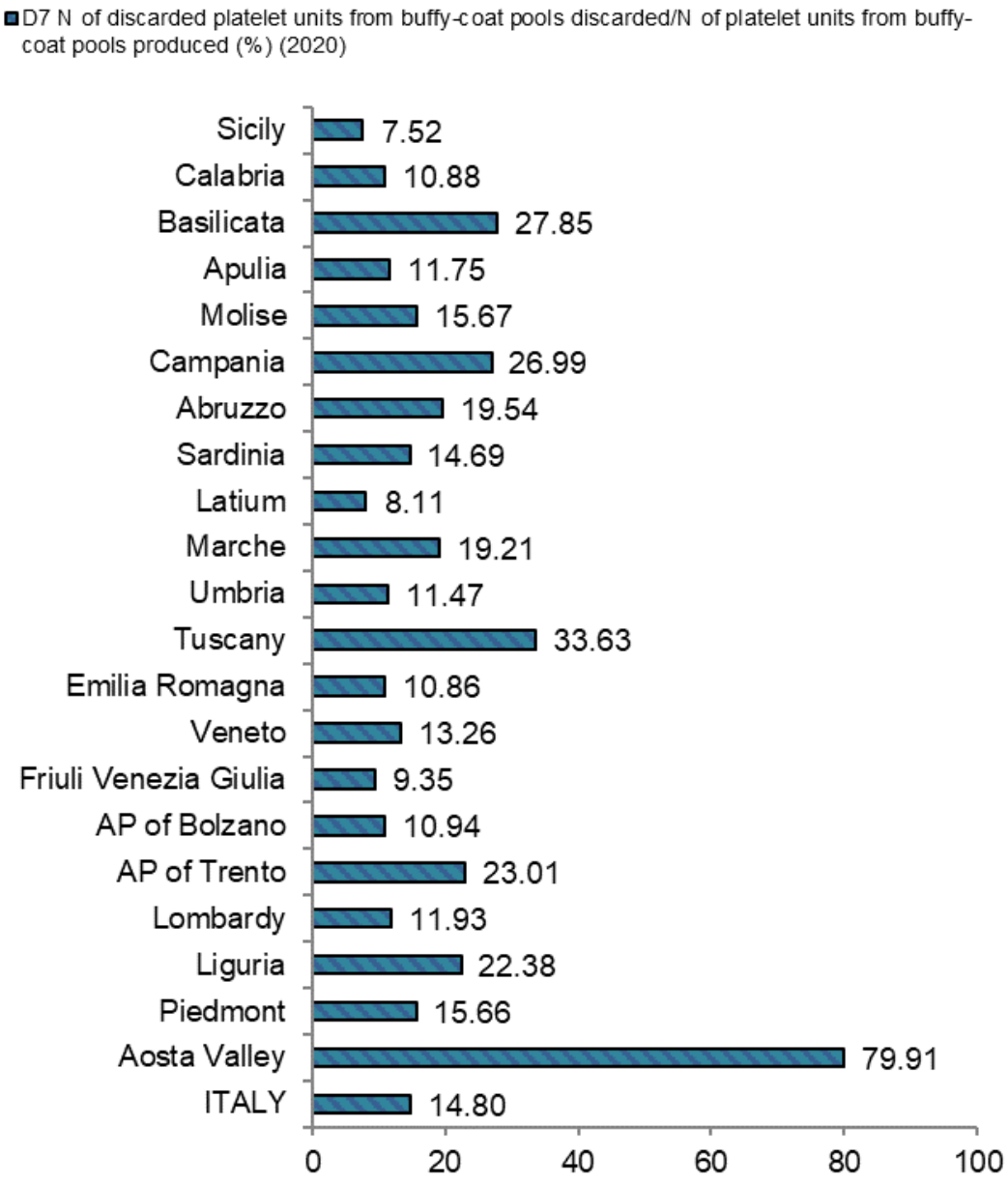
N. number; RBC Red Blood Cells; AP Autonomous Province

Figure A28. INDICATOR D5: N. of RBC units discarded for reasons linked to quality control/N. of discarded RBC units (%) (2021)



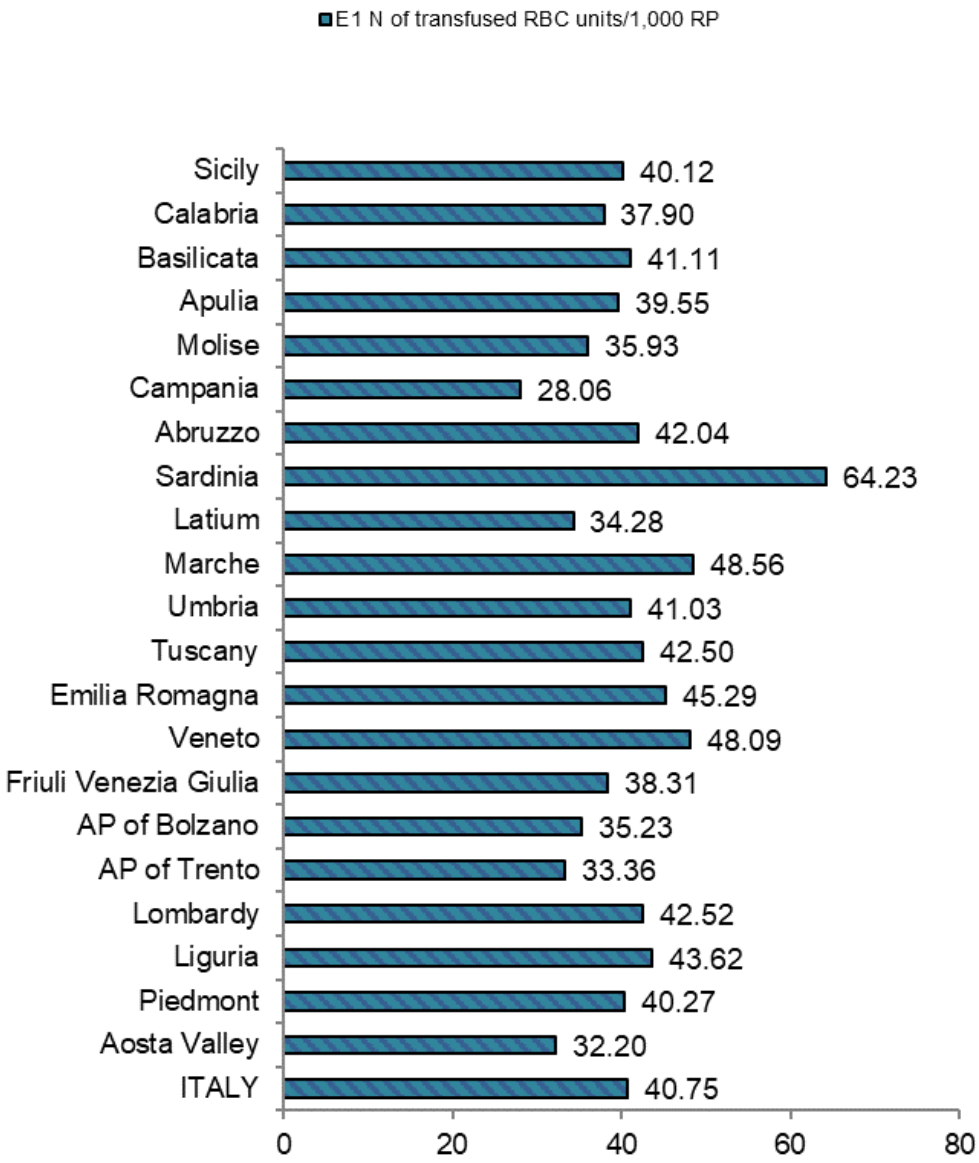
N. number; AP Autonomous Province

Figure A29. INDICATOR D6: N. of platelet units by apheresis discarded /N. of platelet units by apheresis produced (%) (2021)



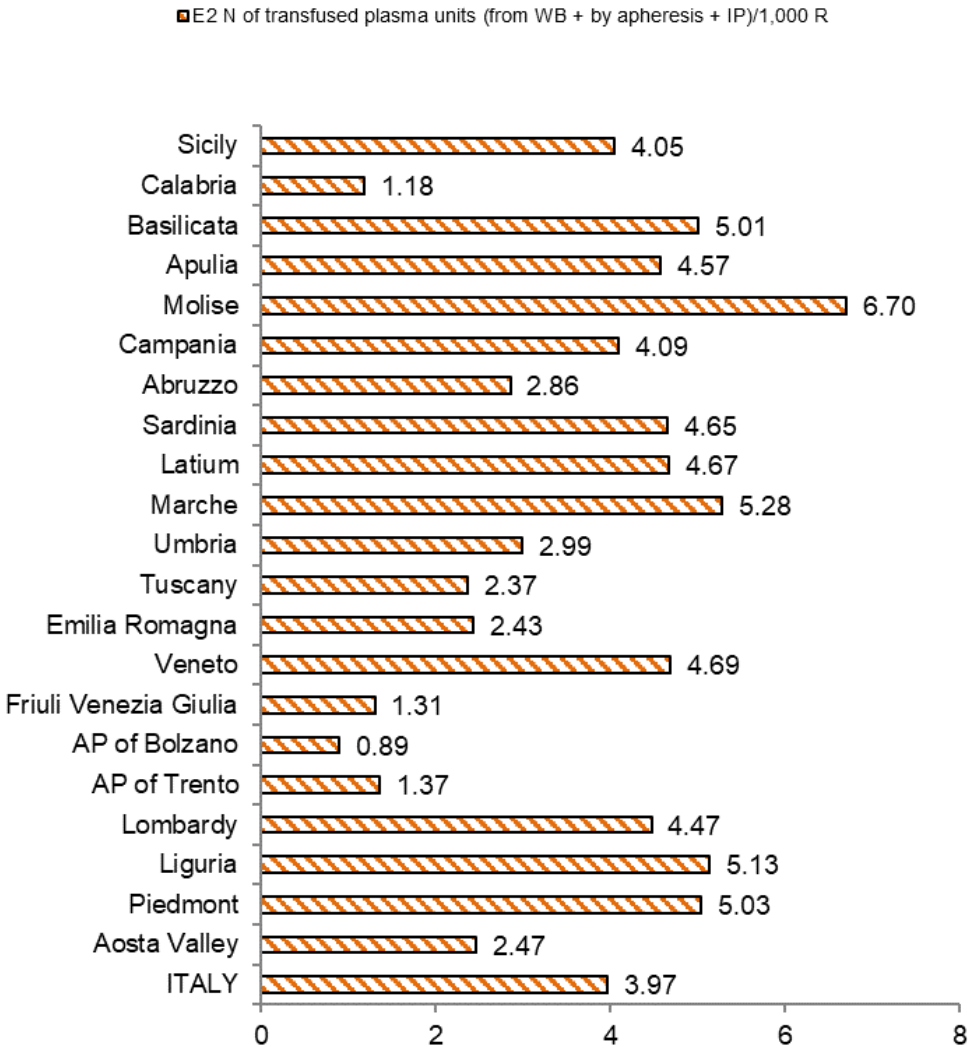
N. number; AP Autonomous Province

Figure A30. INDICATOR D7: N. of platelet units from buffy-coat pools discarded/N. of platelet units from buffy-coat pools produced (%) (2021)



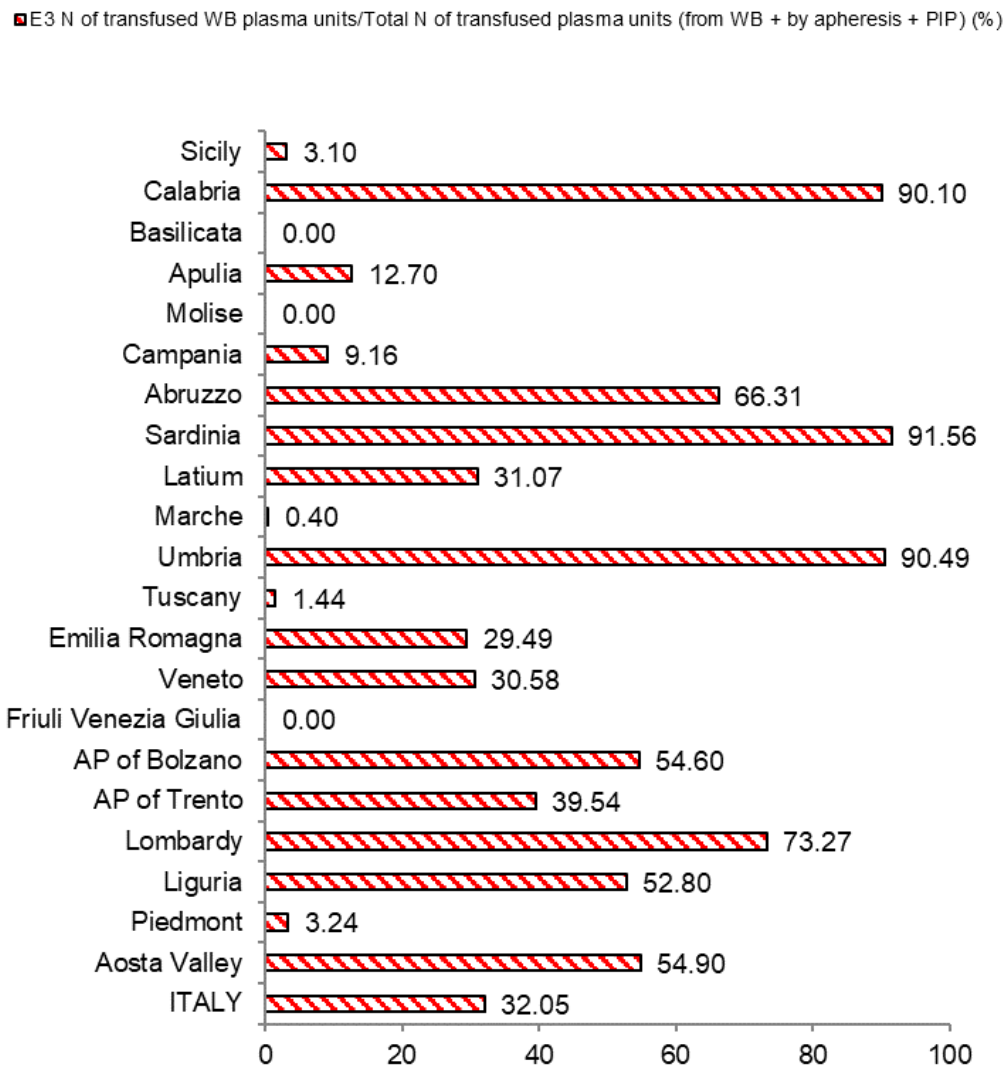
N. number; RBC Red Blood Cells; RP resident population; AP Autonomous Province

Figure A31. INDICATOR E1: N. of transfused RBC units/1,000 resident population (2021)



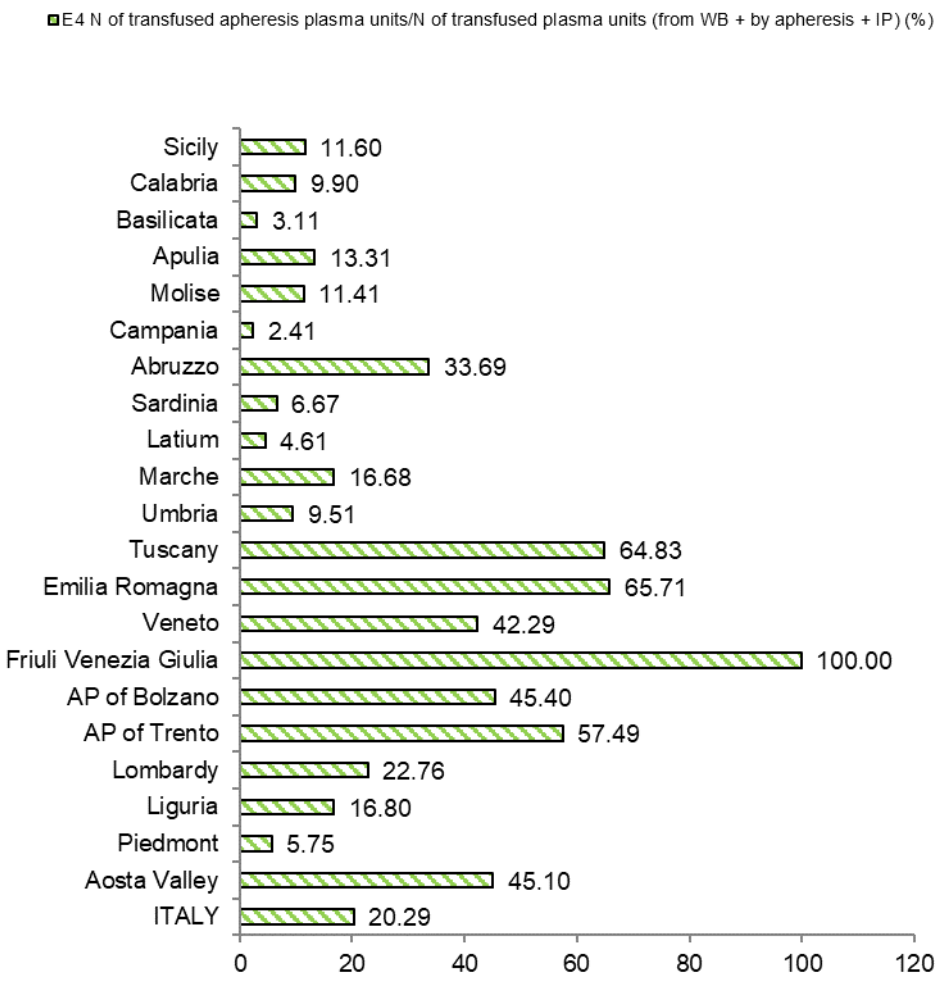
N. number; WB whole blood; PIP pharmaceutical virus-inactivated plasma; RP resident population; AP Autonomous Province

Figure A32. INDICATOR E2: N. of transfused plasma units (from whole blood + by apheresis + pharmaceutical virus-inactivated plasma)/1,000 resident population (2021)



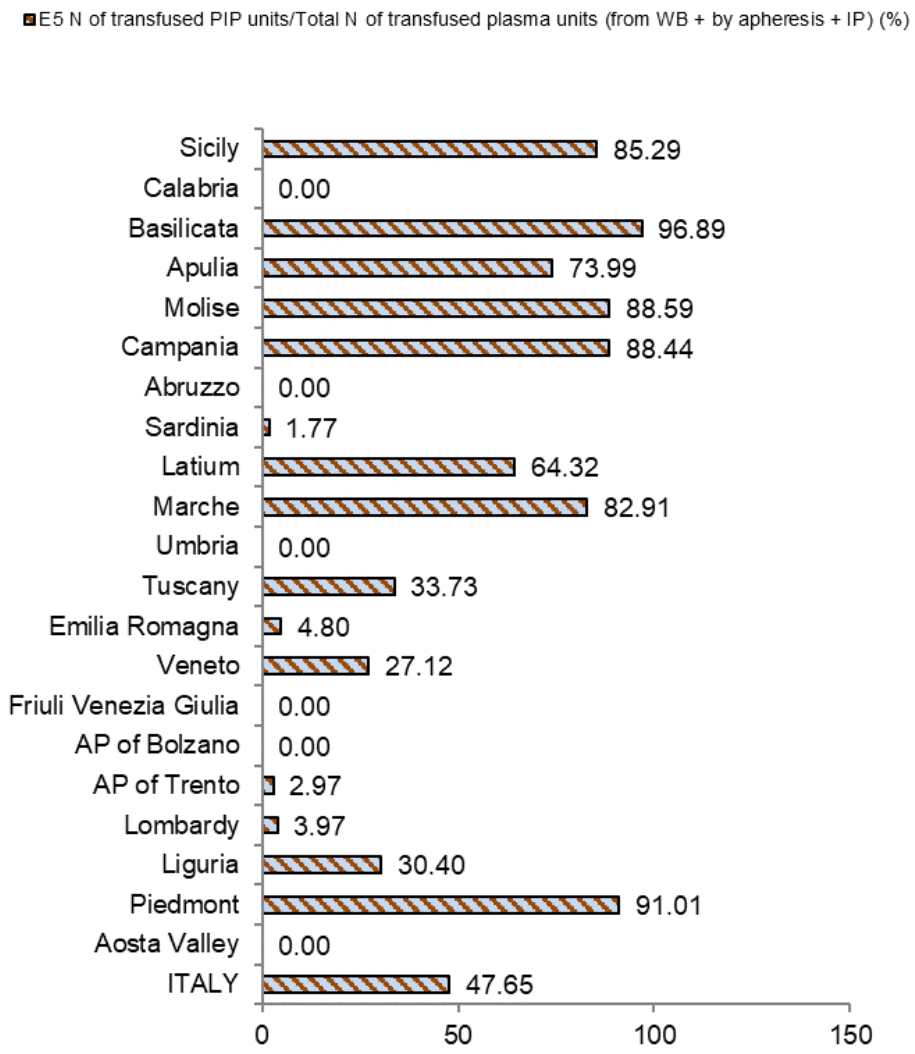
N. number; WB whole blood; PIP pharmaceutical virus-inactivated plasma; AP Autonomous Province

Figure A33. INDICATOR E3: N. of transfused whole blood plasma units/Total N. of transfused plasma units (from whole blood + by apheresis + Plasma pooled and treated for virus inactivation) (%) (2021)



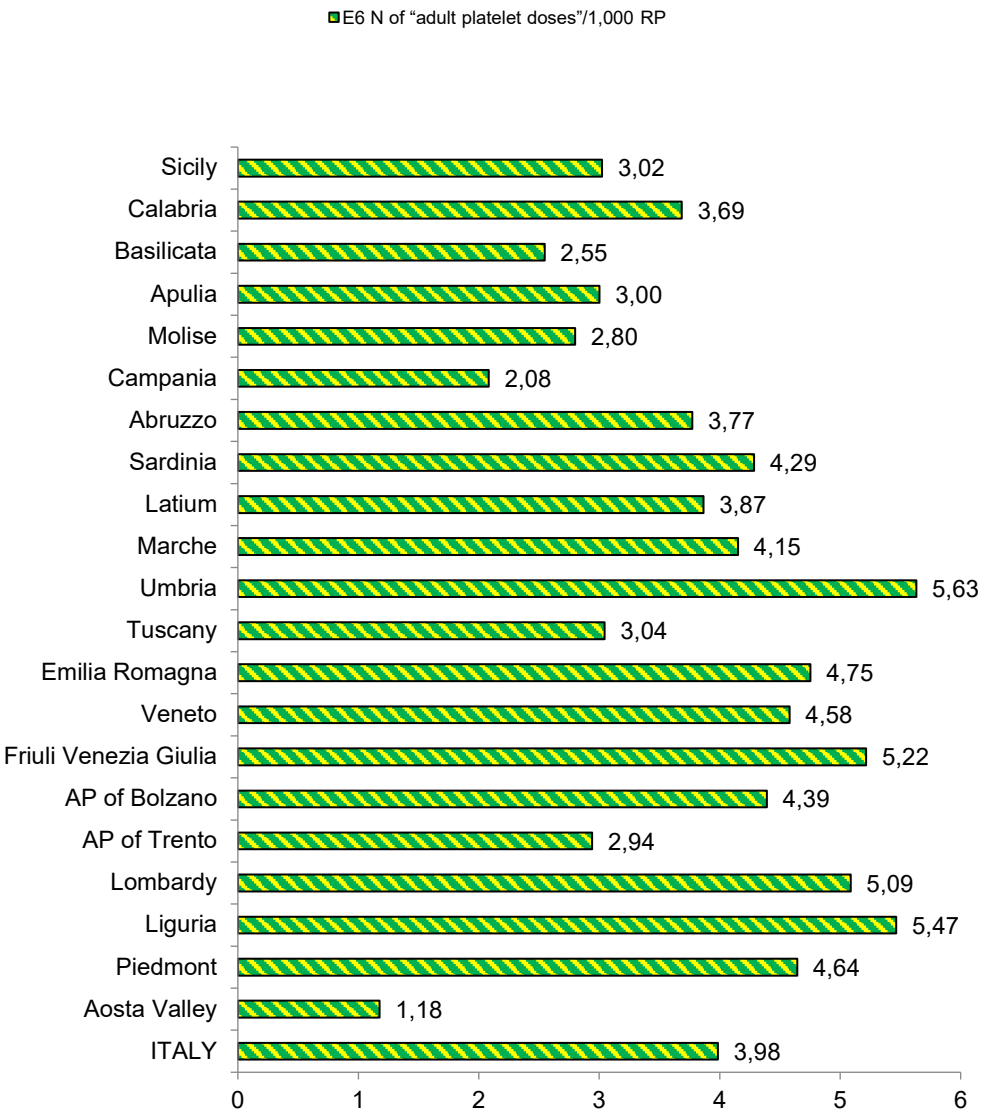
N. number; WB whole blood; PIP pharmaceutical virus-inactivated plasma; AP Autonomous Province

Figure A34. INDICATOR E4: N. of transfused apheresis plasma units/N. of transfused plasma units (from whole blood + by apheresis + Plasma pooled and treated for virus inactivation) (%) (2021)



N. number; WB whole blood; PIP pharmaceutical virus-inactivated plasma; AP Autonomous Province

Figure A35. INDICATOR E5: N. of transfused pharmaceutical virus-inactivated plasma units/Total N. of transfused plasma units (from whole blood + by apheresis + pharmaceutical virus-inactivated plasma) (%) (2021)



N. number; RP resident population; AP Autonomous Province

Figure A36. INDICATOR E6: N. of “adult platelet doses”/1,000 resident population (2021)

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