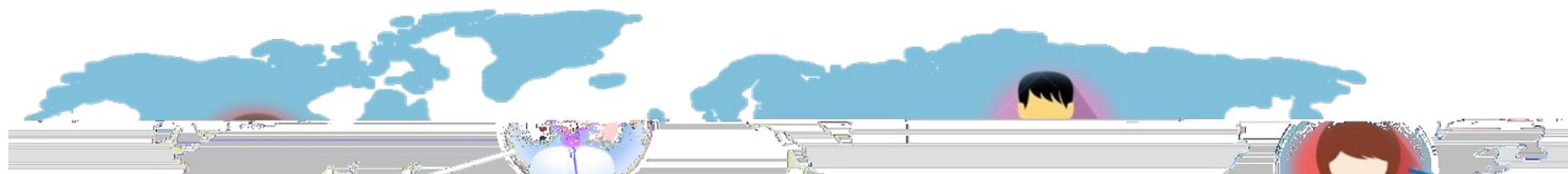


Il trapianto di CSE da non familiare e le criticità della rete



Di cosa parleremo.....

- Dove si trova il donatore giusto ...uno sguardo sul mondo
- Probabilità di matching in Italia e nel mondo
- La gestione della ricerca
- Import export
- Aumento work up
- CP in overbooking
- Miglioramento rete italiana
- Covid e donatori positivi
- Cordone: esiste sempre questa alternativa
- Dati pazienti: numero attivazioni, TX ecc



Uno sguardo sul mondo: numero donatori mondiali



41 million unrelated volunteer donors registered in 59 countries



811 thousand cord blood units banked in 41 countries

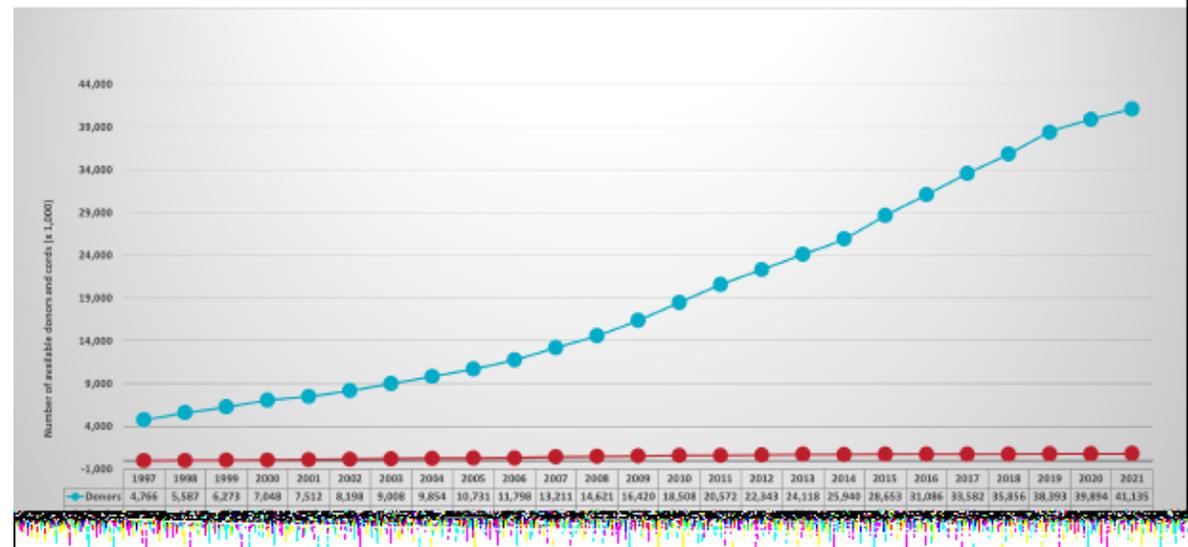
Listing 137 sources with 101 different IONs



ION:

Issuing
Organization
Number

no. donors and CBU globally available



Uno sguardo sul mondo: i registri donatori



| Country | Organisation | ION | Total * | ABDR | ABDR% Typed | DNA Class I | DNA Class II | Date Last File | Accreditation |
|---------|--|------|-----------|-----------|----------------|----------------|-----------------|-------------------|--|
| US | NMDP-National Marrow Donor Program/Be The Match | 3553 | 9,050,931 | 8,749,025 | 96.7 | 8,180,099 | 8,705,205 | 2022-10-06 | WMDA accredited (D/C) 2017 |
| DE | DKMS gemeinnützige GmbH | 5525 | 7,367,070 | 7,313,673 | 99.3 | 7,182,850 | 7,300,822 | 2022-10-10 | WMDA accredited (D/C) 2017 by Affiliation to ION-6939 |
| BR | REDOME - Registro Nacional de Doadores Voluntarios de Medula Ossea | 8766 | 5,053,159 | 5,052,779 | 100 | 5,053,159 | 5,052,827 | 2022-10-06 | WMDA expired (D/C) 2017 (was Qualified until 2022-05) |
| DE | ZKRD - Zentrales Knochenmarkspender-Register Deutschland | 6939 | 2,485,645 | 2,191,178 | 88.2 | 1,970,162 | 2,166,586 | 2022-10-02 | WMDA accredited (D/C) 2017 |
| DE | Fundacja DKMS | 7414 | 1,939,984 | 1,939,457 | 100 | 1,939,984 | 1,939,984 | 2022-10-10 | WMDA accredited (D/C) 2017 |



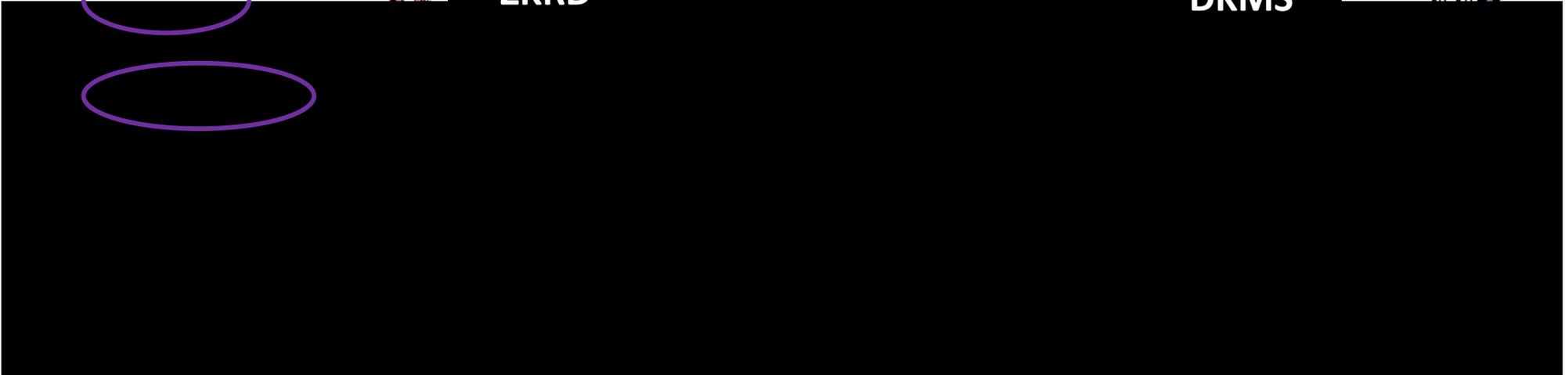
Uno sguardo sul mondo: i registri donatori



| Country | Organisation | Accreditation |
|---------|--|---|
| US | NMDP-National Marrow Donor Program/Be | accredited (D/C) 2017 |
| DE | DKMS gemeinnützige GmbH | accredited (D/C) 2017 by on to ION-6939 |
| BR | REDOME - Registro Nacional de Doadores Vo Ossea | expired (D/C) 2017 (was d until 2022-05) |
| DE | ZKRD - Zentrales Knochenmarkspender-Regis | accredited (D/C) 2017 |
| DE | DKMS | accredited (D/C) 2017 |

ZKRD

DKMS



Uno sguardo sul mondo: le caratteristiche dei donatori

growth of global inventory



2,5 million new unrelated volunteer donors recruited in 2021



15 thousand new cord blood units banked in 2021

donor characteristics



42% of donors are younger than 35 years



57% of donors are female

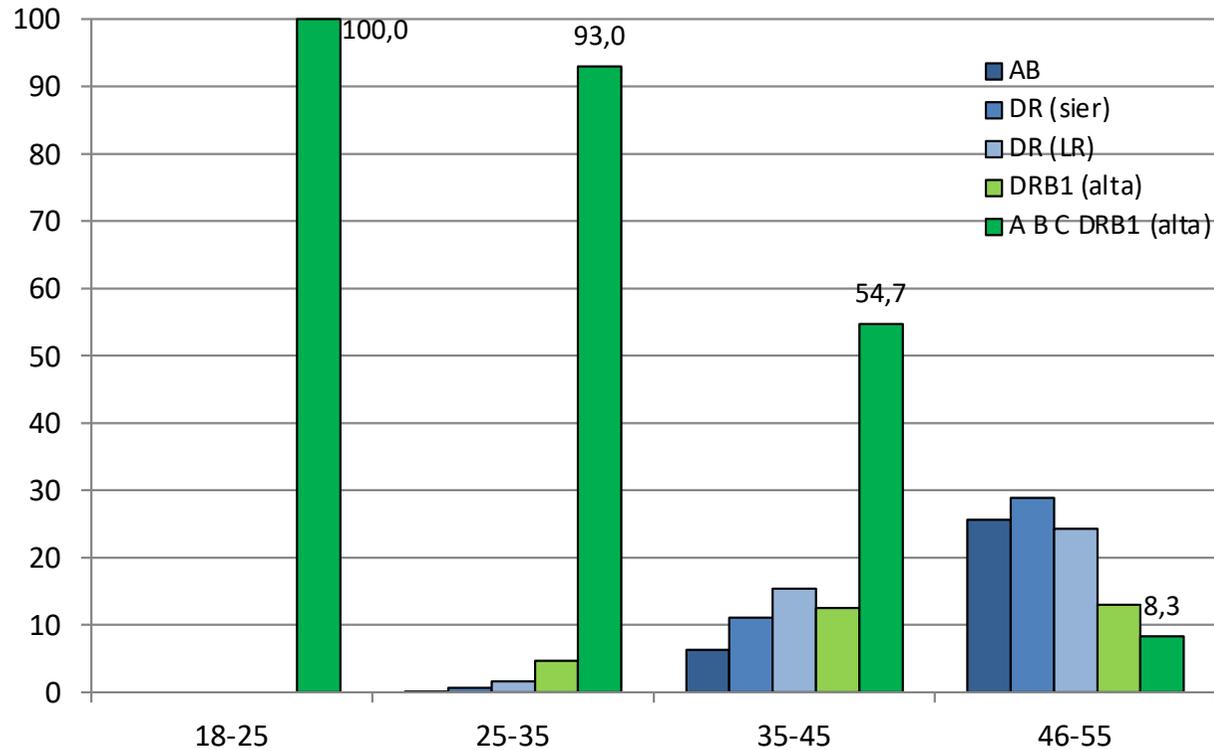
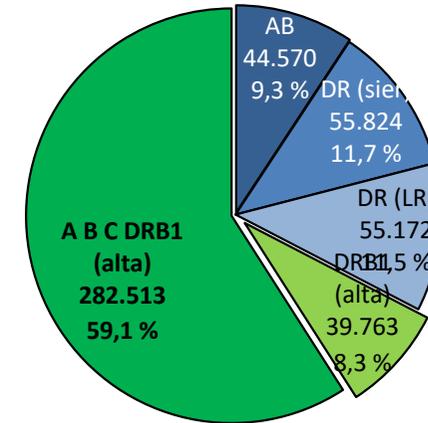


54% of donors and **20%** of CBUs are typed for 5 or 6 loci

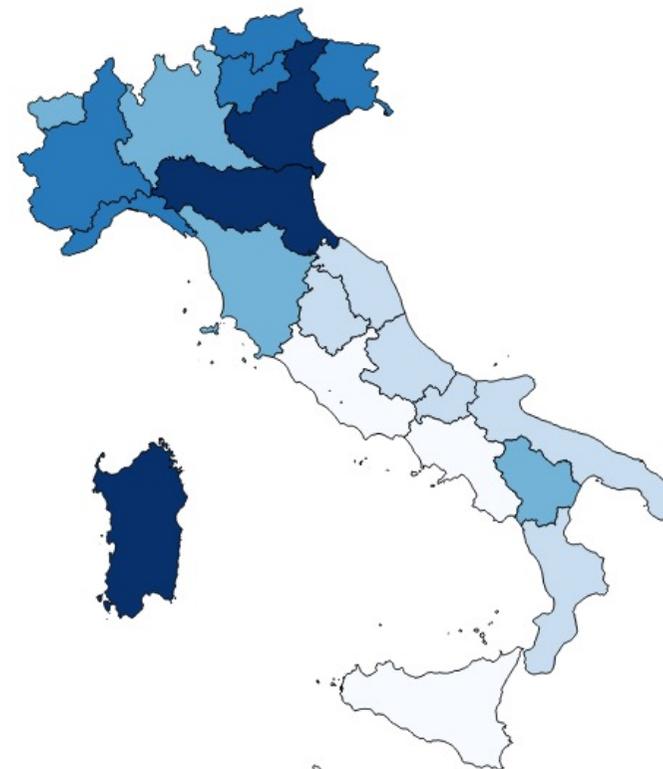
Registro Italiano

Totale donatori attivi
477.842

Livello di tipizzazione dei donatori attivi al 30 settembre 2022 e ripartizione per classe d'età

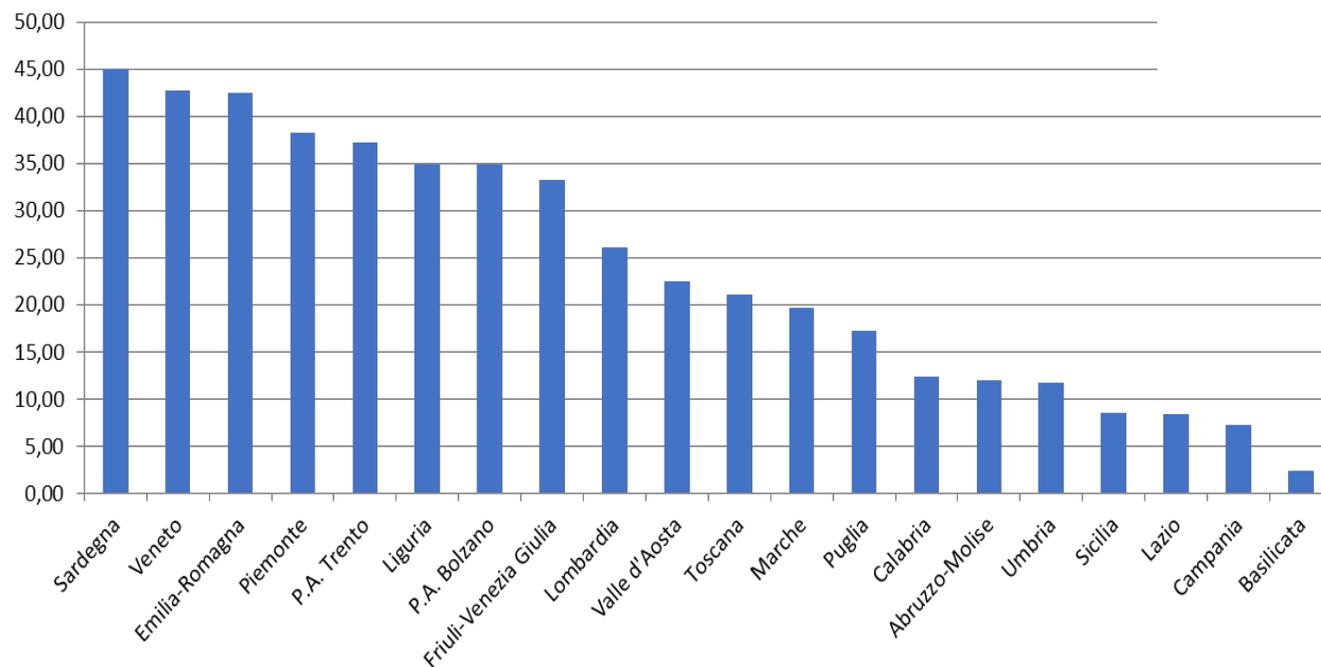


L'archivio nazionale dei donatori: iscrizioni totali per regione

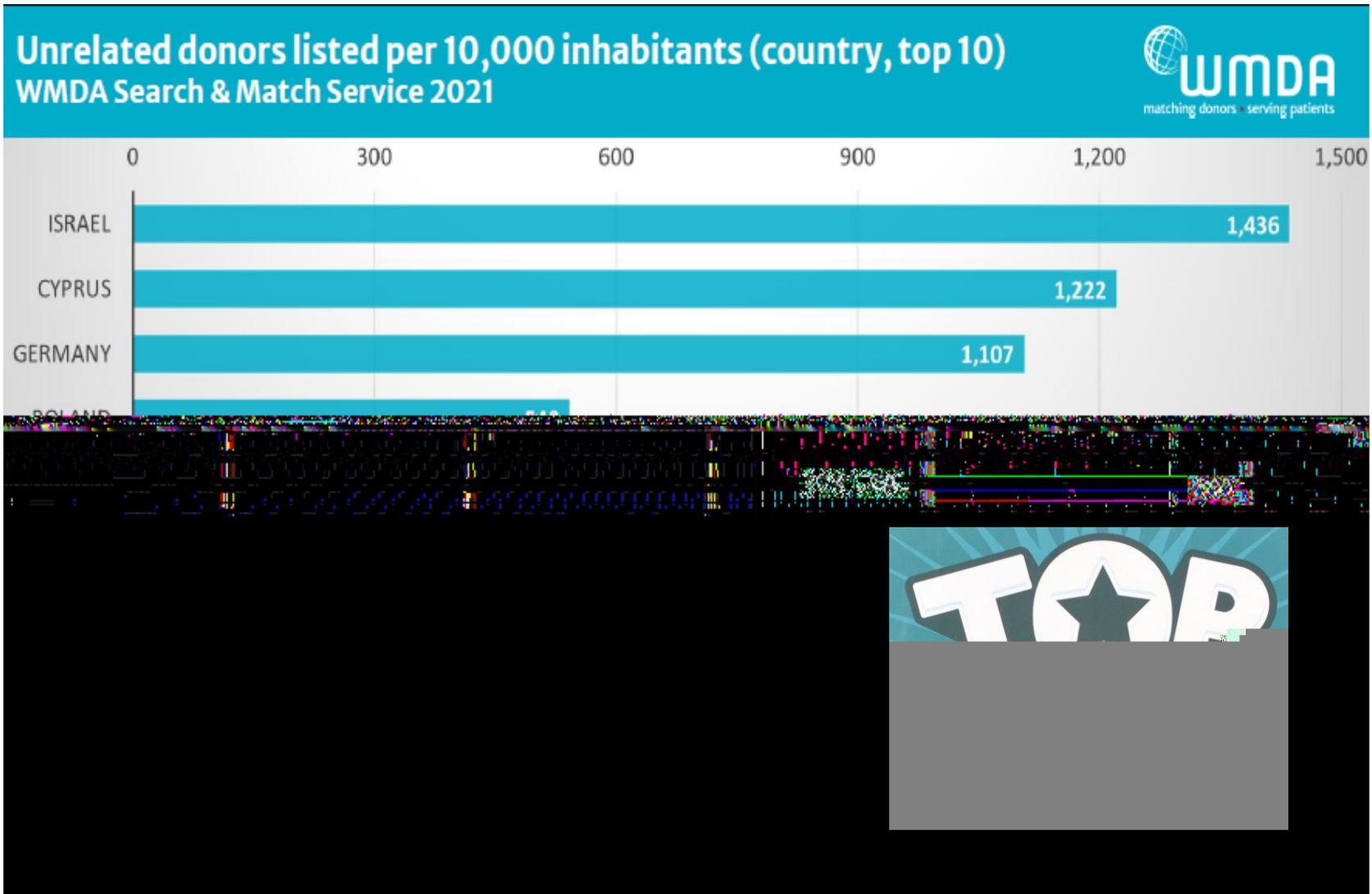


Indice di iscrizione totale

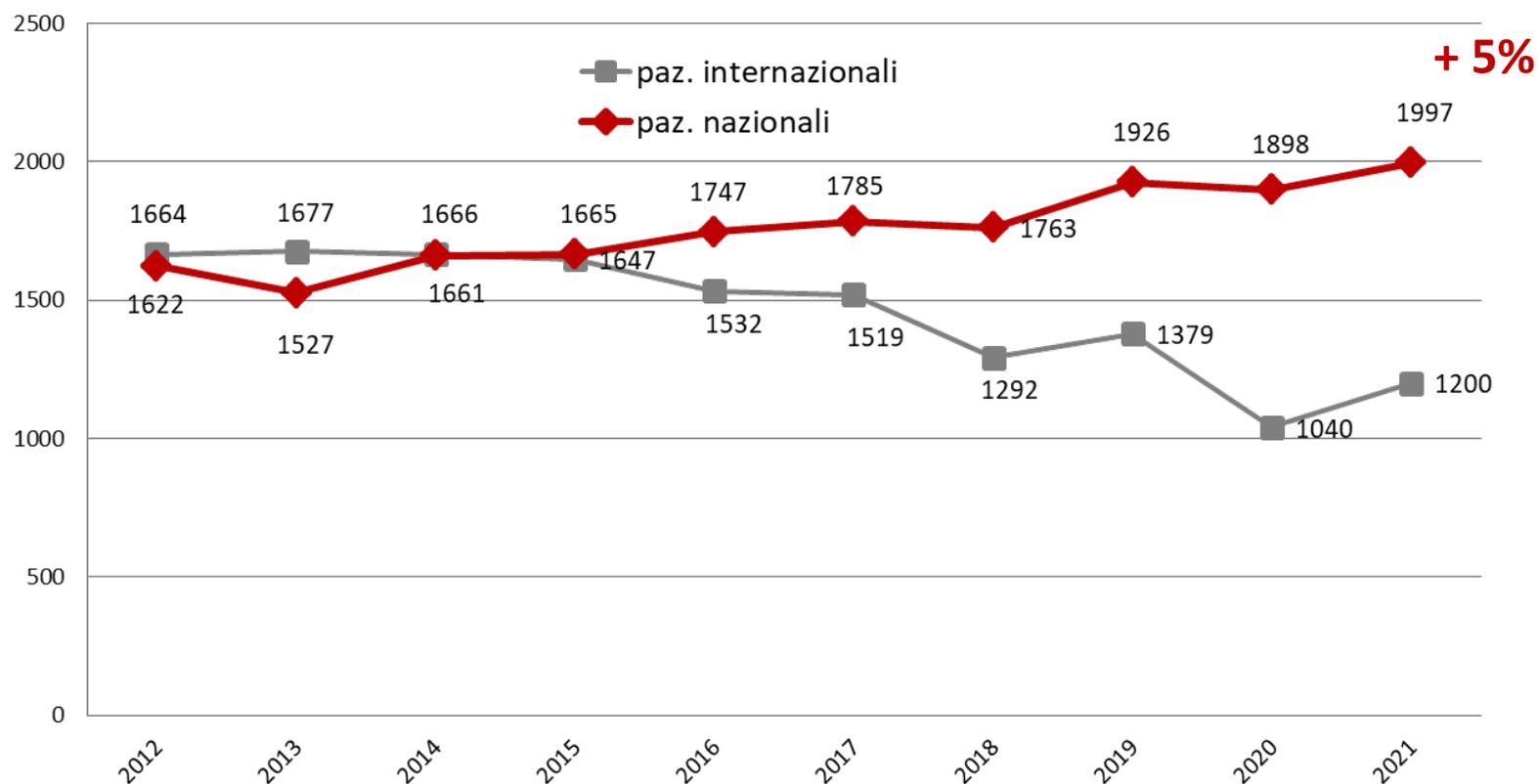
Rapporto (x 1.000 abitanti) tra il numero totale di donatori iscritti e la popolazione residente all'1/1/2022 per regione/PA



Uno sguardo sul mondo



I pazienti: quante ricerche di donatore non familiare attivate



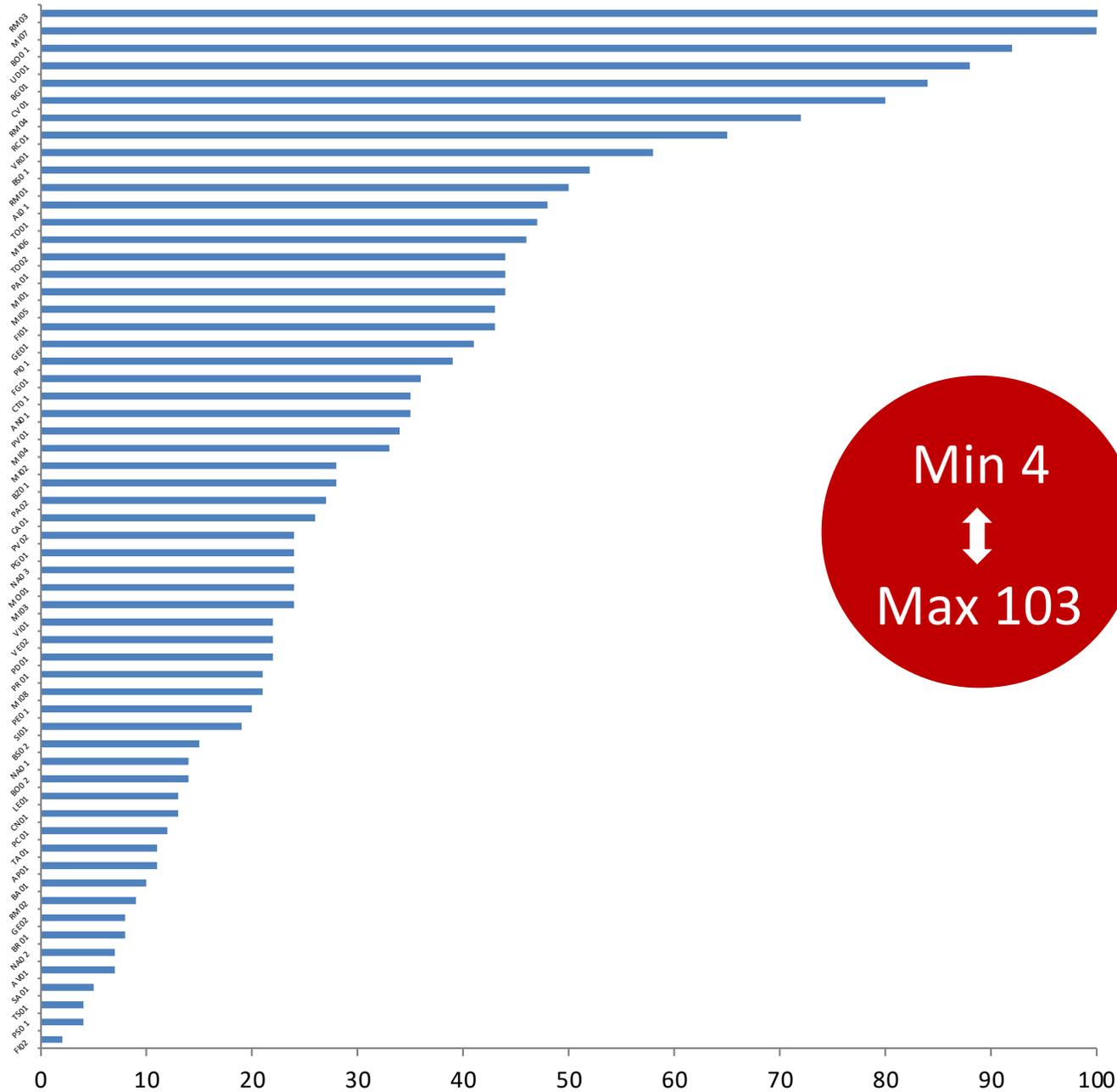
+20%

Incremento numero attivazioni di ricerca negli ultimi 5 anni

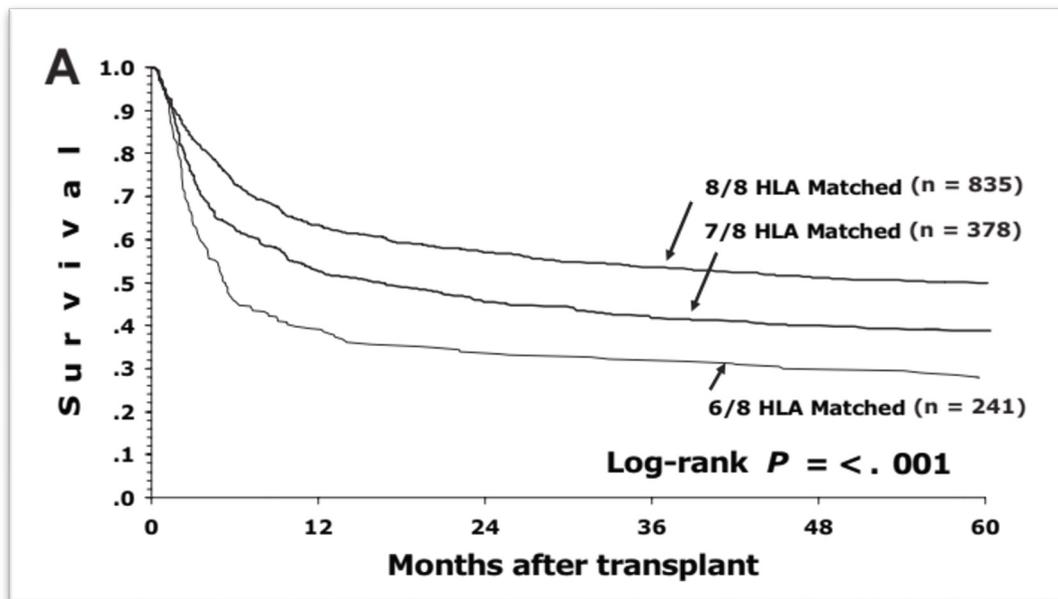
65.627

Pazienti attivati in ricerca in Italia

Numero attivazioni ricerca per CT / anno



Qual'è l'obiettivo ?



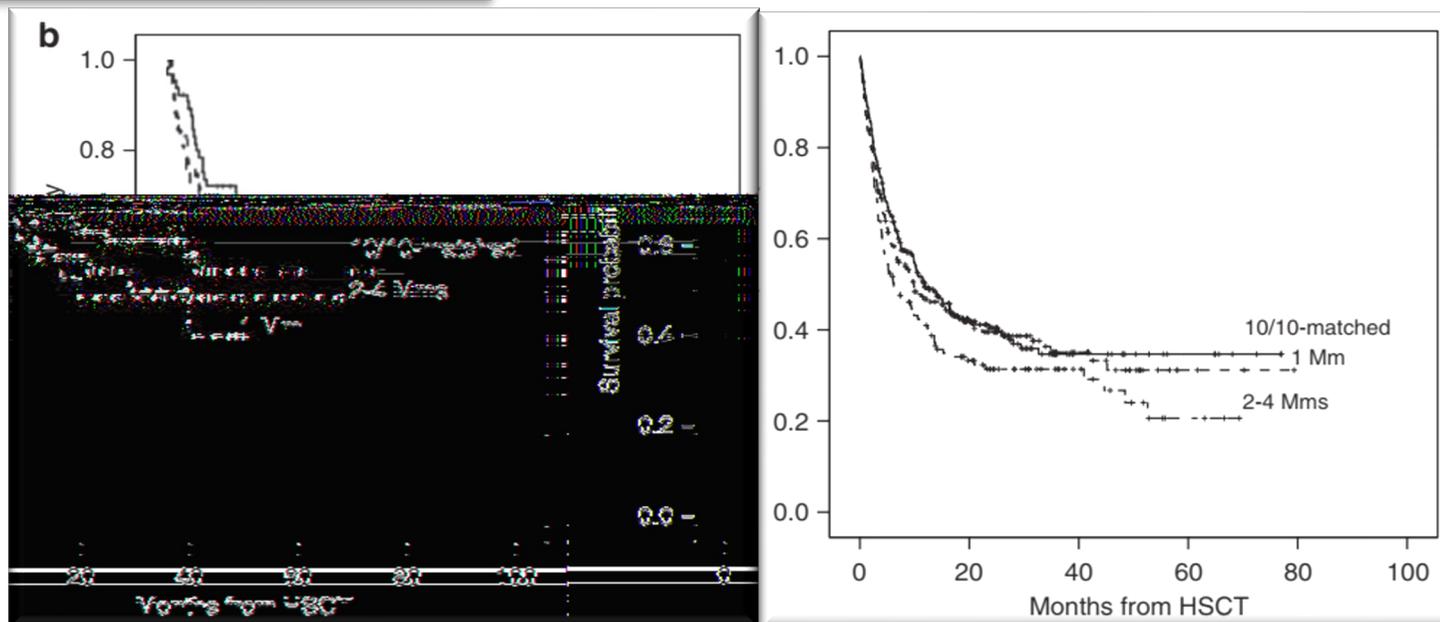
Lee et al., Blood 2007

Pidala et al., Blood 2014

Crocchiolo et al., BMT 2009

Picardi et al., Transpl Cell Ther 2021

antigenic \approx allelic



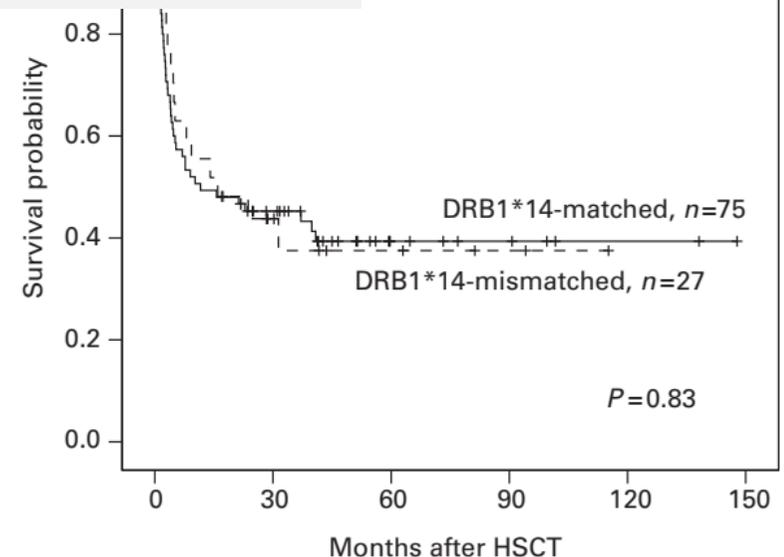
Non tutti i mismatched sono mismatched!



- Non-HLA factors: donor age matters most
- CMV, sex, ABO, pregnancies, weight, registry, distance,...
- Other «competing» donor types: haplo, CBU
- Selection algorithms depend on center-specific experience



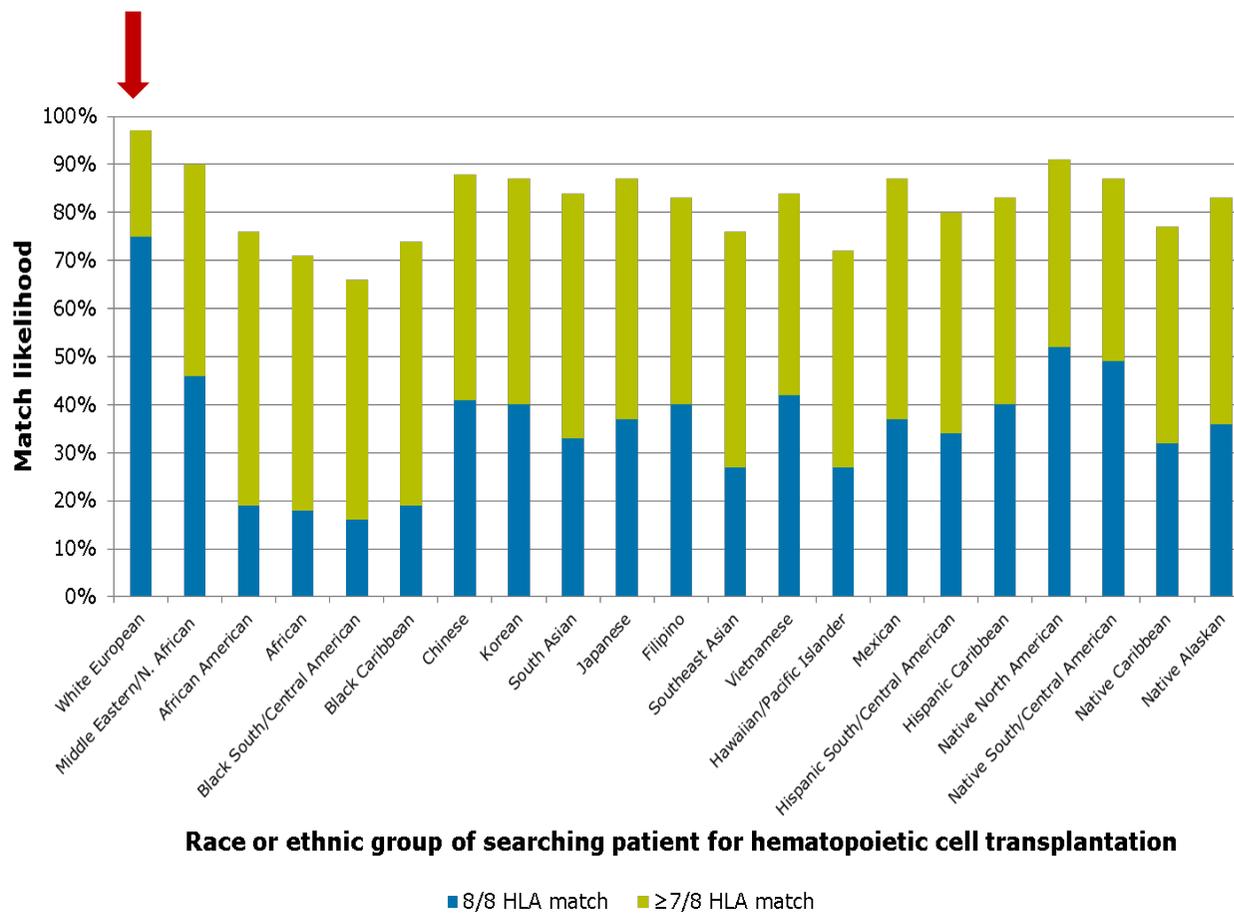
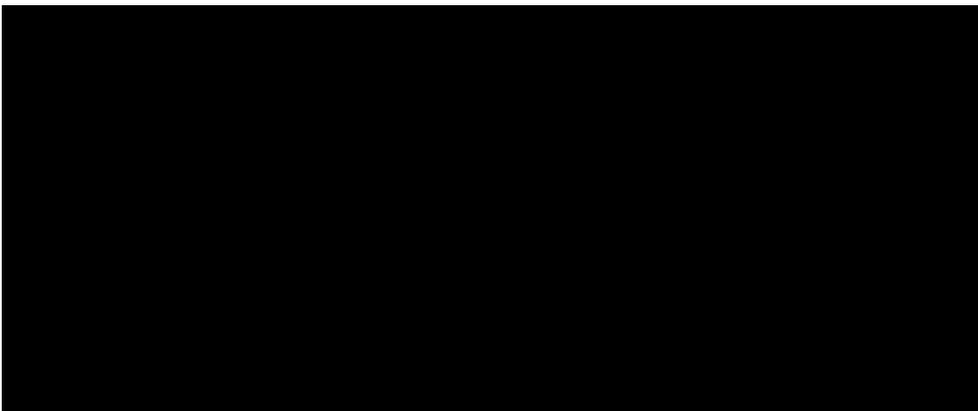
LA-MM at DRB1



The conundrum of HLA-DRB1*14:01/*14:54 and HLA-DRB3*02*02:02 mismatches in unrelated hematopoietic SCT

A Pasi¹, R Crocchiolo², M Bontempelli³, C Carcassi⁴, G Carella⁵, L Crespiatico⁶, L Garbar L Mascaretti⁸, B Mazzi⁹, G Mazzola¹⁰, V Miotti¹¹, B Porfirio¹², C Tagliaferri¹³, T Valentini C Vecchiato¹⁵, K Fleischhauer^{9,16}, N Sacchi¹⁷, A Bosi¹⁸ and M Martinetti¹

Probabilità di trovare un donatore matched a seconda dell'origine etnica



RELATIVE PERCENTAGE OF UNIQUE U-A-A, -B, -OR -S TYPE PHENOTYPES OF STEV. GEN. DONORS PER COUNTRY ATTRIBUTED TO THE ENTIRE DATABASE BY COUNTRY

Age of unique phenotypes in 2015

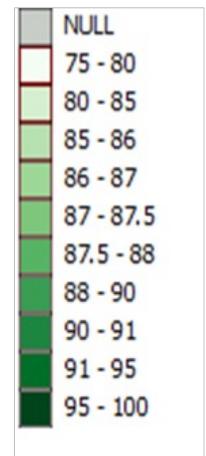
Remark:

Uruguay and United Arab Emirates had too few U-A-

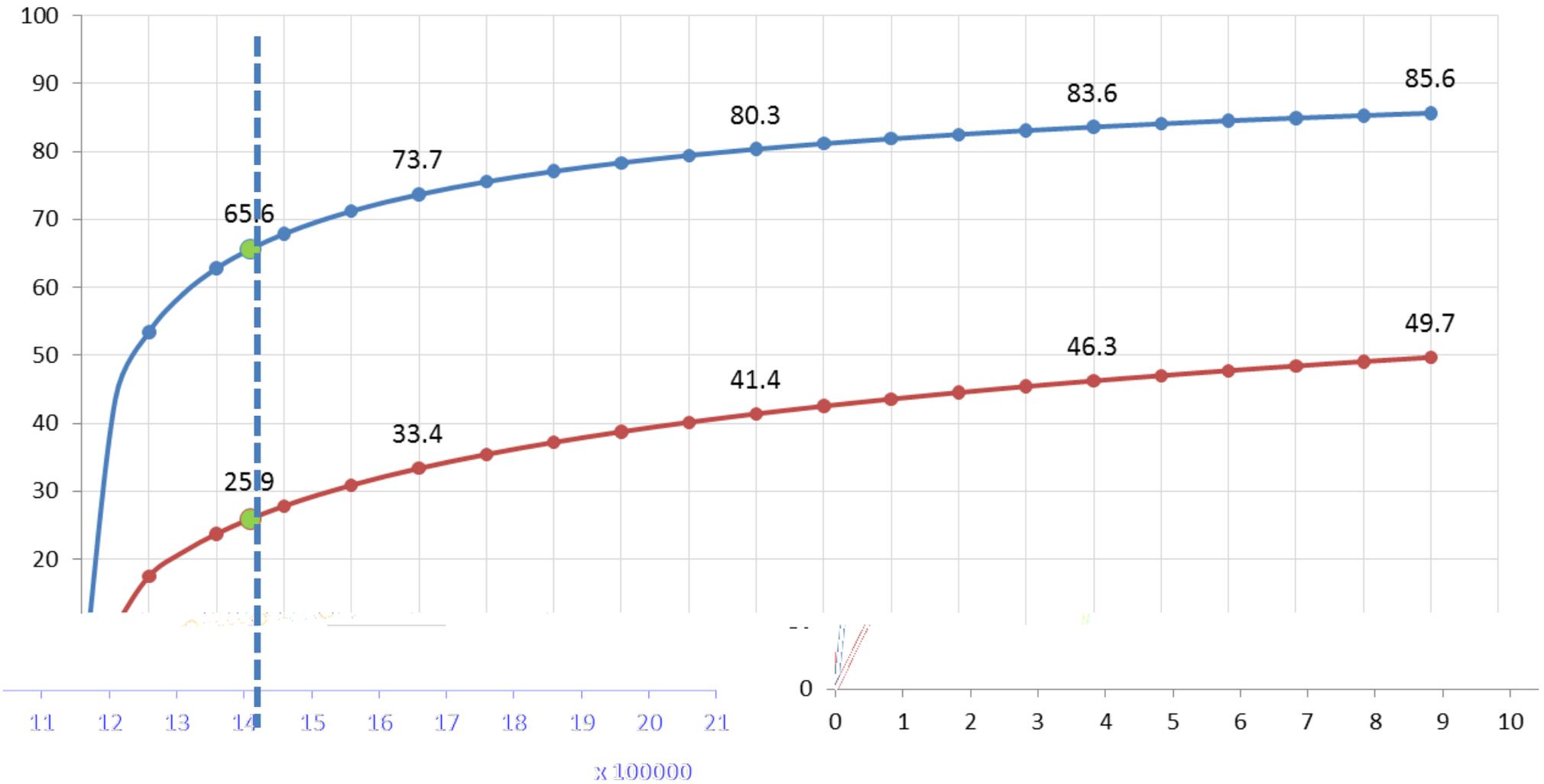
phenotypes to be included in the analysis.



Polimorfismo HLA in Italia

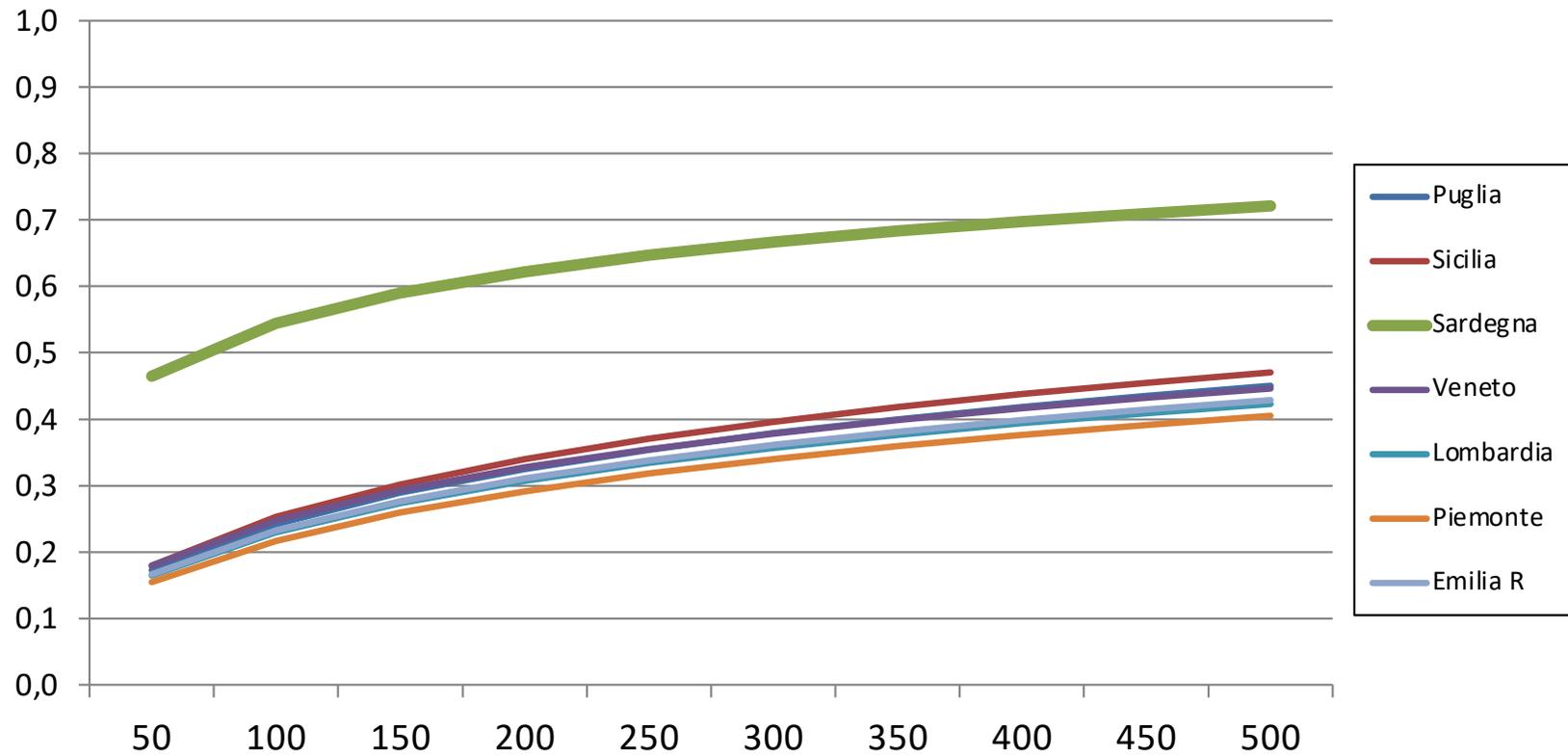


Probabilità di identificare un donatore in un registro di dimensione N



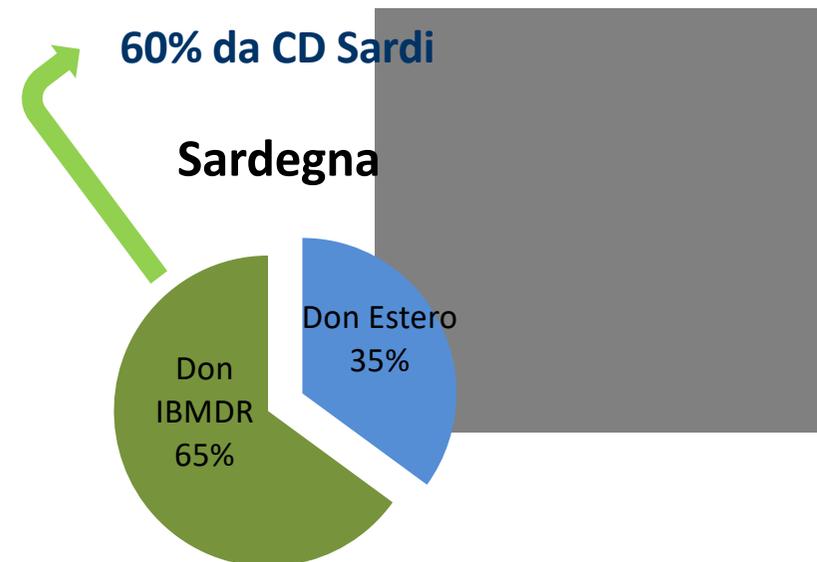
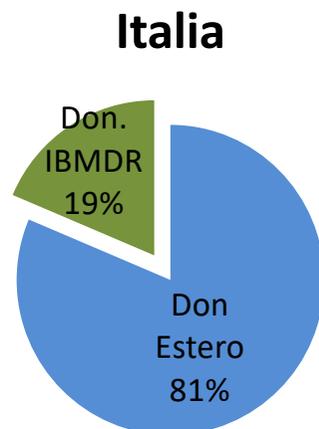
* Con mismatched in I classe

Confronto autosufficienza Sardegna vs altre Regioni



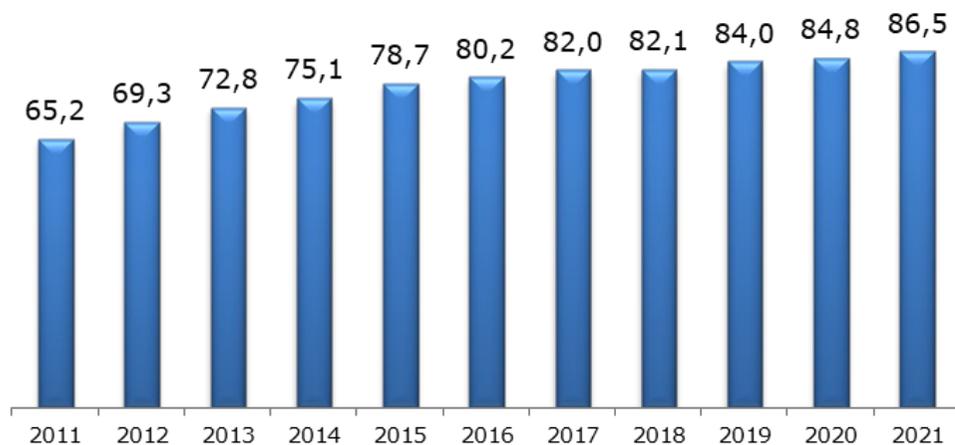
La probabilità in Sardegna

| Set of patients | International donors | IBMDR donors | % IBMDR donors | TOTAL |
|---|----------------------|--------------|----------------|-------|
| Italian patients (Sardegna patients excluded) | 1,264 | 389 | 23.53 | 1,653 |
| SARDEGNA patients | 19 | 15 | 44.12 | 34 |
| Total | 1,283 | 404 | 23.95 | 1,687 |

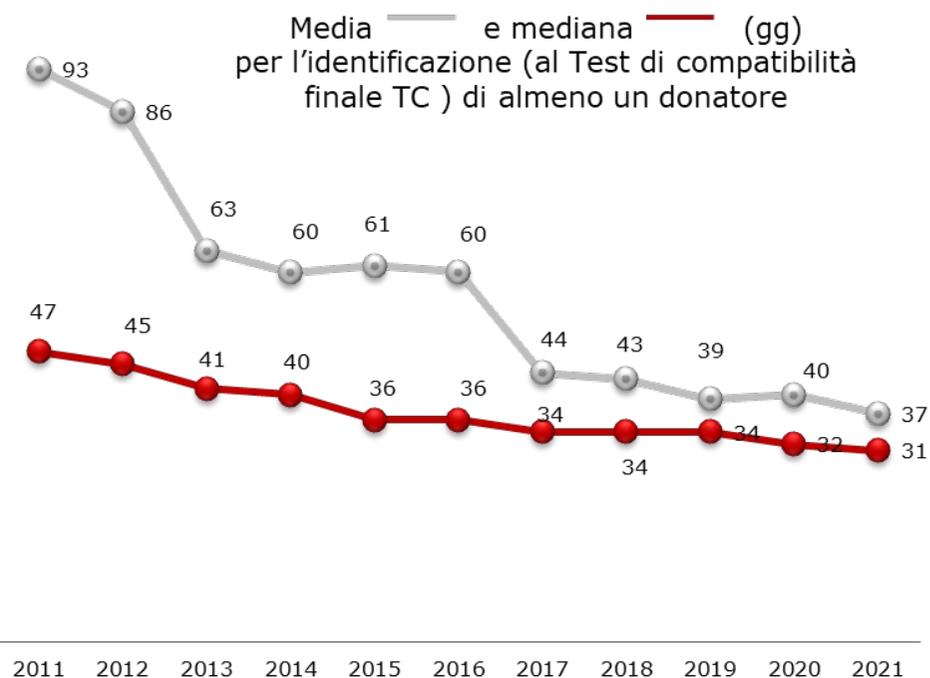


Efficienza della ricerca: quanti pazienti trovano il donatore

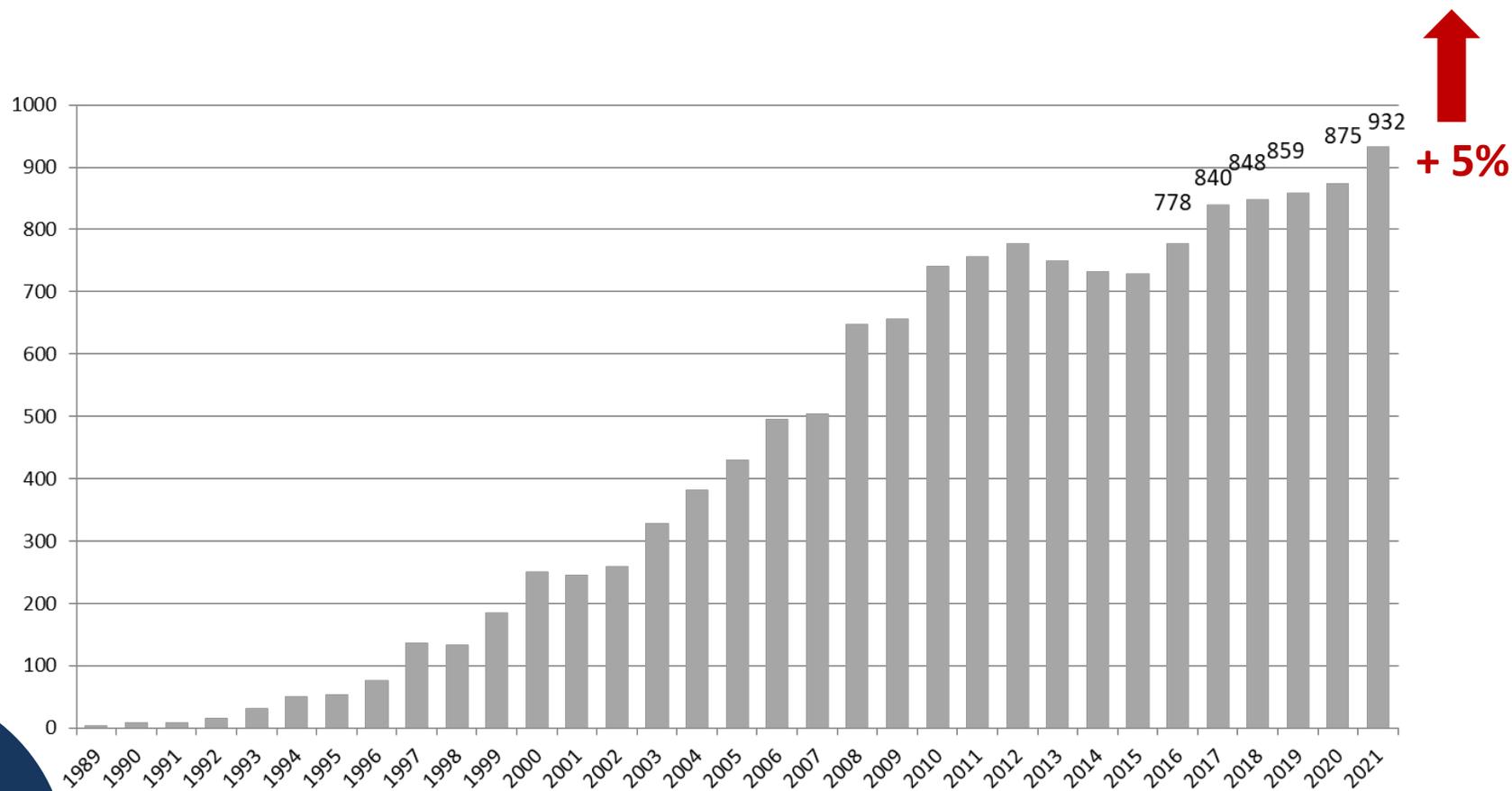
% pazienti per i quali è stato identificato almeno un donatore compatibile al TC



86,5%
dei pazienti trova
almeno un donatore
in circa un mese



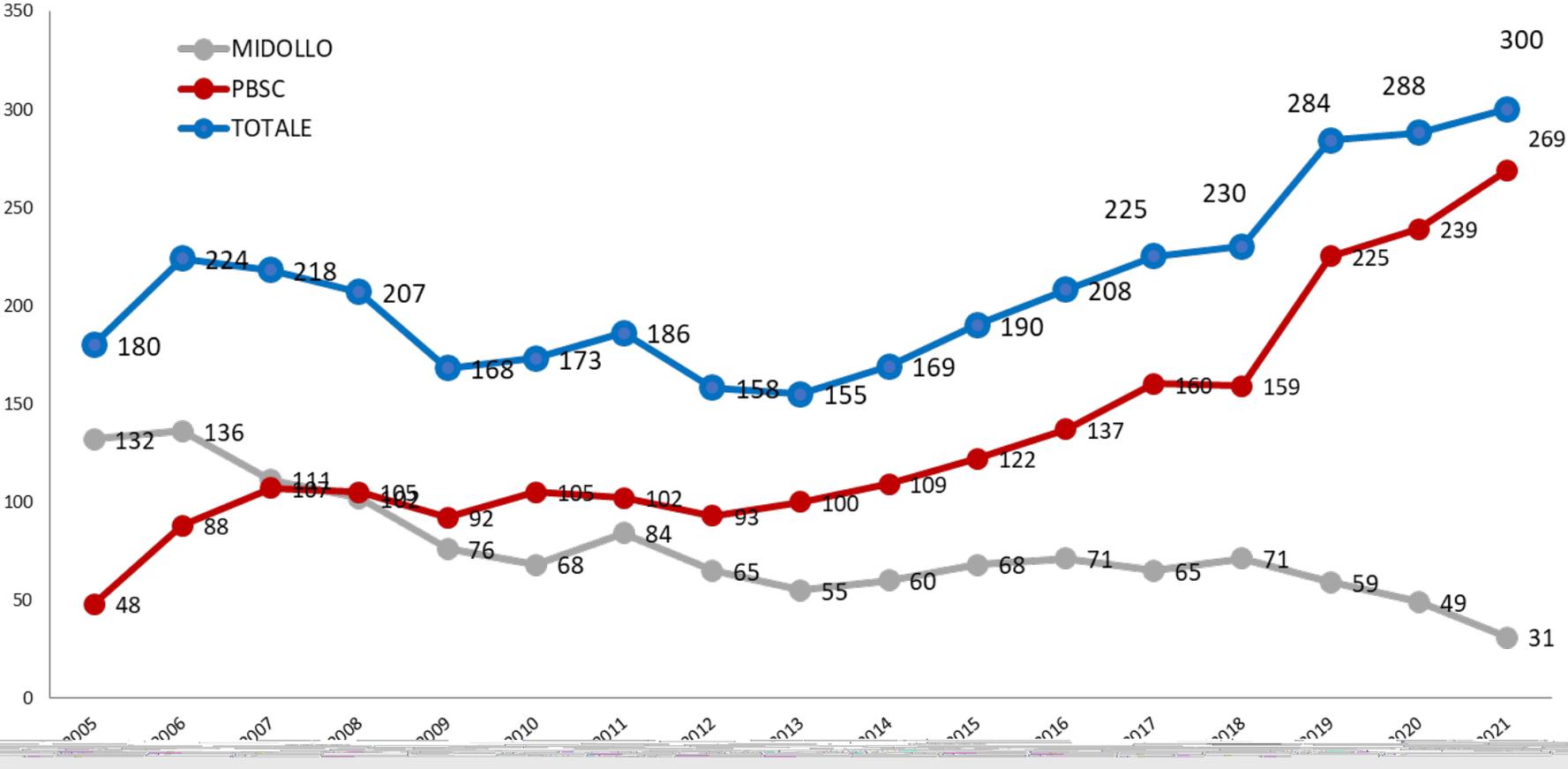
Efficienza della ricerca: quanti pazienti vengono trapiantati



14.522

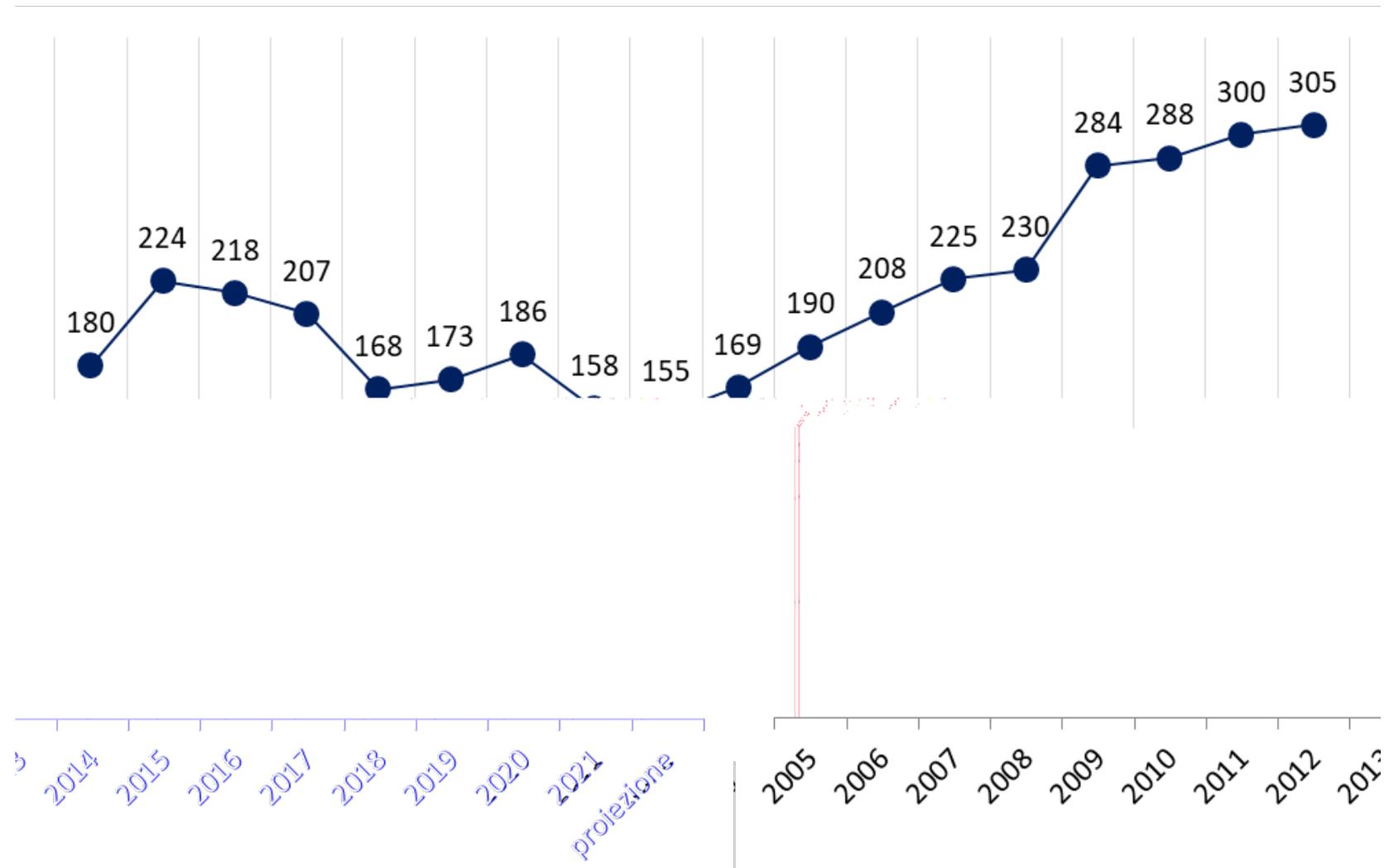
Pazienti trapiantati da
MUD in Italia
(+20% negli ultimi 5
anni)

Le donazioni IBMDR: i numeri

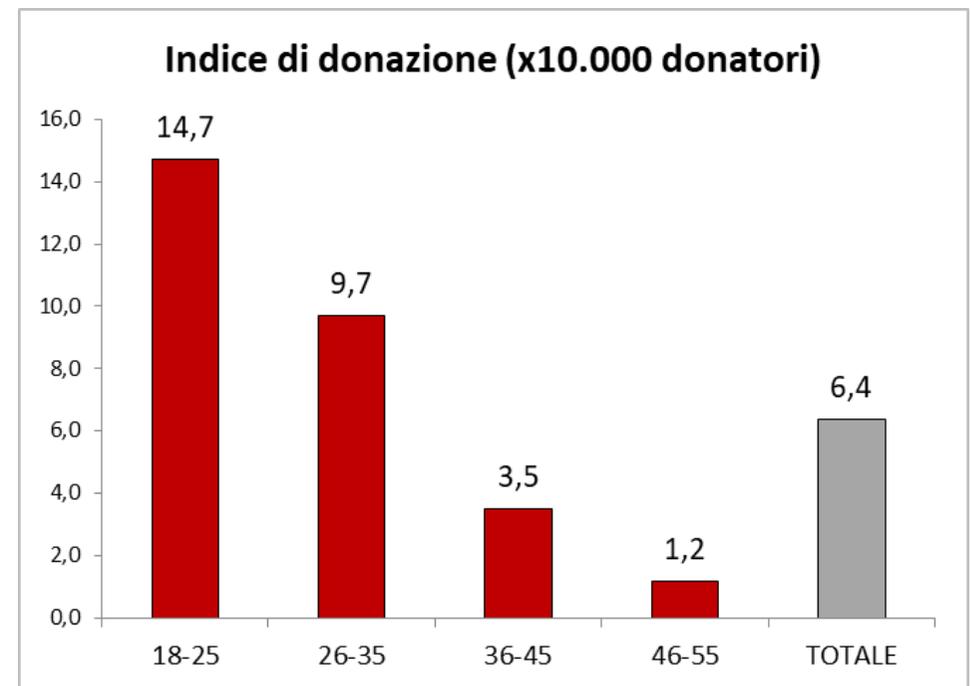
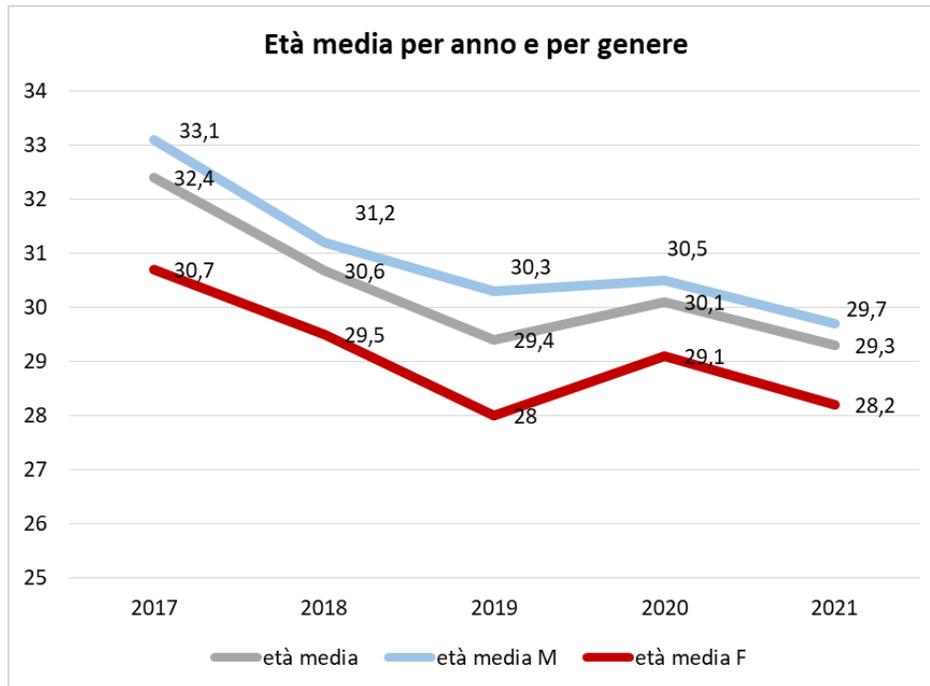


Donazioni IBMDR Trend negli anni

82% PBSC



Le donazioni IBMDR: chi dona

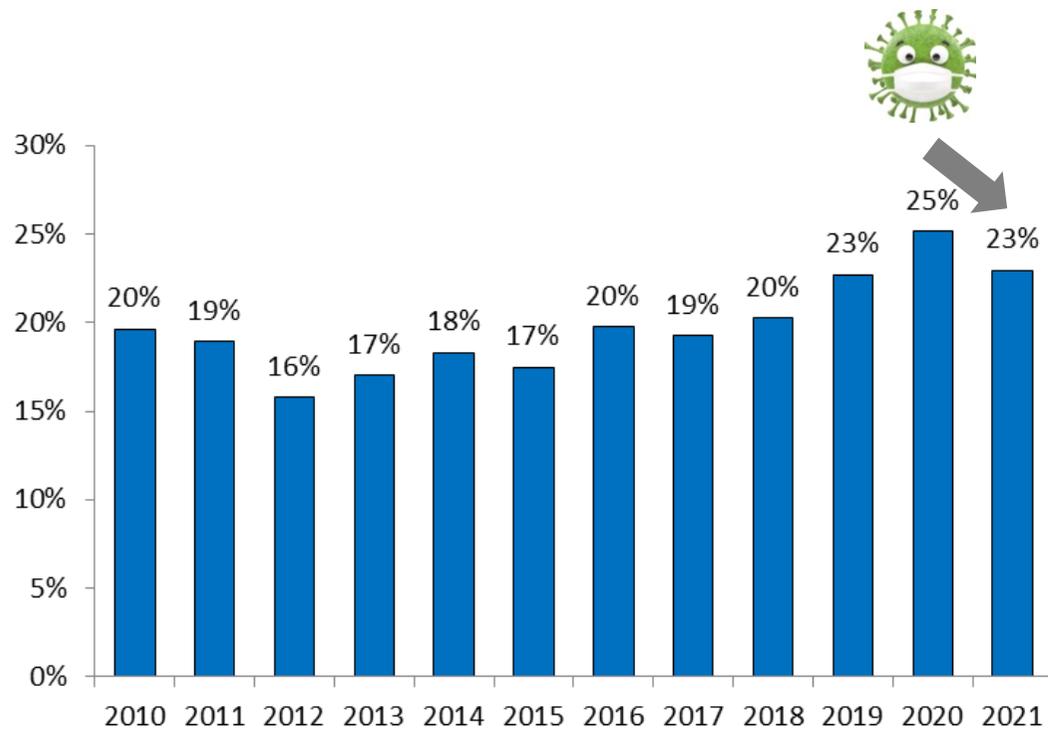


La sostenibilità e l'autosufficienza

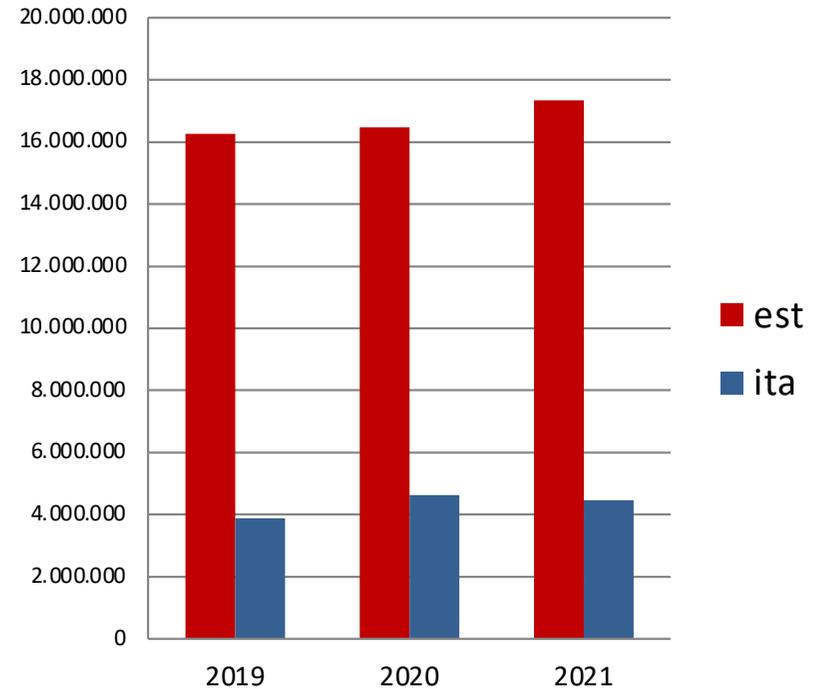


La sostenibilità e l'autosufficienza

Trapianti eseguiti con donatore IBMDR



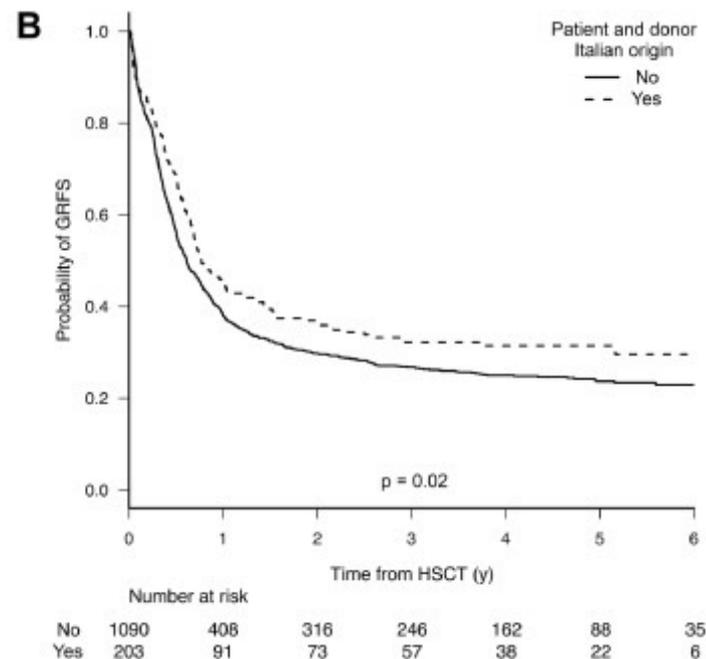
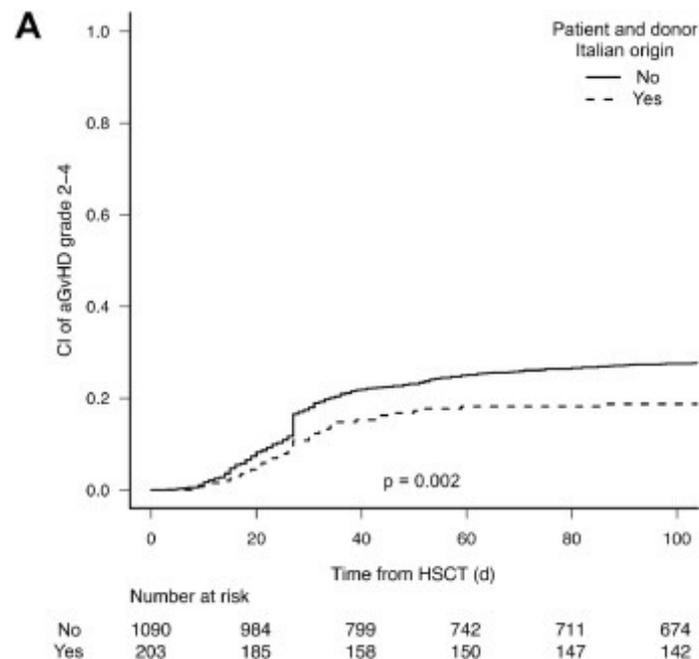
Costi di reperimento e ricerca di CSE da adulto in Italia e all'Estero



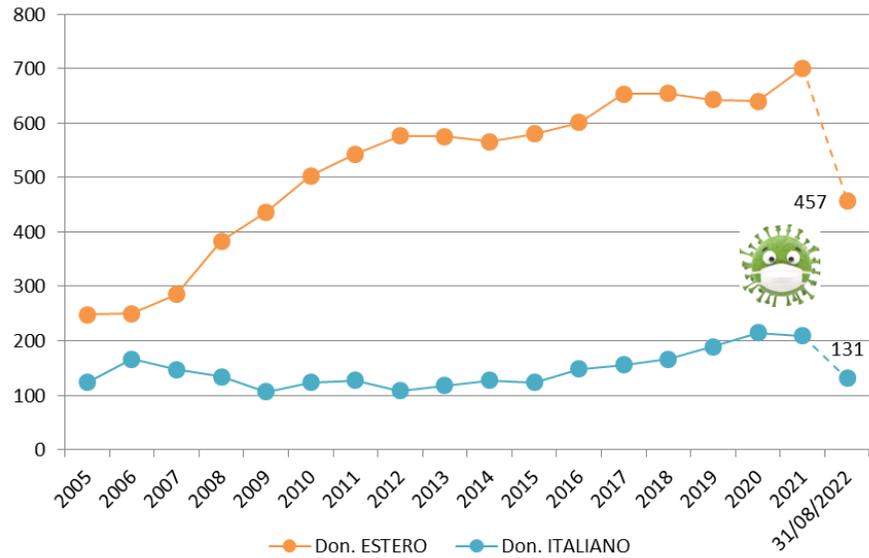
La sostenibilità e l'autosufficienza: solo impatto economico ?

Allelic HLA Matching and Pair Origin Are Favorable Prognostic Factors for Unrelated Hematopoietic Stem Cell Transplantation in Neoplastic Hematologic Diseases: An Italian Analysis by the Gruppo Italiano Trapianto di Cellule Staminali e Terapie Cellulari, Italian Bone Marrow Donor Registry, and Associazione Italiana di Immunogenetica e Biologia dei Trapianti.

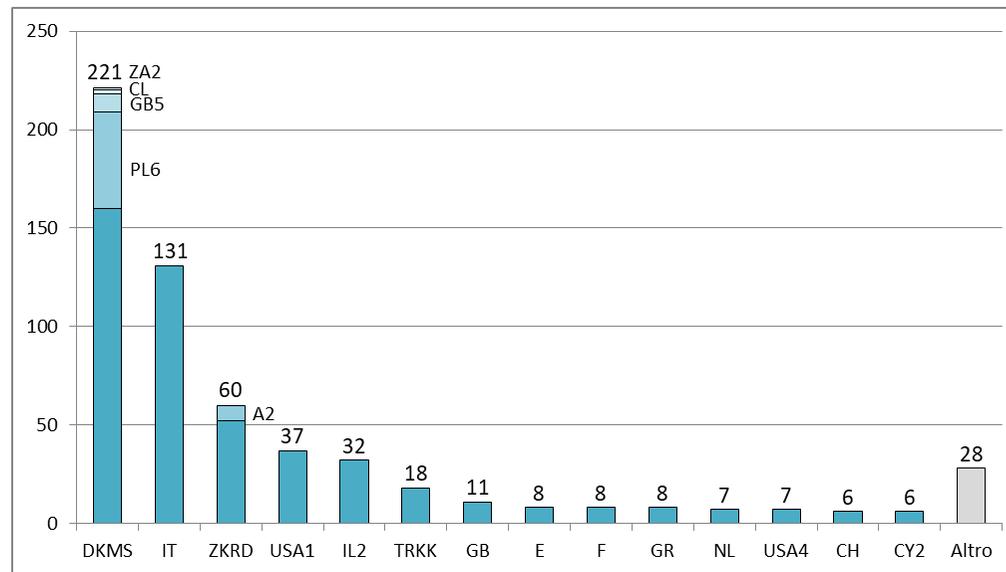
Picardi A et al, Transplantation and Cellular Therapy, 2021, ISSN 2666-6367, <https://doi.org/10.1016/j.jtct.2020.11.021>.



Provenienza dei donatori



78%
prodotti
importati



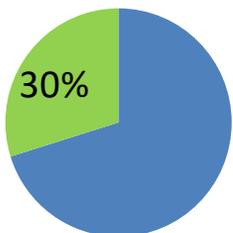
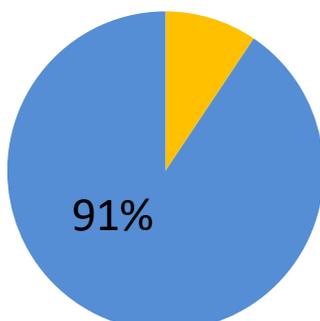
47% da
registri
tedeschi

Cosa succede nel mondo reale

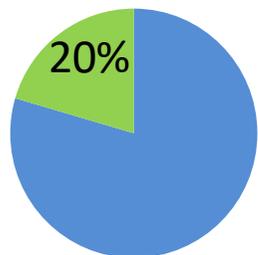
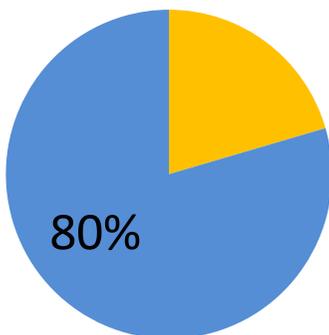
1051 pazienti entrati in ricerca dal 1/1/2022 al 30/6/2022 (dati elaborati settembre 2022)



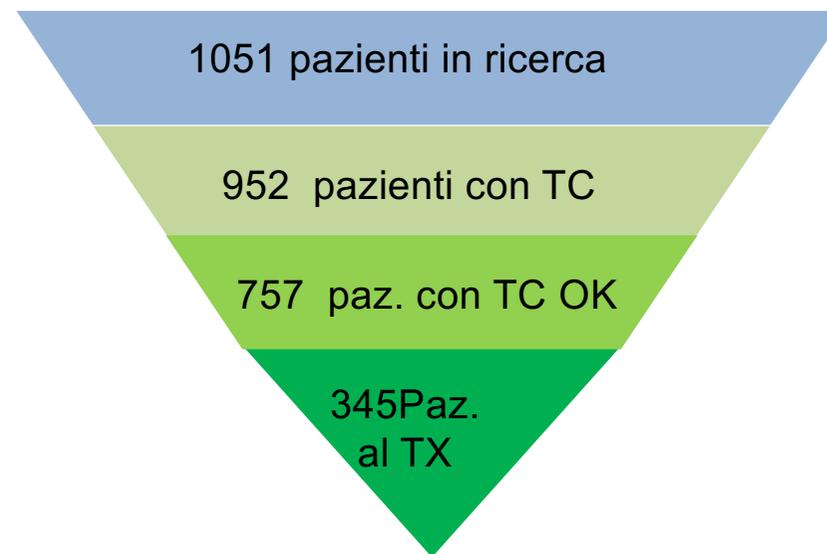
952 pazienti con almeno un TC proposto



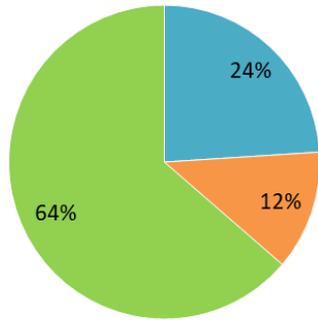
285 con don IBMDR



157 con don IBMDR



Indisponibilità dei donatori 2022 (31.08.2022)

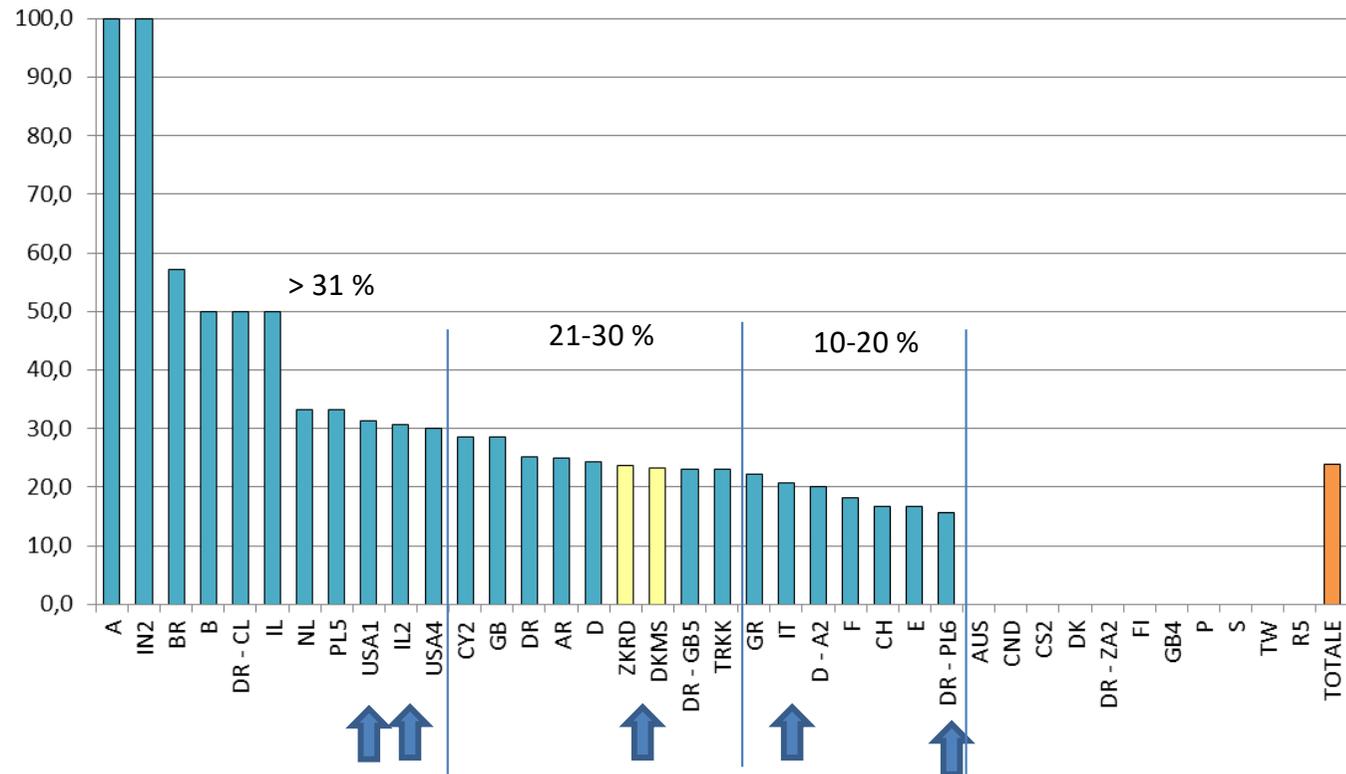


■ Canc causa Donatore ■ Canc causa Paziente
■ Donazione eseguita

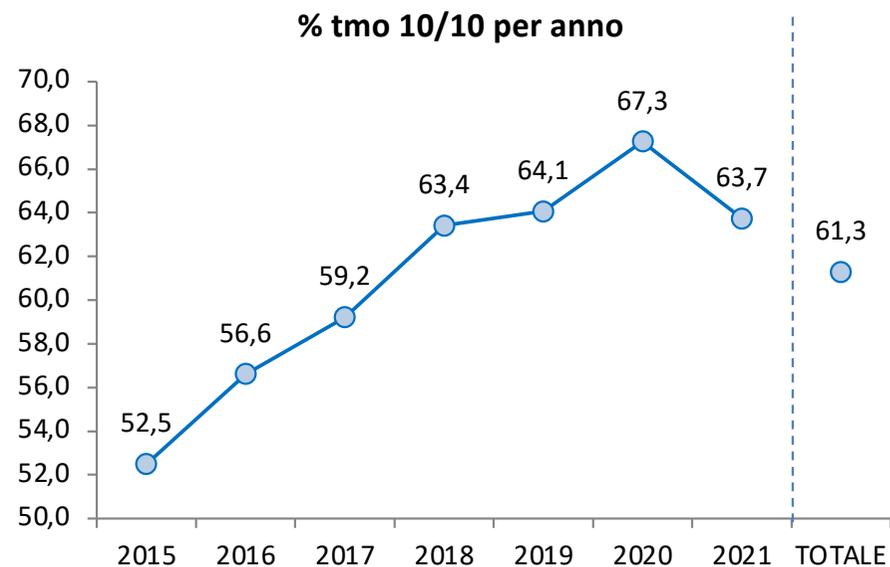
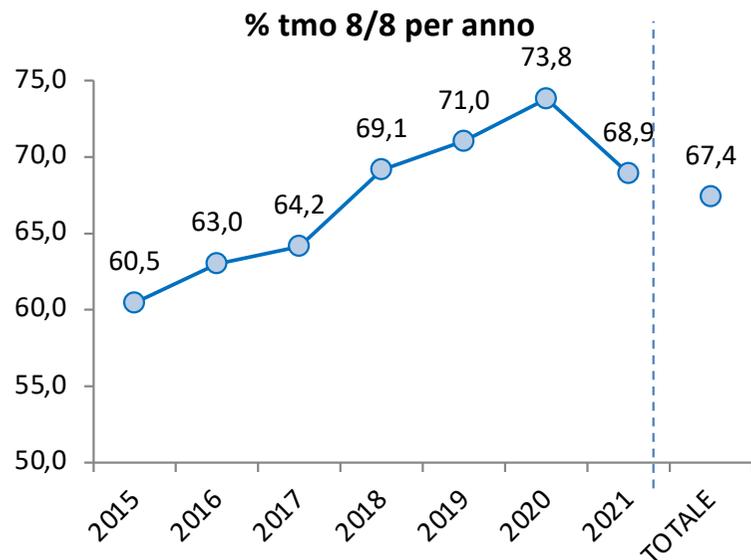
Tot: 884



% indisponibilità del donatore al WU



Livello Compatibilità al TX



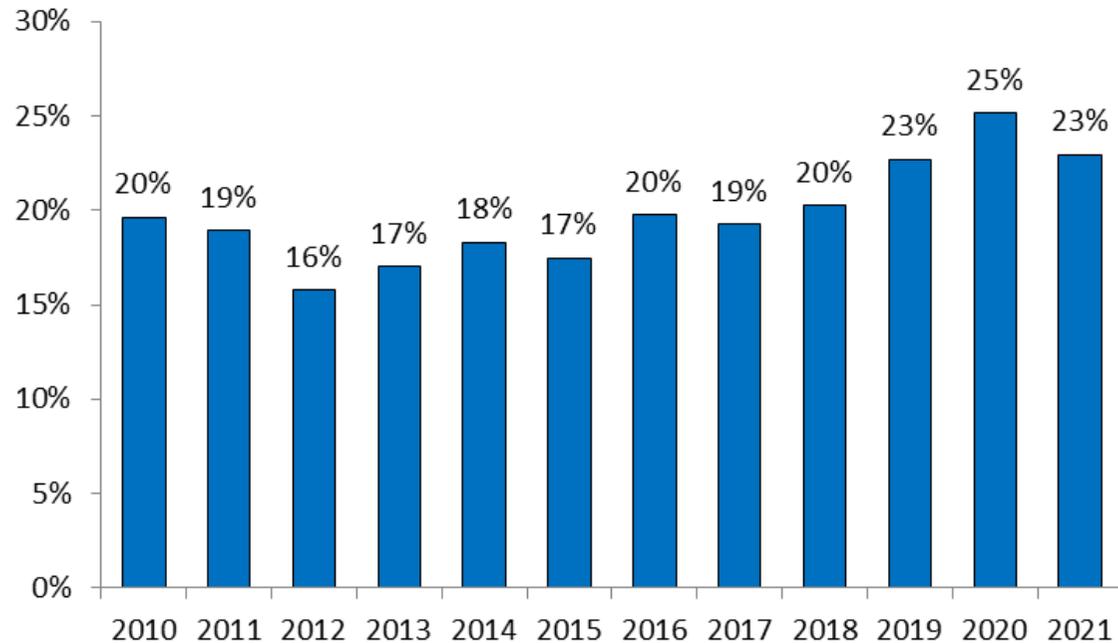
| 2020 | Compatibilità A B C DRB1 | | | |
|---------------|--------------------------|------|------|--------|
| | ≤ 6 | 7 | 8 | Totale |
| Don. Estero | 0,6 | 26,9 | 72,5 | 100,0 |
| Don. Italiano | 0,5 | 21,4 | 78,1 | 100,0 |
| Totale | 0,6 | 25,5 | 73,9 | 100,0 |

| 2021 | Compatibilità A B C DRB1 | | | |
|---------------|--------------------------|------|------|--------|
| | 6 | 7 | 8 | Totale |
| Don. Estero | 0,4 | 31,2 | 68,3 | 100,0 |
| Don. Italiano | 0,0 | 29,2 | 70,8 | 100,0 |
| Totale | 0,3 | 30,8 | 68,9 | 100,0 |



Livello Compatibilità al TX

Autosufficienza



| 2020 | Compatibilità A B C DRB1 | | | |
|---------------|--------------------------|------|------|--------|
| | ≤ 6 | 7 | 8 | Totale |
| Don. Estero | 0,6 | 26,9 | 72,5 | 100,0 |
| Don. Italiano | 0,5 | 21,4 | 78,1 | 100,0 |
| Totale | 0,6 | 25,5 | 73,9 | 100,0 |

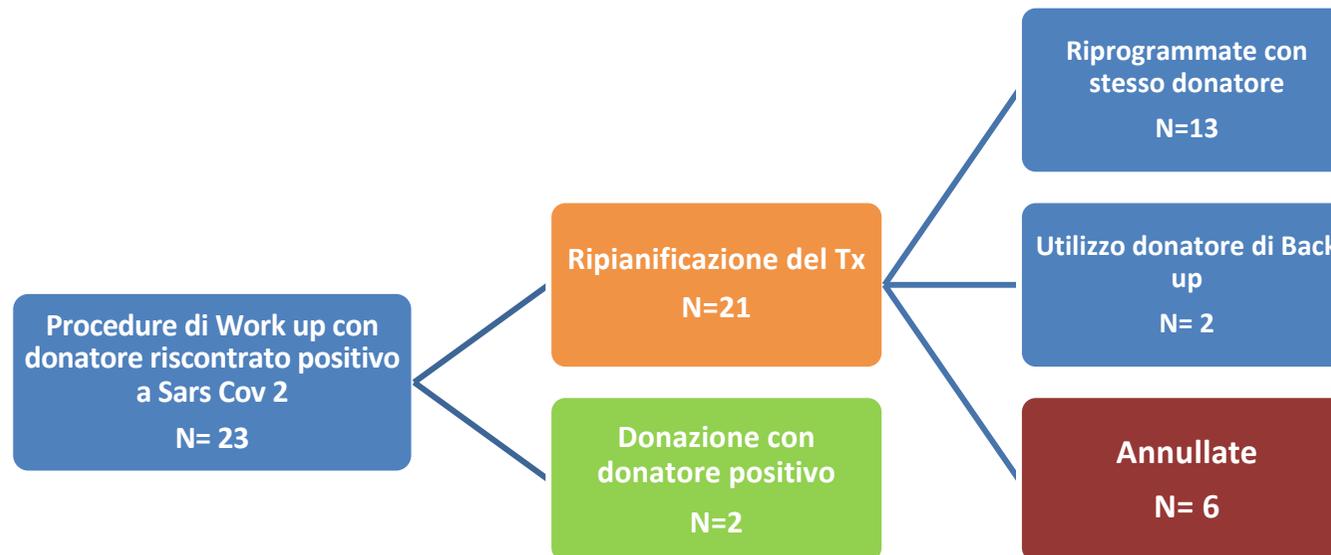
| 2021 | Compatibilità A B C DRB1 | | | |
|---------------|--------------------------|------|------|--------|
| | 6 | 7 | 8 | Totale |
| Don. Estero | 0,4 | 31,2 | 68,3 | 100,0 |
| Don. Italiano | 0,0 | 29,2 | 70,8 | 100,0 |
| Totale | 0,3 | 30,8 | 68,9 | 100,0 |

IBMDR: SPEAR reports: SARS-CoV-2-Related Reports in 2020

Raccolta documentazione relativa alle procedure di work up da donatore IBMDR che non si sono svolte come programmato a causa della positività al COVID del donatore.

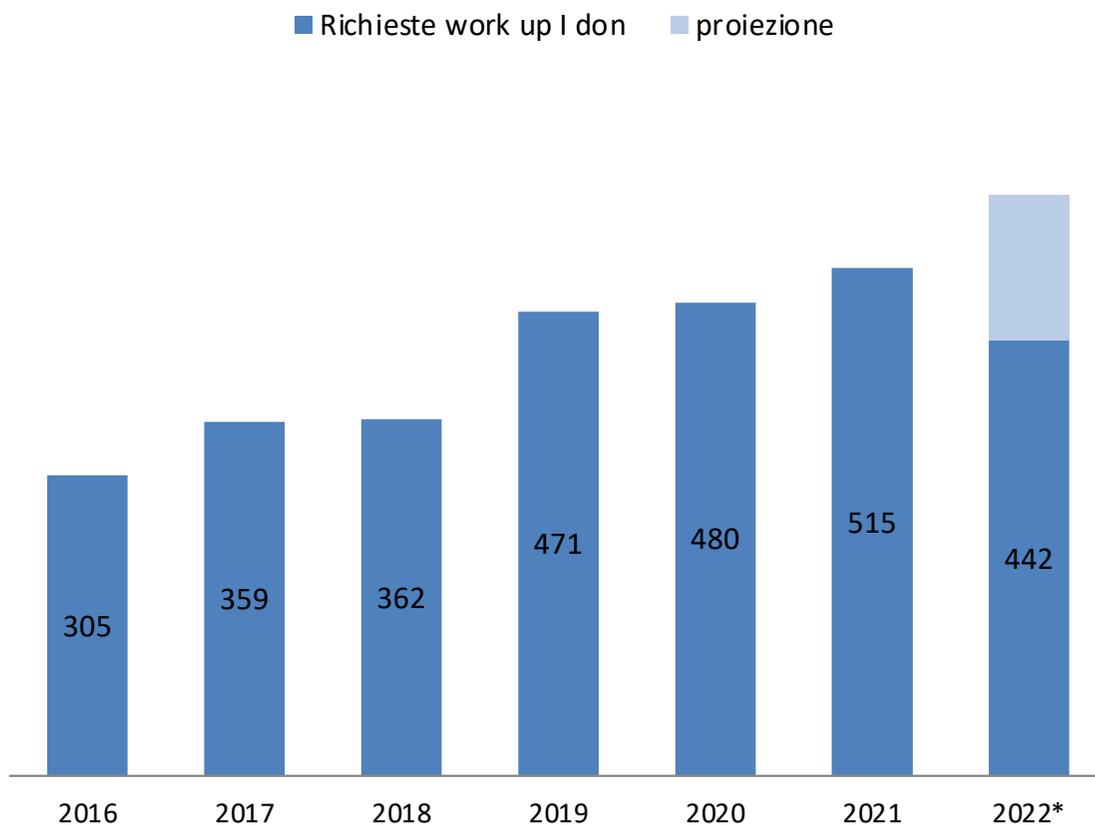
Disponibili le segnalazioni di quasi 2 anni, (1 novembre 2020 - 31 agosto 2022).

Richieste 1012 procedure di raccolta di CSE o DLI da 888 donatori IBMDR e 21 di queste (pari al 2%) hanno subito sostanziale modifica nella programmazione o non sono andate definitivamente a buon fine.





Crescita numero work up da gestire



Richieste W-UP 2021

| REGIONE CD GESTIONE | N RICHIESTE (No Pending) |
|--------------------------|--------------------------|
| ABRUZZO - MOLISE | 8 |
| BASILICATA | 0 |
| CALABRIA | 3 |
| CAMPANIA | 13 |
| EMILIA ROMAGNA | 85 |
| FRIULI VG | 15 |
| LAZIO | 14 |
| LIGURIA | 13 |
| LOMBARDIA | 93 |
| MARCHE | 13 |
| PIEMONTE - VALLE D'AOSTA | 72 |
| PIEMONTE | 72 |
| VALLE AOSTA | 0 |
| PUGLIA | 21 |
| SARDEGNA | 19 |
| SICILIA | 12 |
| TOSCANA | 23 |
| UMBRIA | 3 |
| VENETO - BZ e TN | 108 |
| VENETO | 78 |
| BZ | 9 |
| TN | 21 |
| TOTALE 2021 | 515 |

+90%
negli ultimi 6 anni

... non è un problema solo Italiano

Currently BM dates are available in December (with luck) or January at the earliest.
Kind regards

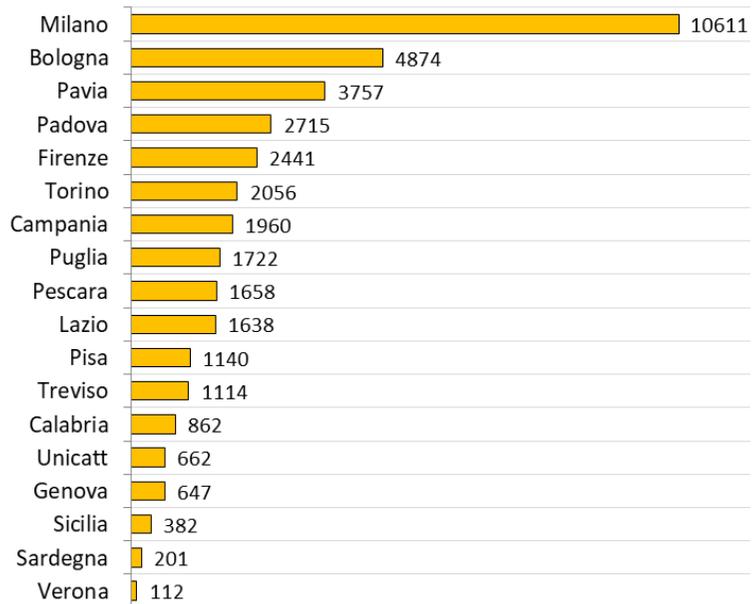
Clarissa Buche
Case Manager
Workup Team 2

DKMS

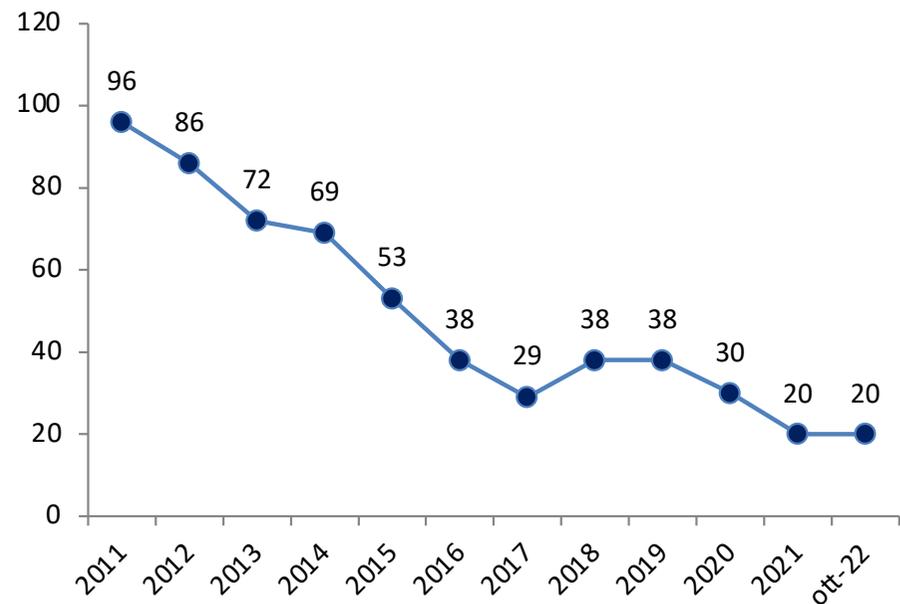


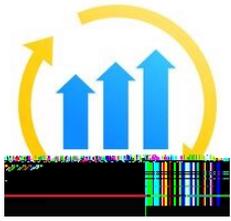
Italian national Cord blood bank inventory

Total CBU in public inventory: **38,552**

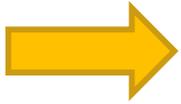


TREND unità rilasciate per anno

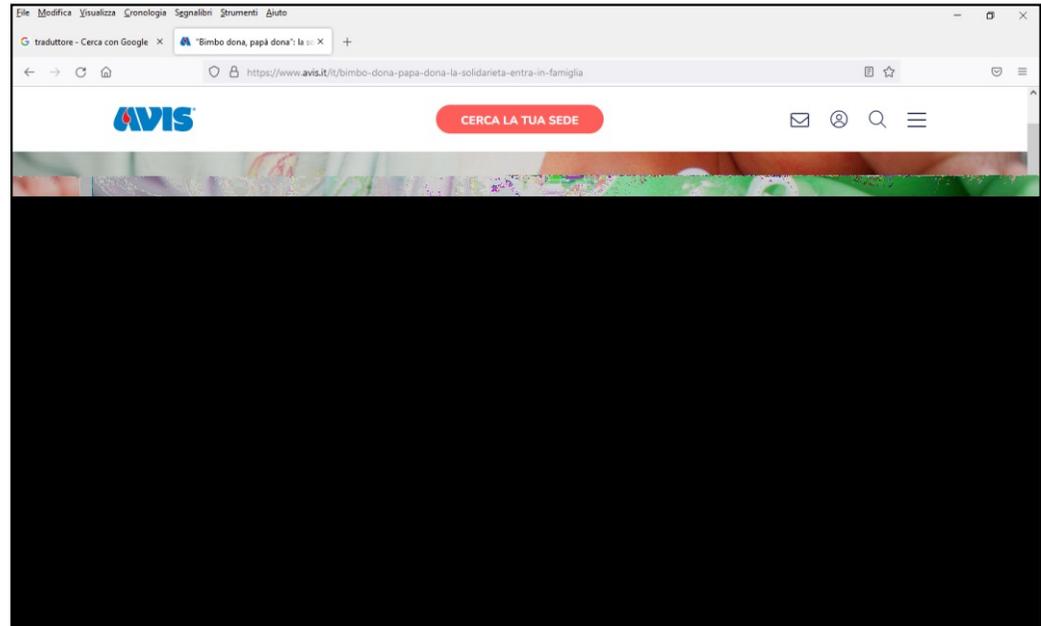




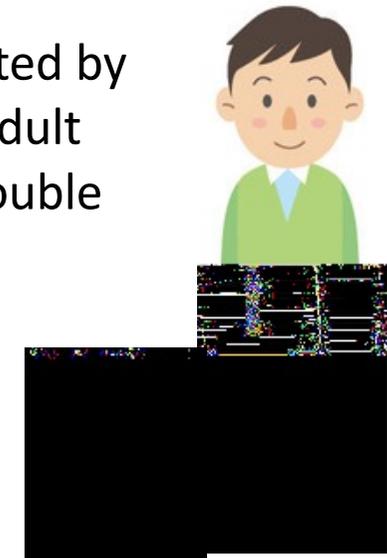
Actions: reinventing inventories



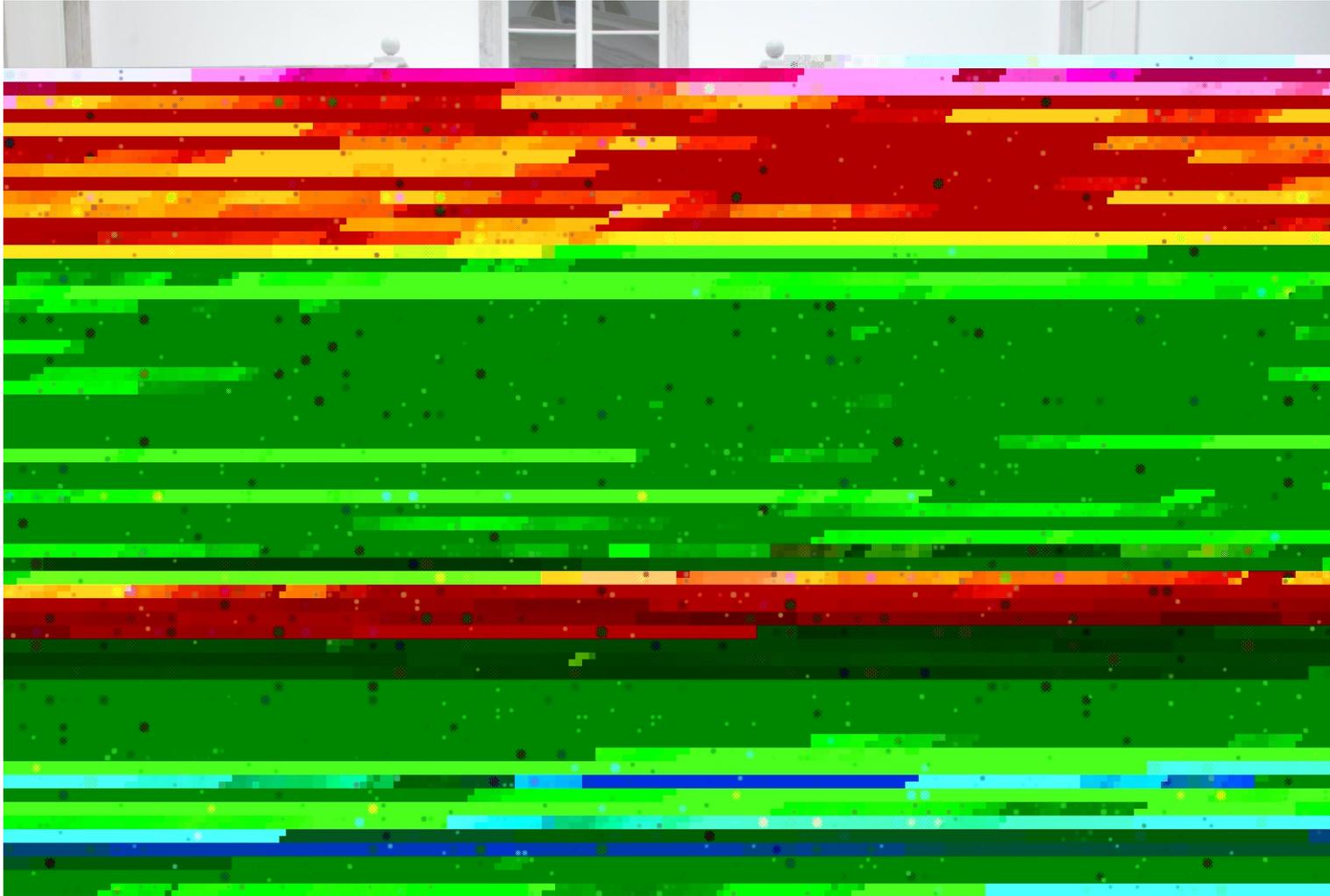
Father& son donation project



CORDONOR project: the CB donor (once 18 aged) are contacted by CBB to propose the enrollment in the adult inventory. Both adult donor and CBU are flagged for letting physicians know the double source availability (1 DLI request !).



Grazie!



@Massimiliano Murgia

@Marco Vitale

@Marina Venzano

@Francesca Vagnozzi

@Renato Marciano

@Simona Pollichieni

@Cristina Costa

@Maurizia Lofrano

@Roberto Scali

@AnnaGallina

@Erika Lonobile

@Roberta Sacco

@Elisa Porta

@Cinzia Lastrego