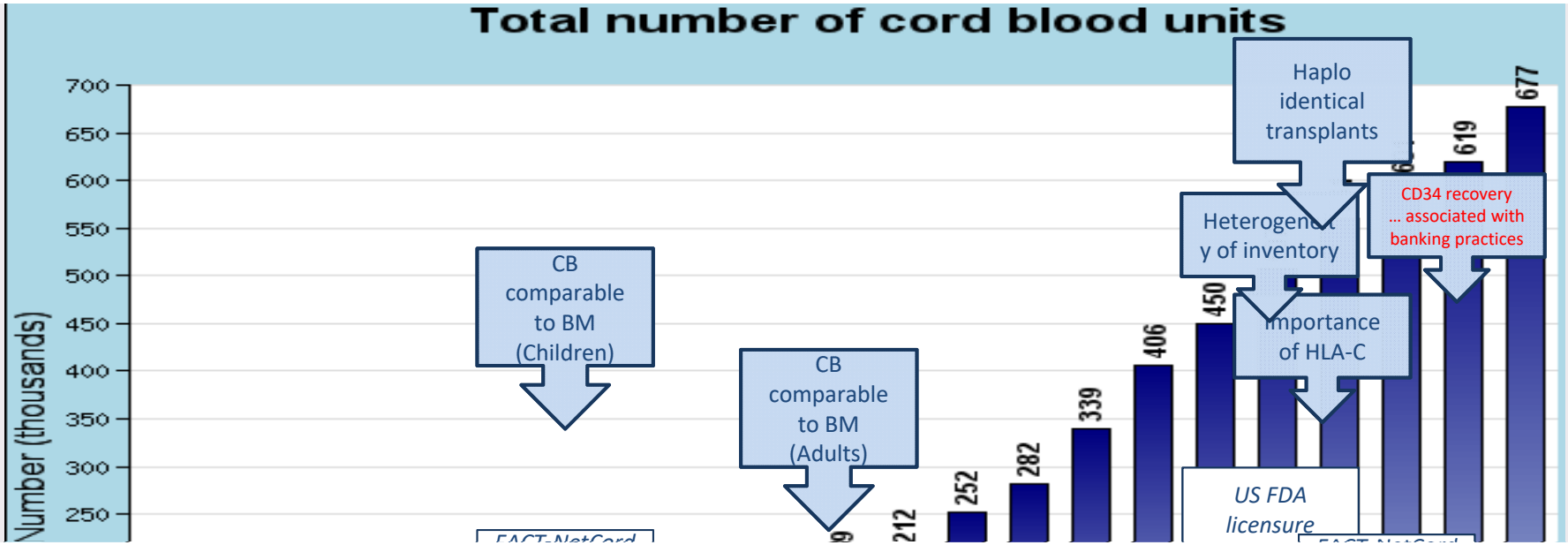
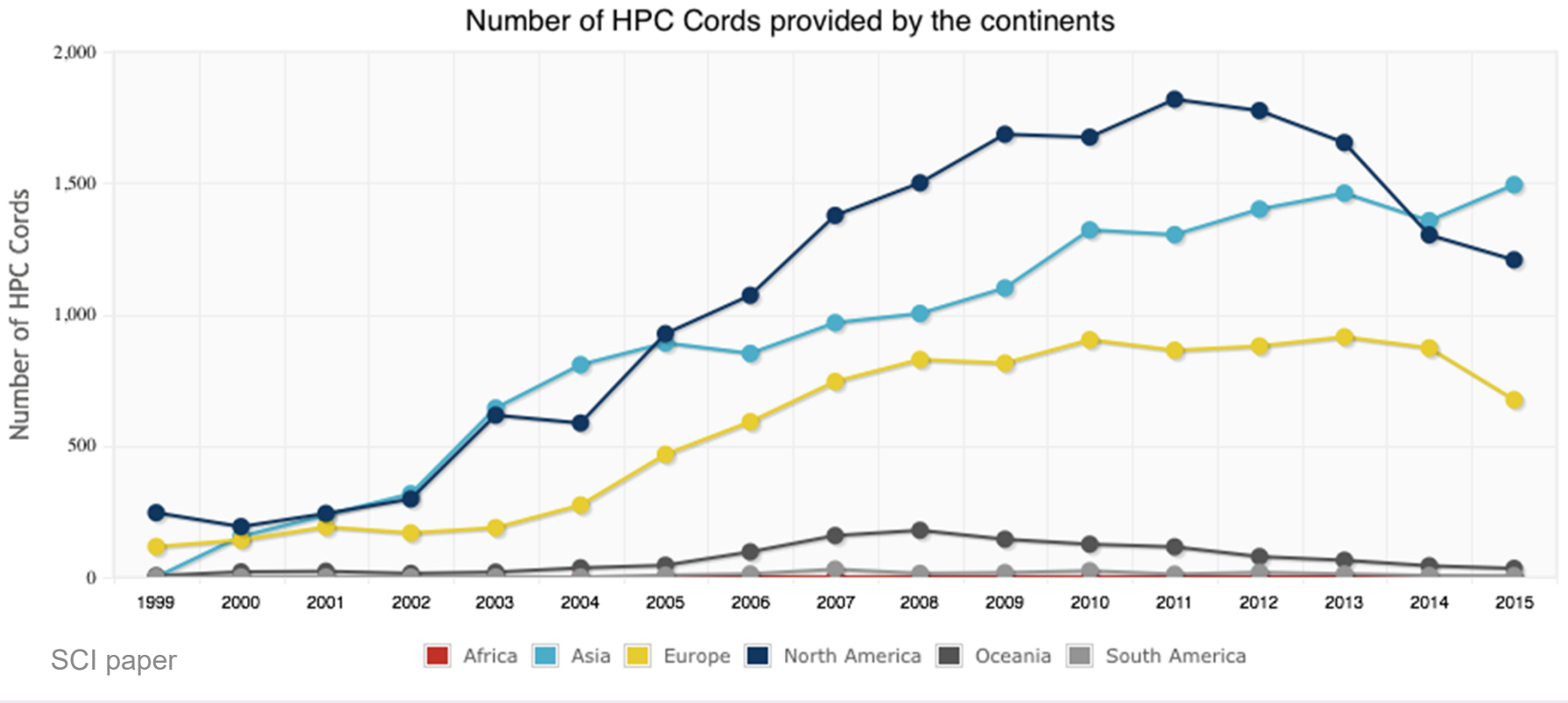
Sang de cordon
État des lieux et perspectives

E. Baudoux

20/12/2016


Total number of cord blood units
Number (thousands)
700
650
600
550
500
450
400
350
300
250
CB comparable to BM (Children)
CB comparable to BM (Adults)
Haplo identical transplants
Heterogeneity of inventory
Importance of HLA-C
CD34 recovery … associated with banking practices
US FDA licensure
212
252
282
339
406
450
619
677

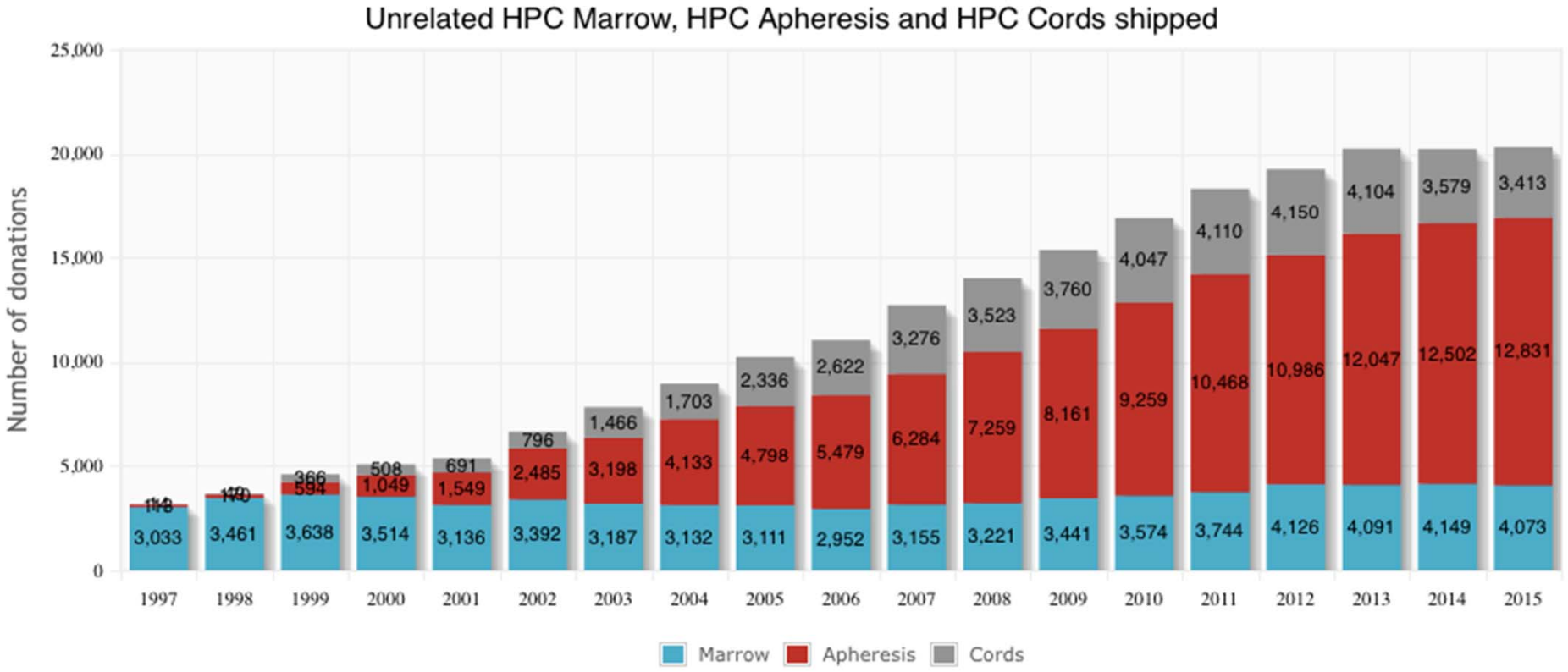

Number of HPC Cords provided by the continents
Number of HPC Cords
2,000
1,500
1,000
500
0
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
Africa
Asia
Europe
North America
Oceania
South America

SCI paper

SITUATION INTERNATIONALE

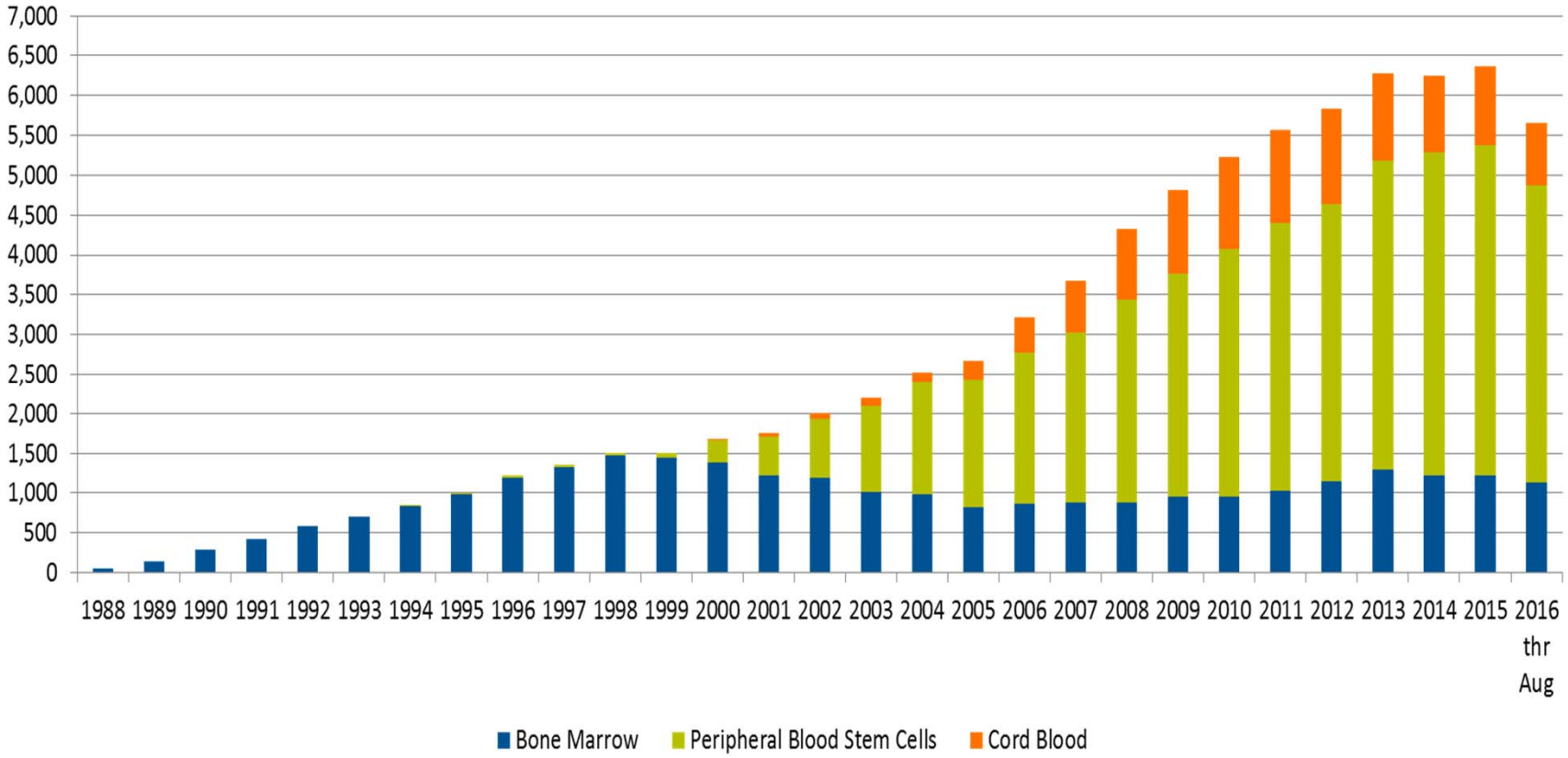
20/12/2016

Number of unrelated HPC donations provided globally from 1997 till 2015



SCI paper

Transplants by Cell Source



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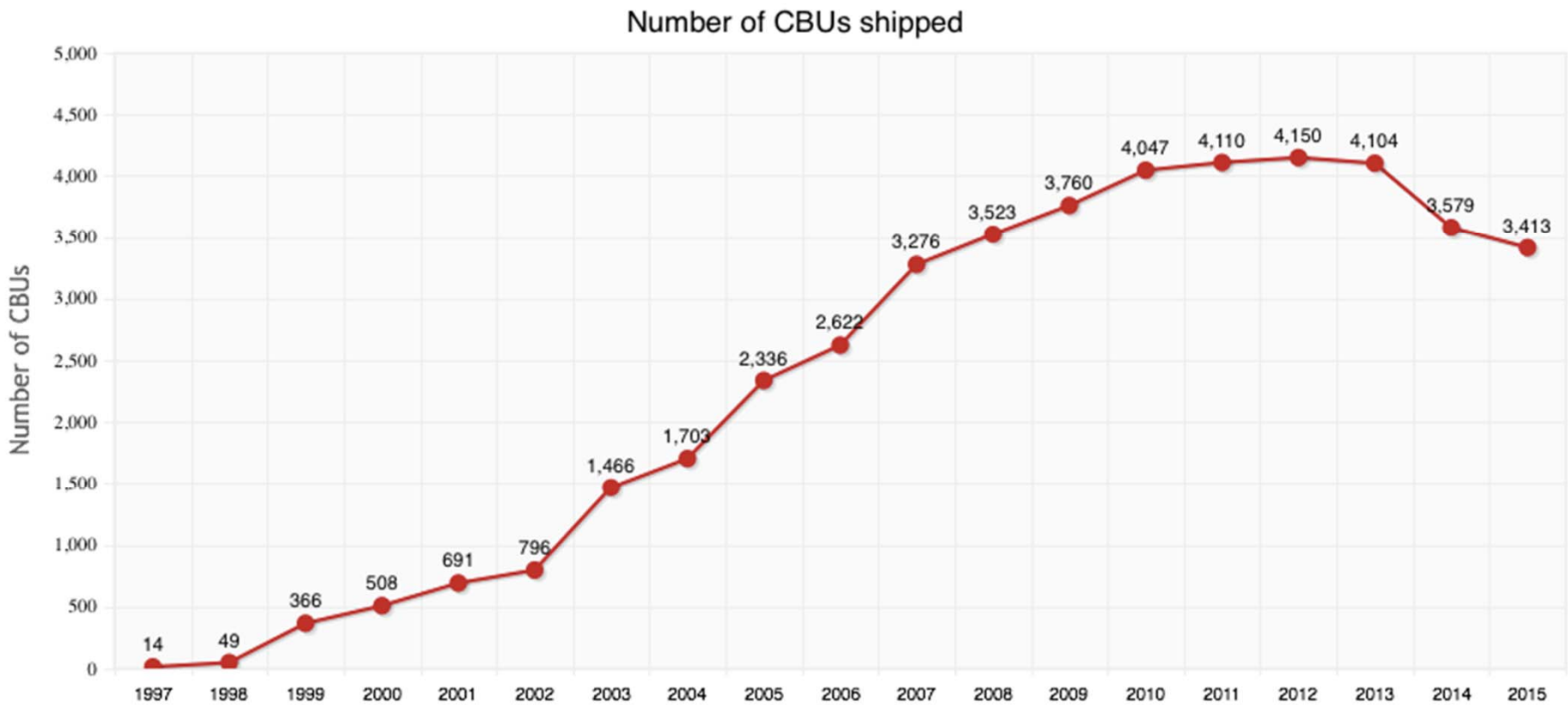
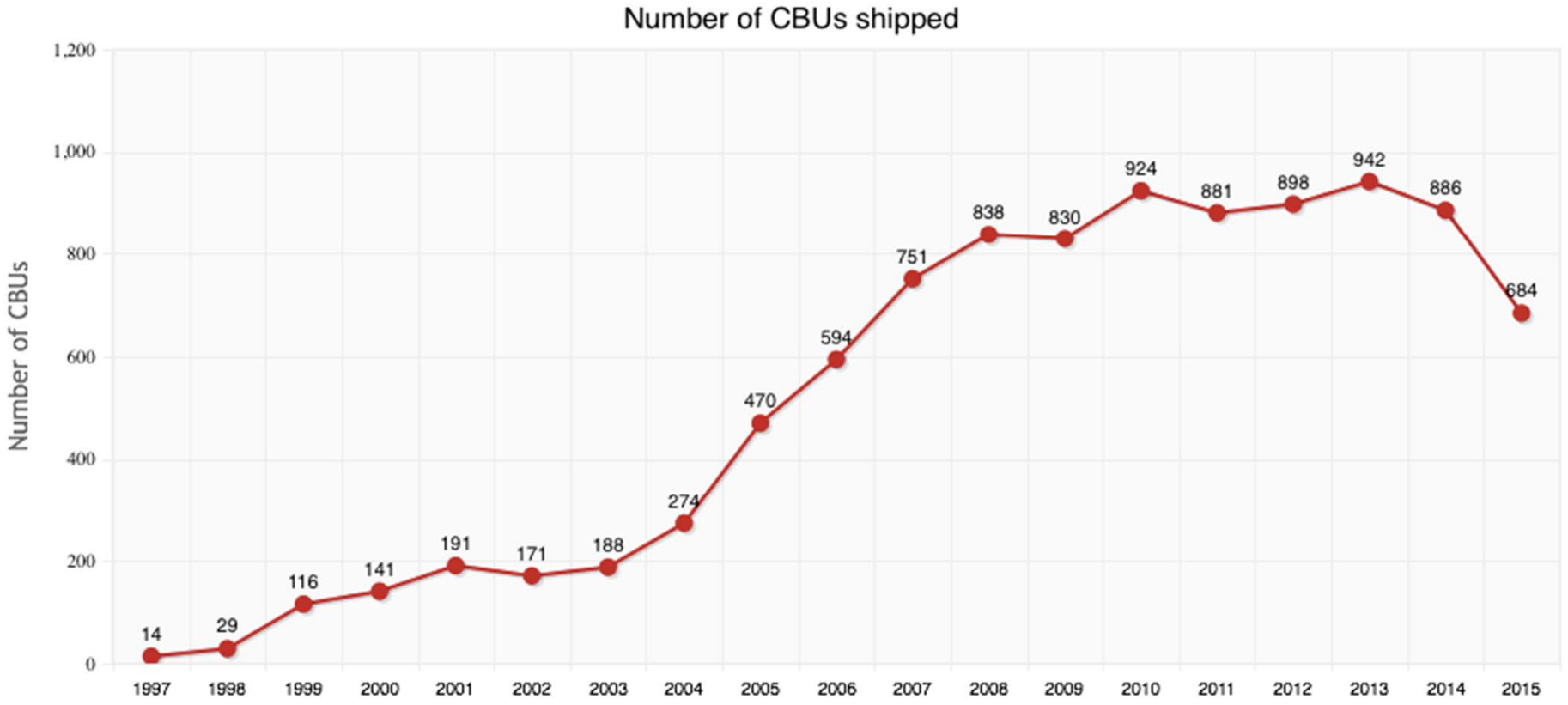
Global CBU shipments



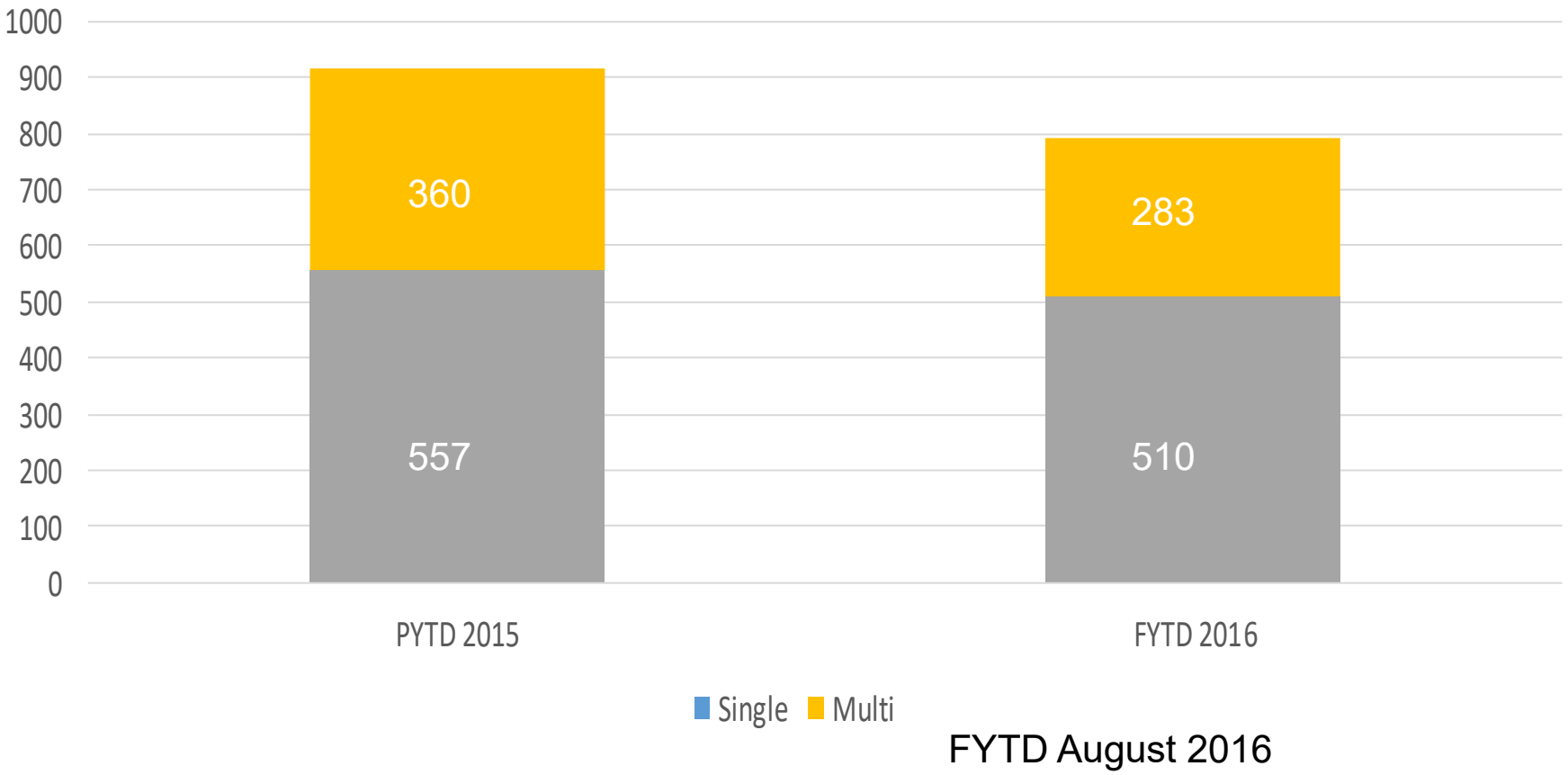
SCI paper

CBU shipments WHO region Europe



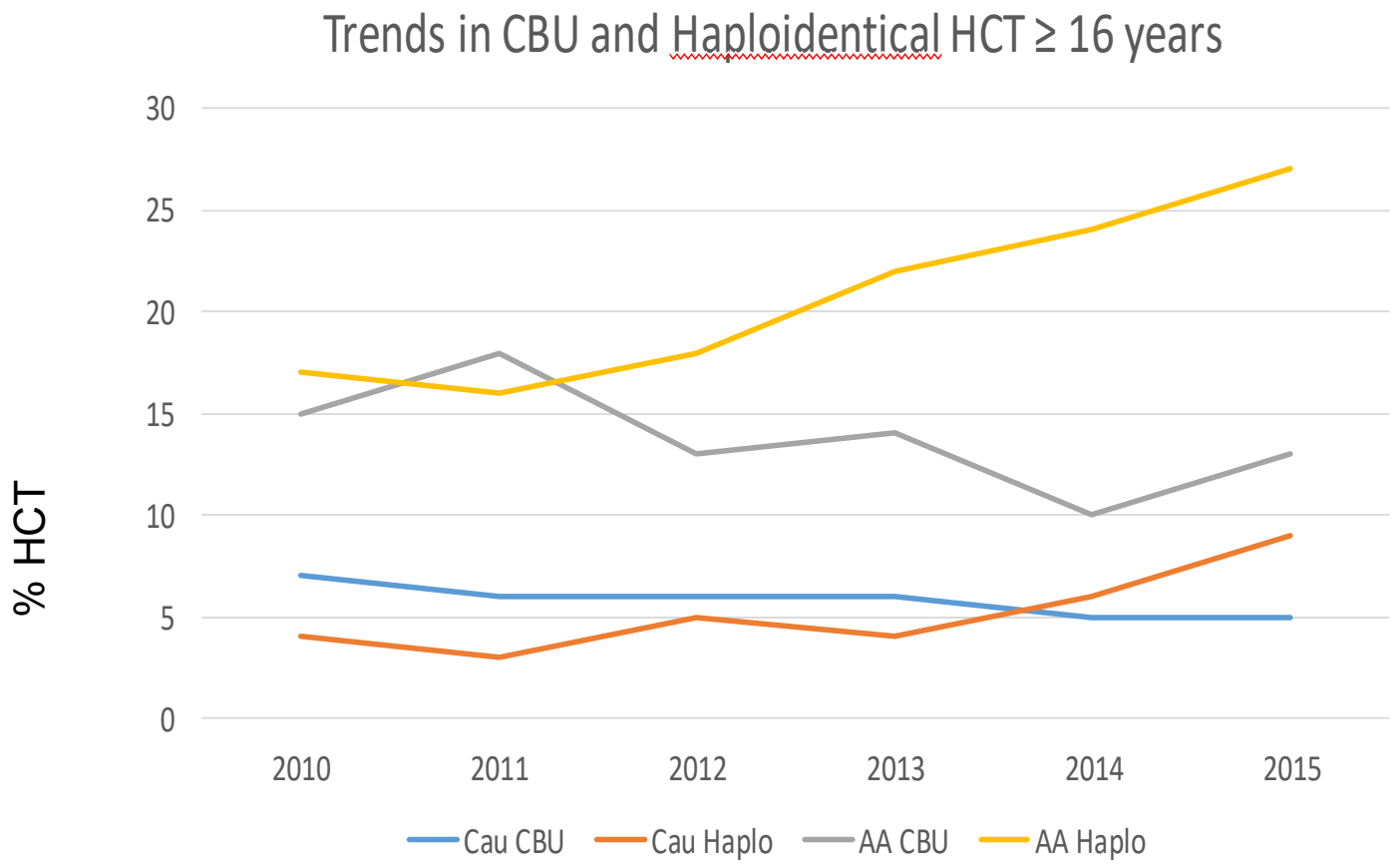
SCI paper

Multiple Cord Transplants are Declining at a Faster Rate than Single Cord



FYTD August 2016

There Appears to be a Transition from Cord Blood to Haploidentical Transplant



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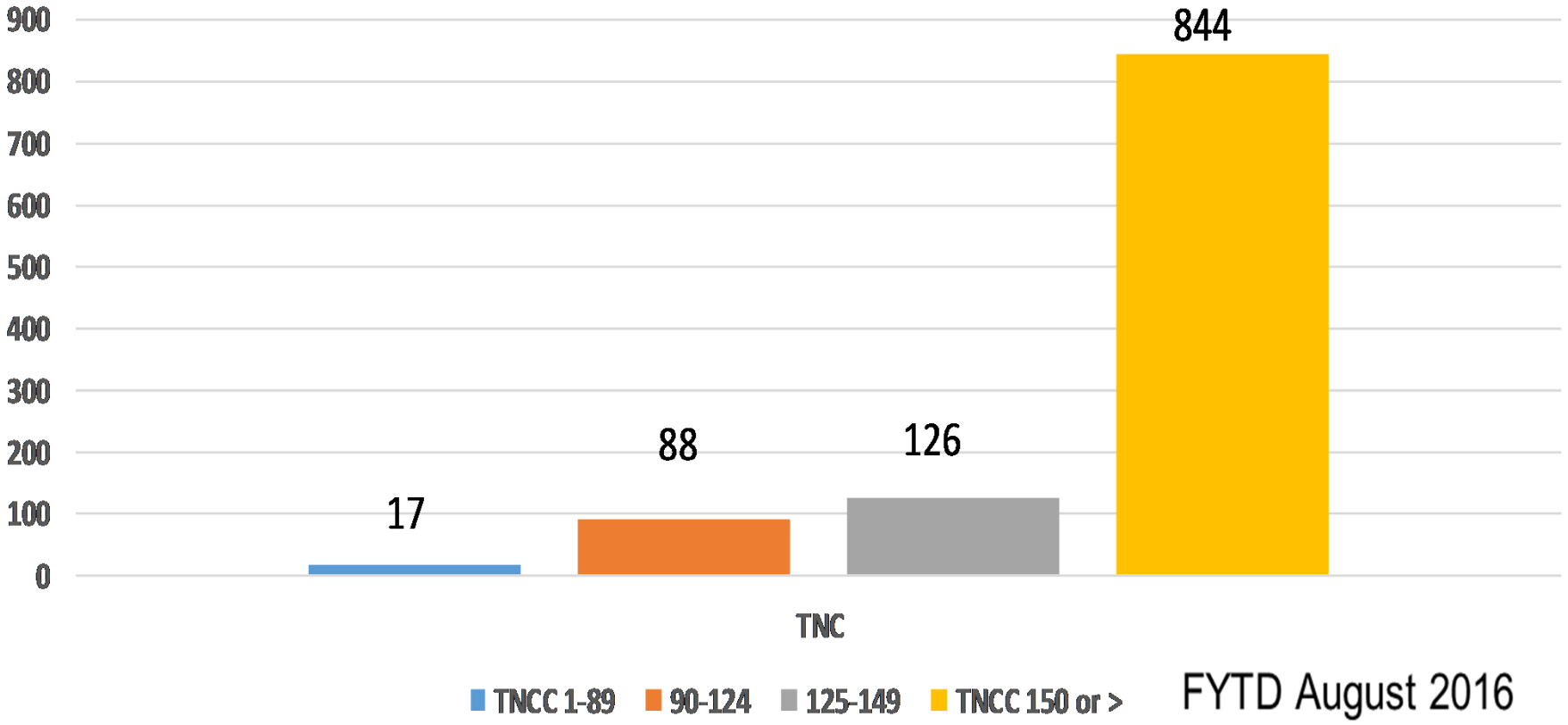
SCI paper

The Greater the TNCC, the Higher the Likelihood of Utilization



Goal of Interviews

- Understand reason(s) for decrease in use of cord blood as a graft source
- Understand if this decrease is temporary or permanent
- If an increase in haplo transplants is a reason for the decrease in cord blood, understand the reason for that preference
- Determine if anything would influence transplant centers to utilize more cord blood again

Selection

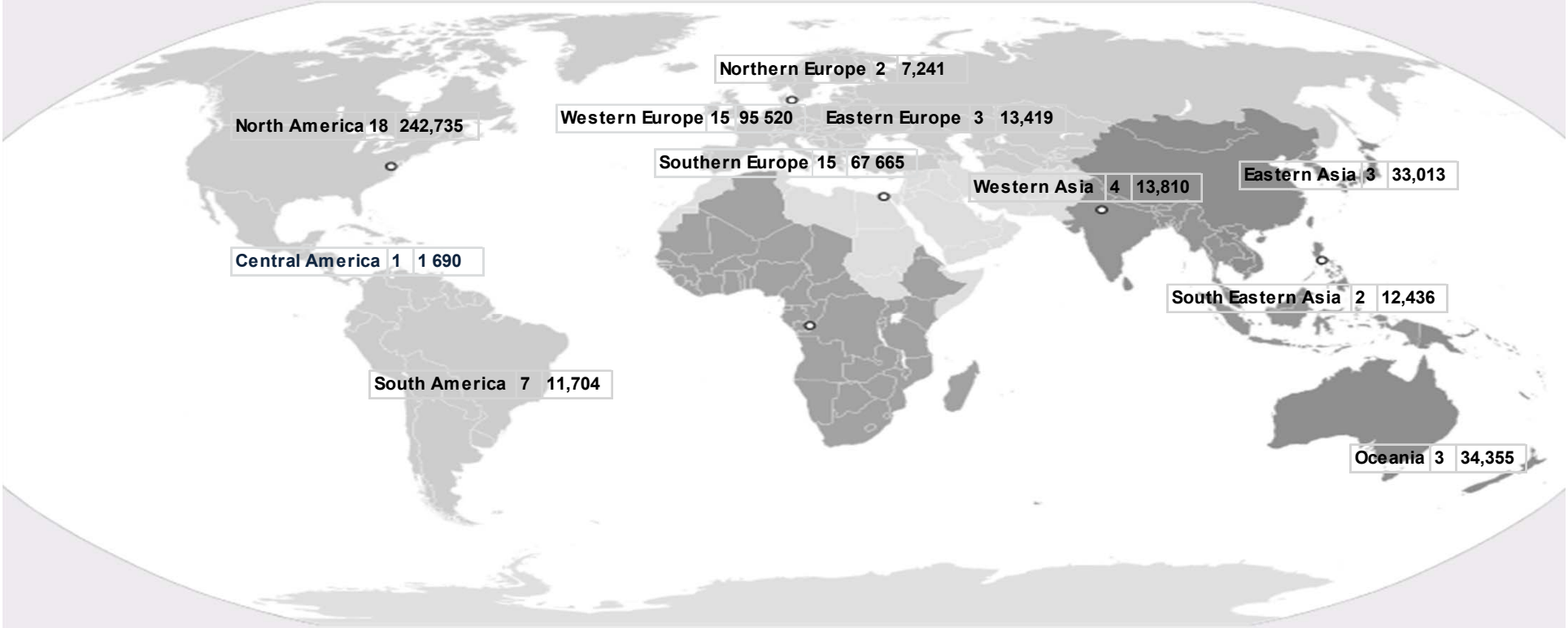
- Reviewed cord blood usage in US transplant centers
- Looked at use over past 5 years
- Looked for those TCs with largest decreases in the past year – looked at numbers and percent
- Interviewed 17 TCs – Dr. Linda Burns

Cord Blood Bank Technology Survey

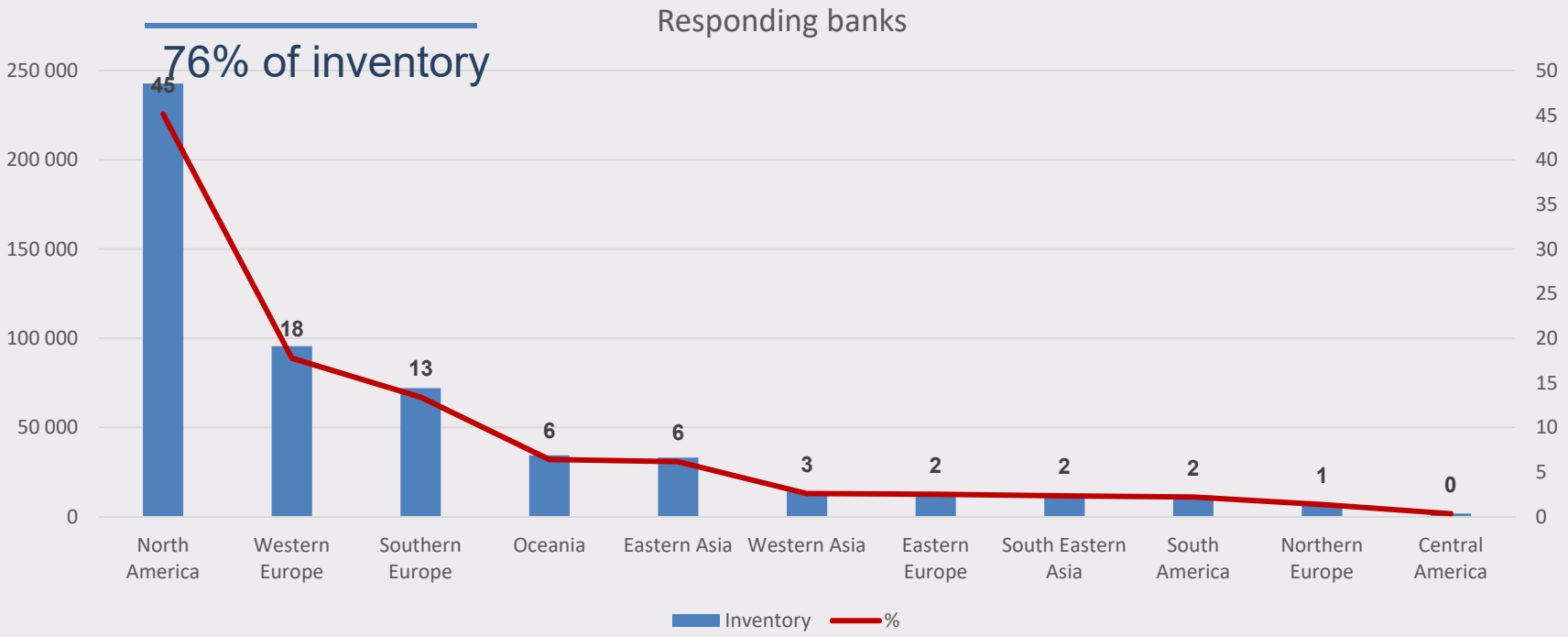
E. BAUDOUX
M. JÖRIS

Accès public: https://share.wmda.info/display/WMDAREG/Database

73 responding banks - 30 countries



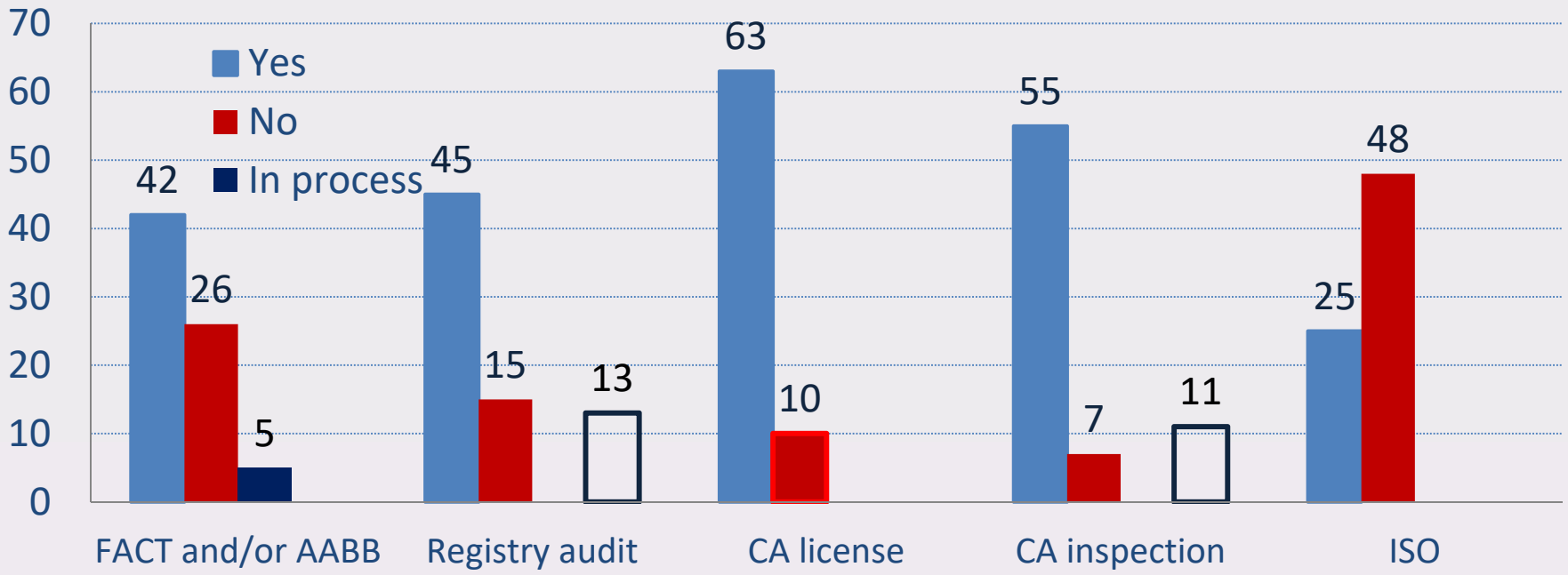
73 responding banks



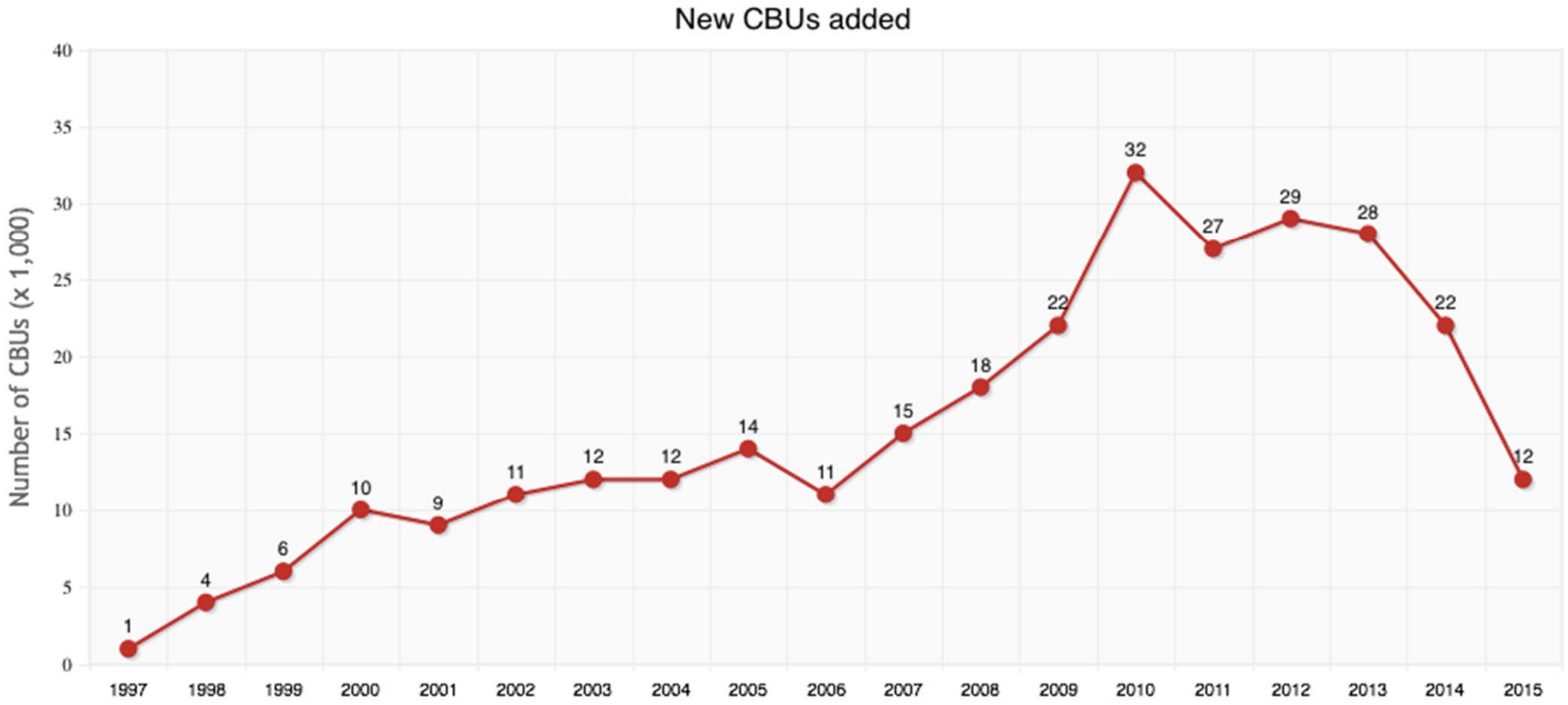
SCI paper

Accreditations and State license

Both (FACT+AABB)	FACT Only	AABB only	None
• 3 banks	• 30banks	• 9 banks	• 26 banks



WHO Region Europe Cord Blood Units added to the global database in 2015

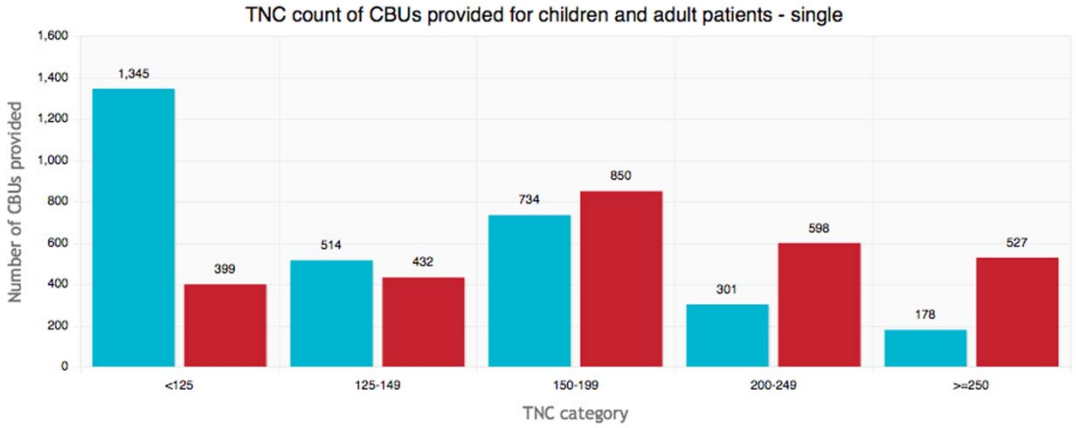


SCI paper

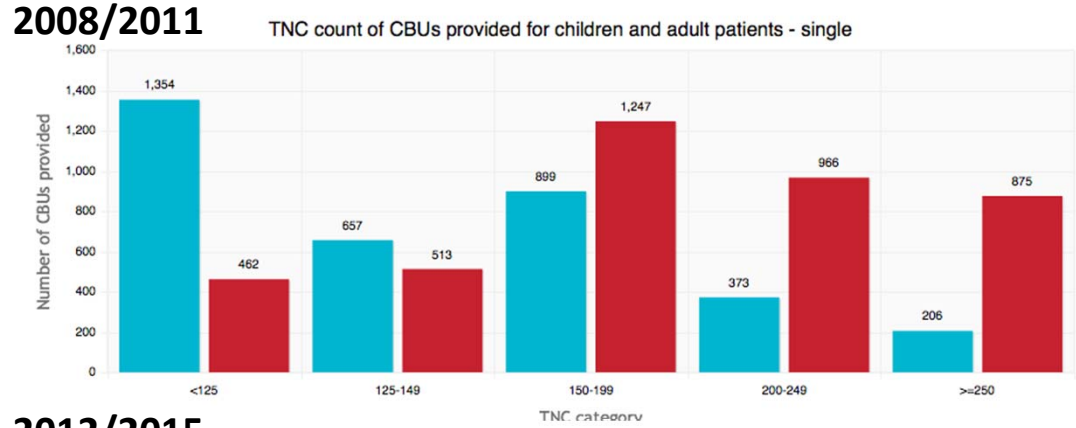
EU Countries that have stored new CBUs in 2015

Country	Number of CBUs added in 2015
Spain	2,538
UK NHS and Anthony Nolan	1,170+934 = 2,104
Belgium	1,140
France	910
Germany and Düsseldorf	842+769=1,611
Cyprus	550
Italy	494
Sweden	366
Bulgaria	145
Netherlands	138
Poland	69
Czech Republic	40

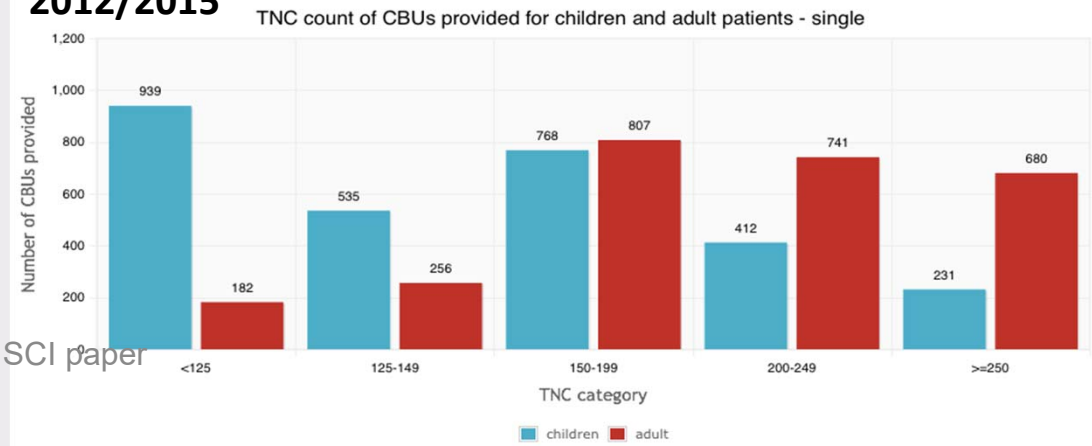
2004/2007



2008/2011



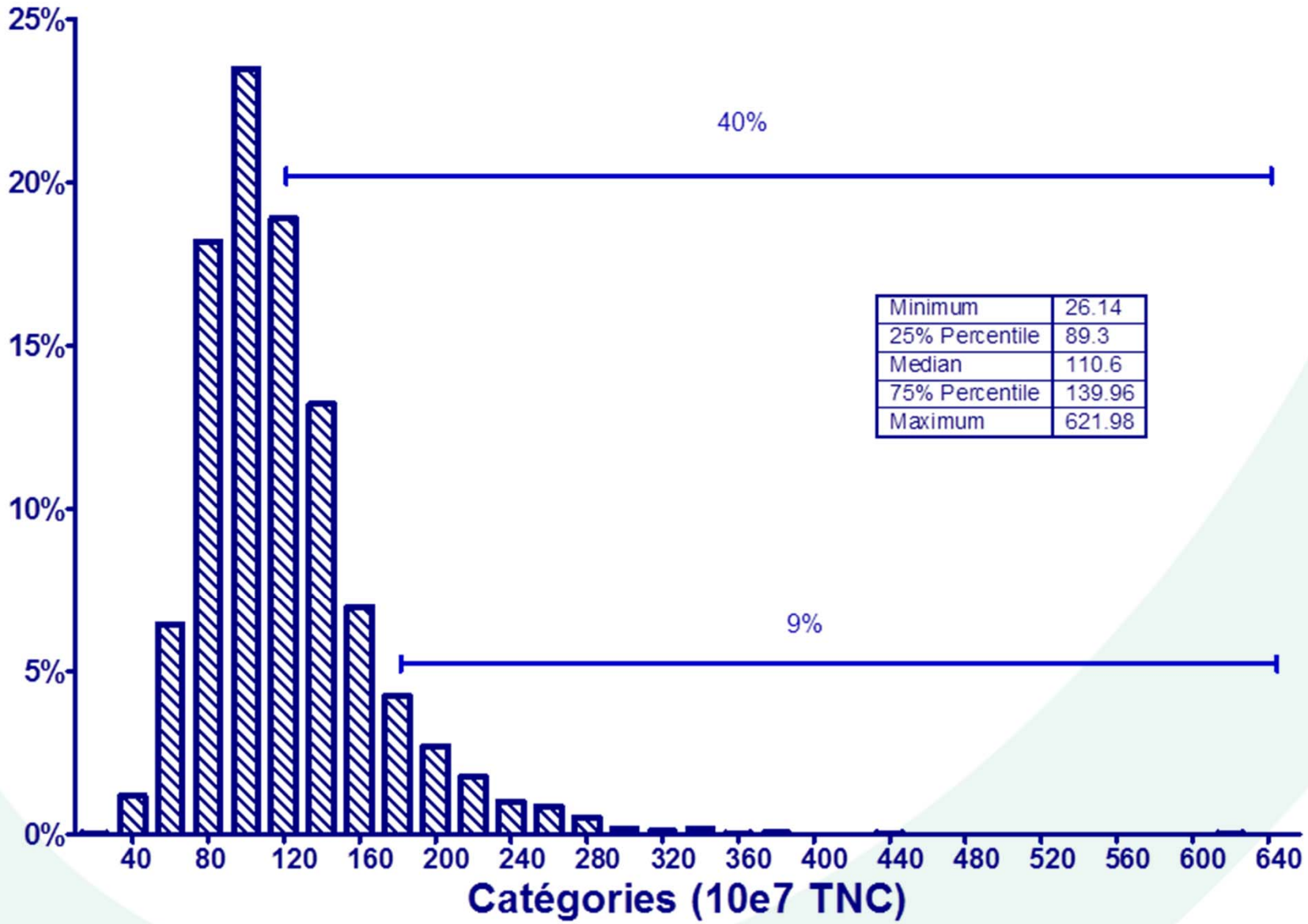
2012/2015



TNC	% in BMDW
<90	32
90-124	35
125-149	15
150-199	**13**
200-249	**3.2**
250-299	**0.8**
>300	**0.3**

SCI paper

Inventaire BSC Liège



20/12/2016

(SÉLECTION DE LA) LITTÉRATURE RÉCENTE

20/12/2016

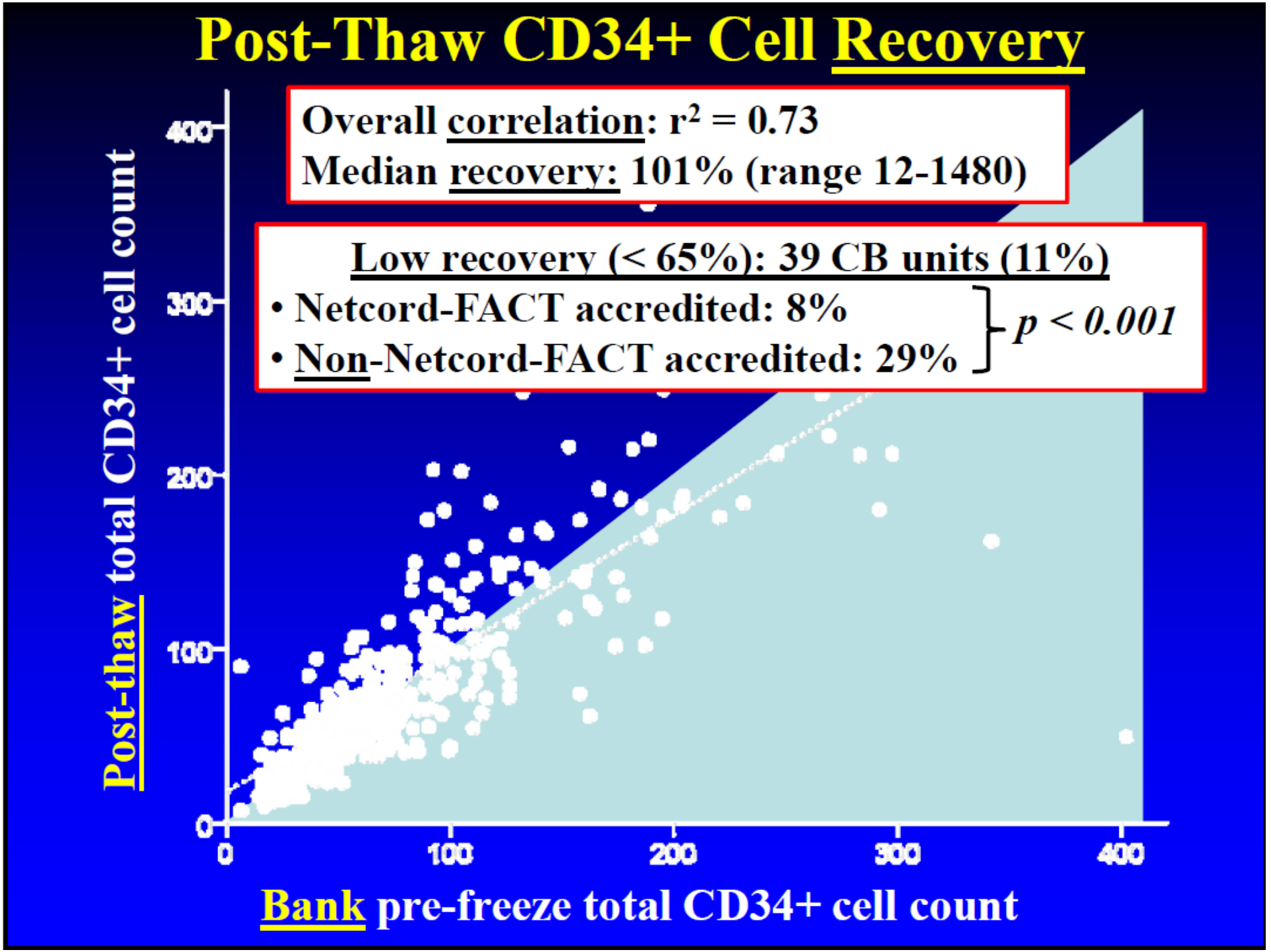
Eapen et al. ***Lancet oncology, 2011***	Avoiding a mismatch at HLA-C in the presence of a single mismatch at HLA-DRB1 significantly lowers mortality risks
Rocha et al. ***Biol Blood Marrow Transplant 2012***	HLA MM CBT with NIMA match show lower TRM (A) and better OS (B) When HLA MM CBT, preferably NIMA match
Eapen et Al. ***Blood 2013***	If full allele match not available: • 1-2 allele MM better tolerated than 3+ allele MM (10-15% difference in NRM) • Single MM HLA A, C, DRB1➔NRM x 3
Ruggeri et al. ***Hematologica 2014***	Engraftment kinetics and graft failure after single umbilical cord blood
Ruggeri et al. ***Leukemia 2015***	Results after UCBT and unmanipulated Haplo are likely comparable, indicating that both transplant strategies are suitable for patients lacking an HLA matched donors or when transplantation cannot be delayed
Saccardi et al. ***Transfusion 2016***	Cell viability assessment varied among the banks, suggesting that efforts to improve the standardization of CBU quality controls are needed

Cord Blood Graft Selection Criteria

- **Cell Dose**
- **HLA Match**
- **Bank of Origin**
- **Processing / Cryovolume**
- **Other Factors**

Barker et al, How I Treat, Blood 2010
Purtill, Blood 2014; Purtill et al, BBMT 2015

Post-Thaw CD34+ Cell Recovery



Selecting Cord Blood Units: TNC & CD34+ Cell Dose

Total Nucleated Cells

- Single Unit: ≥ 2.5 x 10^7/kg
- Double Unit: ≥ 1.5 x 10^7/kg

CD34+ Cells

- Single Unit: ≥ 1.5 x 10^5/kg
- Double Unit: ≥ 1.0 x 10^5/kg

blood
2014 124: 2905-2912
doi:10.1182/blood-2014-03-566216 originally published online September 2, 2014

Plenary Paper

TRANSPLANTATION

Dominant unit CD34$^+$ cell dose predicts engraftment after double-unit cord blood transplantation and is influenced by bank practice

Duncan Purtill,[1] Katherine Smith,[2] Sean Devlin,[3] Richard Meagher,[2] Joann Tonon,[2] Marissa Lubin,[1] Doris M. Ponce,[1,4] Sergio Giralt,[1,4] Nancy A. Kernan,[5] Andromachi Scaradavou,[5] Cladd E. Stevens,[1] and Juliet N. Barker[1,4]

[1]Adult Bone Marrow Transplantation Service, Department of Medicine, [2]Department of Laboratory Medicine, [3]Department of Epidemiology and Biostatistics, Memorial Sloan-Kettering Cancer Center, New York, NY; [4]Weill Cornell Medical College, New York, NY; and [5]Bone Marrow Transplantation Service, Department of Pediatrics, Memorial Sloan-Kettering Cancer Center, New York, NY

Post-thaw CD34+ dose can be predicted at the time of unit selection.

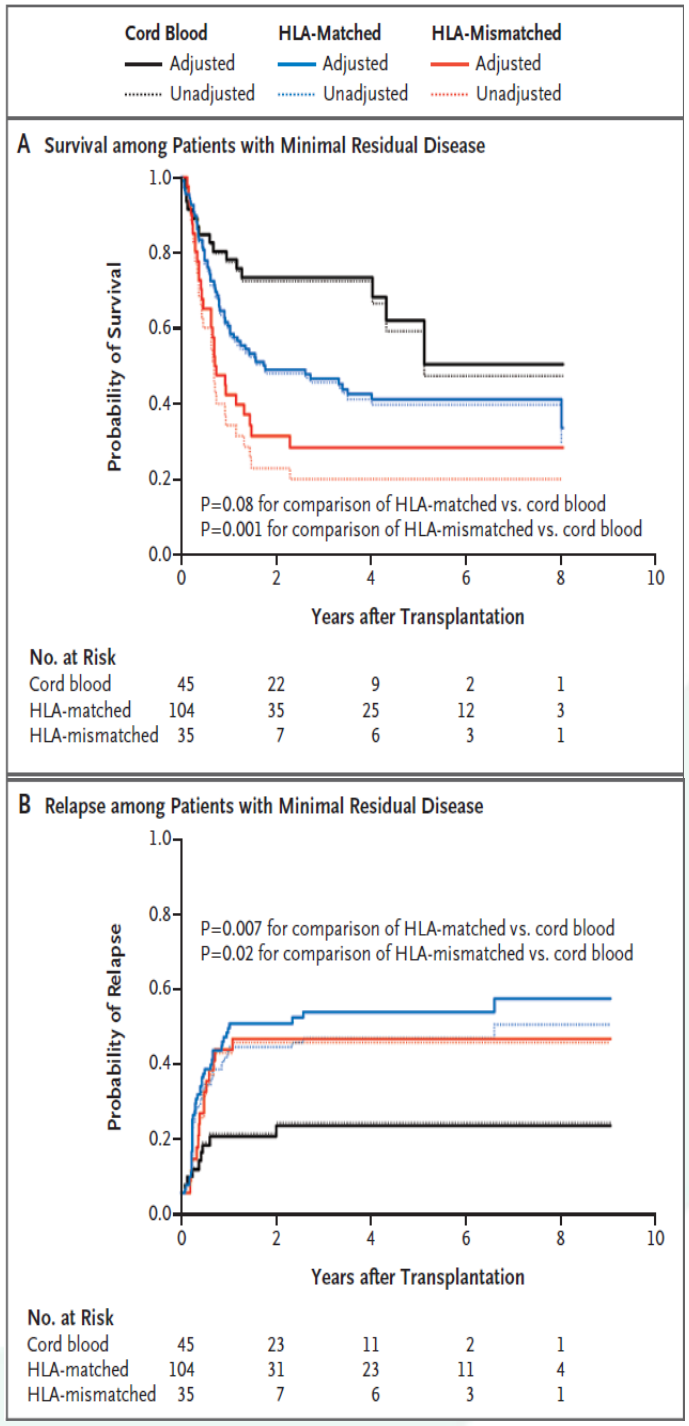
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Cord-Blood Transplantation in Patients with Minimal Residual Disease

Filippo Milano, M.D., Ph.D., Ted Gooley, Ph.D., Brent Wood, M.D., Ann Woolfrey, M.D., Mary E. Flowers, M.D., Kristine Doney, M.D., Robert Witherspoon, M.D., Marco Mielcarek, M.D., Joachim H. Deeg, M.D., Mohamed Sorror, M.D., Ann Dahlberg, M.D., Brenda M. Sandmaier, M.D., Rachel Salit, M.D., Effie Petersdorf, M.D., Frederick R. Appelbaum, M.D., and Colleen Delaney, M.D.

In conclusion, our results showed that in patients with minimal residual disease, the use of cord blood as the donor source for hematopoietic-cell transplantation led to a higher rate of survival and a lower rate of relapse than the use of a transplant from an HLA-mismatched unrelated donor. Our data also showed that the risk of relapse was higher after receipt of a transplant from an HLA-matched unrelated donor than after receipt of a transplant from a cord-blood donor,



- **OS: SC meilleur que donneur non apparenté HLA MM**
- **Rechute: SC meilleur que donneur non apparenté MM ou M**

RESEARCH ARTICLE

Banking or Bankrupting: Strategies for Sustaining the Economic Future of Public Cord Blood Banks

Jeremy Magalon[1,2,3], Martin Maiers[4], Joanne Kurtzberg[5], Cristina Navarrete[6], Pablo Rubinstein[7], Colin Brown[6], Catherine Schramm[8], Jérome Larghero[9], Sandrine Katsahian[8,9], Christian Chabannon[10], Christophe Picard[11], Alexander Platz[12], Alexander Schmidt[12], Gregory Katz[1]*

Conclusion

Our study shows that the utilization rate of CBUs is paramount to the economic sustainability of public banks. We found that a swift transition from strategy A to C can play a vital role in preventing public banks worldwide from bankrupting. We also found that a pre-freezing level of 18 x 10^8 TNC would be a cost-effective strategy to deliver therapeutic value to patients with a minimum financial deficit for the bank. In a context of limited public spending on health systems, banking decisions based on stronger selection criteria are essential if public banks are to remain financially sustainable and maximize their long-term therapeutic value for patients.

20/12/2016

Réduction des capacités de prélèvement

- France
  - Limitation du développement du RFSP
- Finlande
  - Arrêt des prélèvements en 2014
  - Activités de la banque limitée à la distribution
  - Décision de fermer la banque en suspens (coût/bénéfice défavorable)
- Belgique
  - Pas de stratégie de recrutement coordonnée au niveau national
  - Leuven: réduction drastique du nombre de maternités (20^{+} ➔ 1)
  - Liège: stockage de +/- 200 unités/an

Réaménagement des inventaires

- Mise à jour des critères de qualité et sélection des unités éligibles pour transplantation
  - TNC, CD34, typage,…
  - Complément de typage/tests si nécessaire
- Suppression des unités inéligibles
  - Données
  - Destruction?

Attentes des utilisateurs

- À paraître dans BBMT
  Consensus de 6 centres US à haut niveau d'expertise:
  MSKCC, Duke, U of Mn, Boston, FHCRC, MDA

Match	8 allèles
Dose TNC	❶
Match	❷
Dose TNC	>2.5 x10^7/Kg 5 x10^7/Kg si match 4/6
Dose CD34	1-2 x10^6
Banque d'origine	
Accréditation	Obligatoire
RBC replete	NO (5/6)
Segment	Obligatoire
Délai	1-3 semaines

Études randomisées

BMT CTN Protocol 1101

A Multi-Center, Phase III, Randomized Trial of Reduced Intensity(RIC) Conditioning and Transplantation of Double Unrelated Umbilical Cord Blood (dUCB) versus HLA-Haploidentical Related Bone Marrow (Haplo) for Patients with Hematologic Malignancies

- Protocol Synopsis, version 7.0 dated January 7, 2015
- Protocol, version 7.0 dated January 7, 2015
- Summary of Changes from version 6.0 to 7.0
- Informed consent and assent, version 7.0 dated January 7, 2015
- Participating Centers
- Frequently Asked Questions
- This study is posted on clinicaltrials.gov as NCT01597778
- Cost-Effectiveness Analysis (CEA) Companion Substudy
  - CEA Overview
  - CEA Quick Reference Guide and Patient Faxes
  - CEA FAQs
  - CEA Protocol, version 4.0
  - CEA Summary of Changes from version 3.0 to 4.0
- Key Personnel
  Protocol Co-Chair: Ephraim Fuchs, MD (410-955-8143) fuchsep@jhmi.edu
  Protocol Co-Chair: Paul O'Donnell, MD, PhD (206-667-1968) podonnel@fhcrc.org
  Protocol Co-Chair: Claudio Brunstein, MD (612-625-3918) bruns072@umn.edu
  Protocol Officer: Mary Eapen, MD (414-805-0700) meapen@mcw.edu
  Protocol Coordinator: Kate Bickett (301-251-1161) kbickett@emmes.com
  Protocol Coordinator: Achintya Jaitly (301-251-1161) ajaitly@emmes.com
  Medical Monitor: Angie Smith smith719@umn.edu

Projet Fit CB panel

- Inspiré du fit donor panel (Anthony Nolan)
  https://www.anthonynolan.org/sites/default/files/670CM_DesinationCureReport_Final_digital.pdf

The UK Stem Cell Strategy 2014 also highlights the need to recruit males to the stem cell registries, who are more likely to be picked as viable donors. Anthony Nolan places a focus on the recruitment of young male potential donors for high-resolution genetic typing, known as a 'fit panel'. This

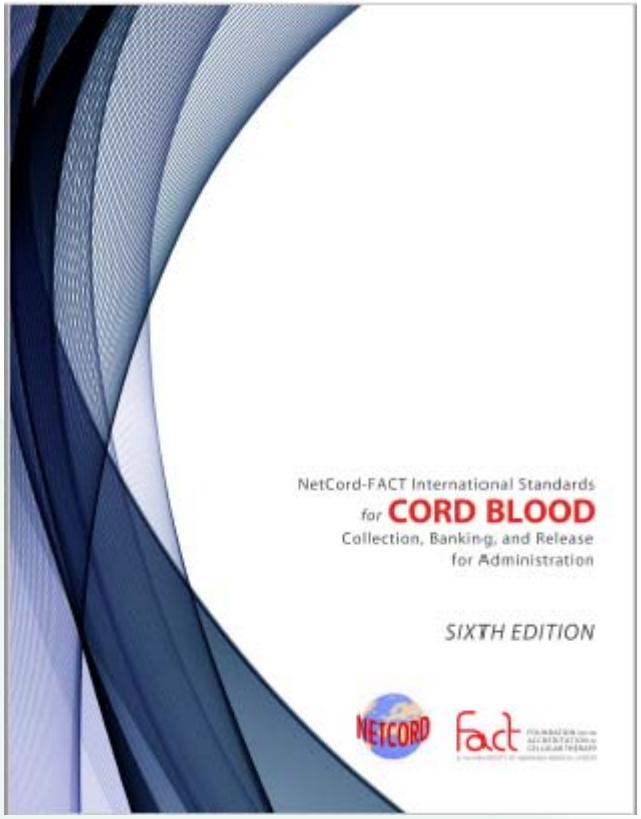
- Sélectionner
  - 50 000 Unités de SC
  - Banques accréditées
  - Réaliser les typages complémentaires
  - Établir un "pro-engraftment score" (typage HR, NIMA, KIR, IPA)
  - Établir un protocole d'essai clinique prospectif pour mesurer l'effet GVL de greffons

STANDARDISATION-ACCREDITATION

20/12/2016

Standards FACT-Netcord

- Standards de référence
  - ✔ 6e édition



APPENDIX V

SPECIFICATION REQUIREMENTS FOR CORD BLOOD UNITS STORED FOR CLINICAL ADMINISTRATION

Test	Unrelated Specification		Related Specification	
	Fresh Post-Processing Sample	Post-Thaw Attached Segment or Representative Sample Prior to Release	Fresh Post-Processing Sample	Post-Thaw Attached Segment or Representative Sample Prior to Release
Total nucleated cell count	≥ 5.0×10^8		Enumerated	
Total nucleated cell recovery	Should be ≥60%		Should be ≥60%	
Total viability	≥ 85%		≥ 70%	
Viable CD34 count	≥ 1.25×10^6			
Viability of CD34 cells	≥ 85%	≥ 70%	≥ 85%	≥ 70%
Viability of CD45 cells		≥ 40%		≥ 40%
CFU (or other validated potency assay)[1]		Growth (or positive result for potency)		Growth (or positive result for potency)
Sterility	Negative for aerobes, anaerobes, fungus		Negative for aerobic and anaerobic bacteria and fungi – OR – identify and provide results of antibiotic sensitivities	
Donor screening and testing	Acceptable as defined by Applicable Law and NetCord-FACT Standards		Acceptable as defined by Applicable Law and NetCord-FACT Standards	
Identity		Verified		Verified

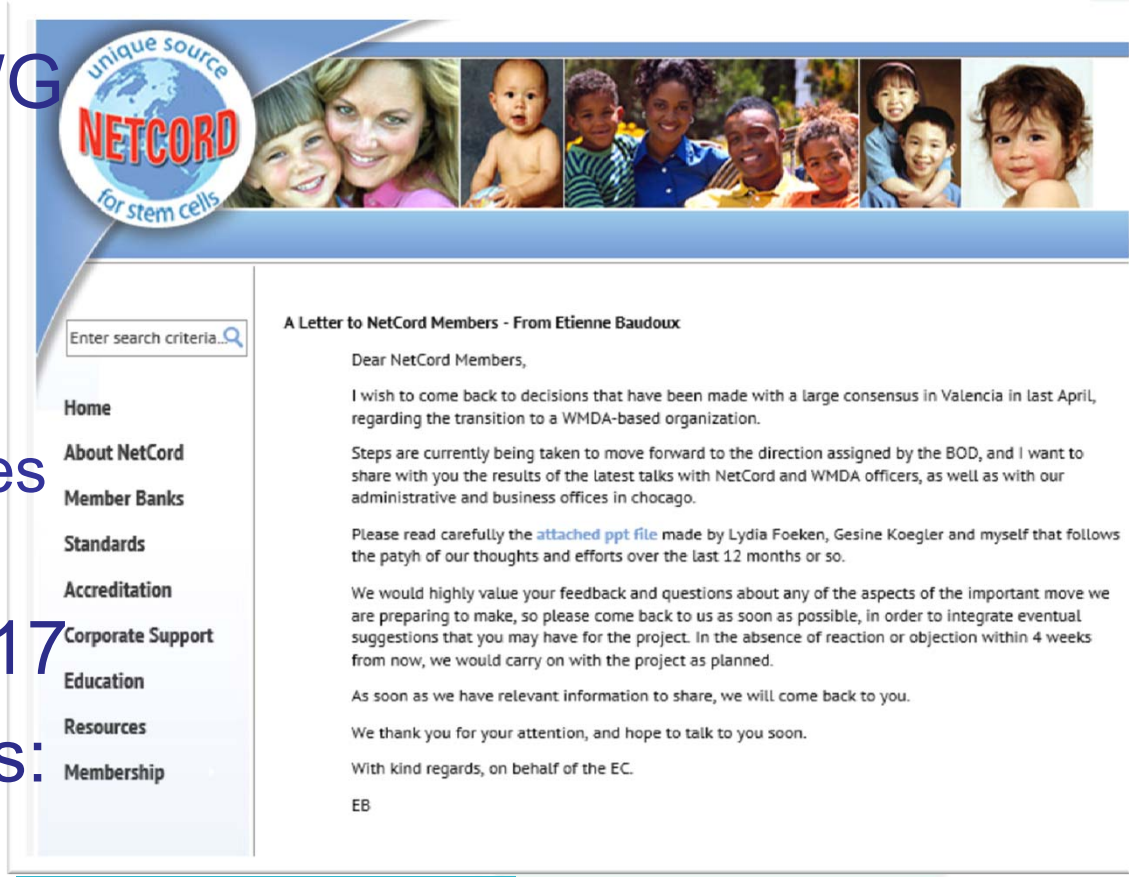
[1]There should be evidence of potency by CFU or other validated potency assay on a fresh post-processing sample.

Conditionnement

1997 **2009** **2013-2016**

The NetCord Foundation

- Fusion avec le CBWG de la WMDA
- Sont maintenus:
  - ✔ Missions et valeurs
  - ✔ Liens avec organismes partenaires
- À partir du 01/01/2017
- Banques intéressées: me contacter



WMDA

Cord Blood Association

CORD BLOOD ASSOCIATION

Member Logi

Home | Who We Are | Leadership | Join/Renew | Advocacy | Global Programs | Resources | Parent Inform

Our Mission

The Cord Blood Association is an international nonprofit organization that promotes the work of the cord blood community for the purpose of saving lives, improving health and changing medicine.

Our members include both public and family banks and individuals in and served by the cord blood community including cord blood bank personnel, research investigators, laboratory technicians, patients, donors, regulatory officials, vendors and health care providers such as transplant physicians, obstetricians, pediatricians, nurses and midwives.

(EN GUISE DE) CONCLUSION?

20/12/2016

Themes / Conclusions

- CB still has a role in pediatric patients and those patients without a Haplo or unrelated donor
- Need effective protocols to improve immune function engraftment of cord blood
- Need to decrease complications seen in CB tx
- Cost of graft – not the primary factor, but are starting to get questions from insurers
- Competing trials that don't involve cord blood
- Would take an improvement in all of the above to move back to CB

Rapid Reversal of Declining Cord Blood Activity Appears Unlikely

- Transplant center “deep dive” survey reveals practice trends and perceptions
- Updated financial modeling indicates that the breakeven point for the industry is declining
- Results of comparison studies of cord vs. other therapies are years away

Future of Cord Blood

- Despite recent decreases in use Cord remains a vital and important source of cells and will likely represent 10 to 15% of unrelated transplants and 7 to 10% of all allo transplants
- Especially important in pediatric patients with non-malignant disease
- Transplant physicians will continue to make decisions that are in the best interests of their patients understanding that they may face more economic constraints within their institutions
- Outcomes data will help sort out the best therapy by disease, age and medical status

Conclusions

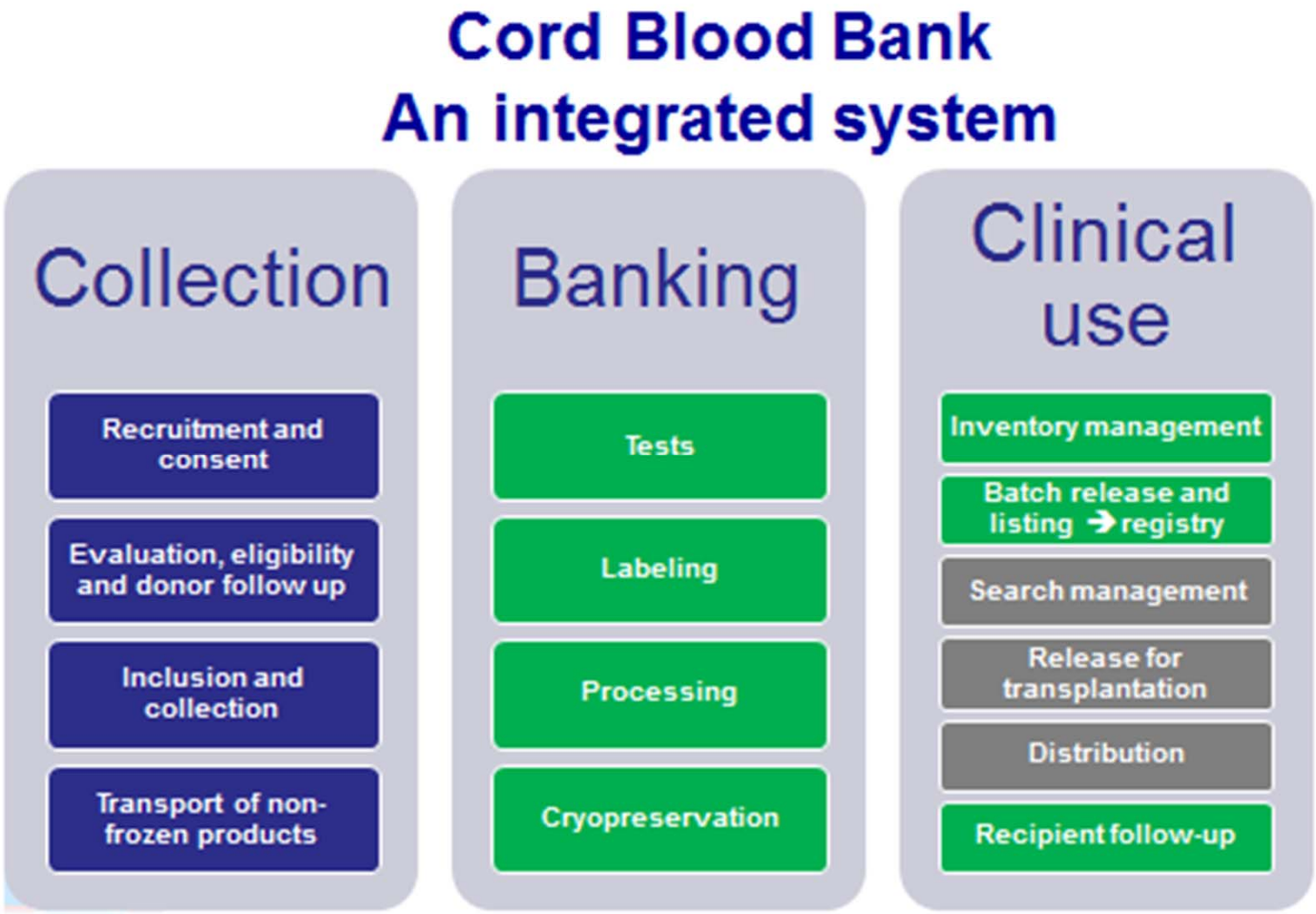
- In Europe the number of CB products provided has decreased from 886 (2014) to 684 (2015)
- Twelve European countries have stored new CBU in 2015 (four countries stored more than 1,000 CBUs in 2015)
- **17.3% from the CBUs globally listed have a TNC count >150*10E7**

Time to rethink about the cord blood field

Hematopoietic stem cell transplantation (HSCT) has become an accepted therapy for many congenital or acquired disorders of the hematopoietic system and has seen major changes in indications and use of transplant techniques over the years.

20/12/2016

Fonctions


Cord Blood Bank
An integrated system
Collection
Recruitment and consent
Evaluation, eligibility and donor follow up
Inclusion and collection
Transport of non-frozen products
Banking
Tests
Labeling
Processing
Cryopreservation
Clinical use
Inventory management
Batch release and listing → registry
Search management
Release for transplantation
Distribution
Recipient follow-up

Conclusion

- Imprévisibilité et rapidité des développements
- Évolution rapide des pratiques de transplantation pas en phase avec leur validation par des données publiées (études surtout rétrospectives)
- Succès des greffes de SC soumis à une chaîne d'expertises (prélèvement➔processing➔usage clinique)
- Transplantation: recherche du meilleur greffon
- Banques: maintien du savoir-faire (prélèvement➔greffe) et des accréditations

Remerciements

- Lydia Foeken

  WMDA
- Merry Duffy

  NMDP-Be the Match

  WMDA CBWG