
UMBILICAL CORD BLOOD STATISTICS

INTRODUCTION

- Stem cells are the next frontier in medicine.
- Stem cells are thought to have great therapeutic and biotechnological potential. This will not only to replace damaged or dysfunctional cells, but also rescue them and/or deliver therapeutic proteins after they have been engineered to do so.¹
- In the last 10 yr, umbilical cord blood has been shown to be therapeutically useful for rescuing patients with bone marrow-related deficits and inborn errors of metabolism.
- Umbilical cord blood offers advantages over bone marrow because cord blood does not require perfect human leukocyte antigen (HLA) tissue matching, has less incidence of graft vs host disease, and may be used allogeneically. ^{2,3}

1. Mark I. Weiss and Deryl L. Troyer, 2006. Stem Cells in the Umbilical Cord. *Stem Cell Reviews*; 2(2) :155-16.

2. Kurtzberg J, Lyerly AD, Sugarman J, 2005. Untying the Gordian knot: policies, practices, and ethical issues related to banking of umbilical cord blood. *J Clin Invest.* ;115(10):2592-7.

3. Laughlin MJ, Barker J, Bambach B, Koc ON, et al., 2001. Hematopoietic engraftment and survival in adult recipients of umbilical-cord blood from unrelated donors. *N Engl J Med.* ; 344(24):1815-

FIRST-IN-HUMAN

- The first transplant using CB was performed in a 5-year old boy with Fanconi anemia, an inherited bone marrow failure syndrome which can only be cured by allogeneic HSCT. ¹
- The mother was pregnant with a girl who was known, before birth, to be HLA-identical to her brother and not a carrier of the same genetic defect. The sister's CB was collected and cryopreserved at birth and transplanted to the patient.
- More than 22 years later, the patient is alive and well with a normal hematologic and immunological reconstitution provided by his donor cells.

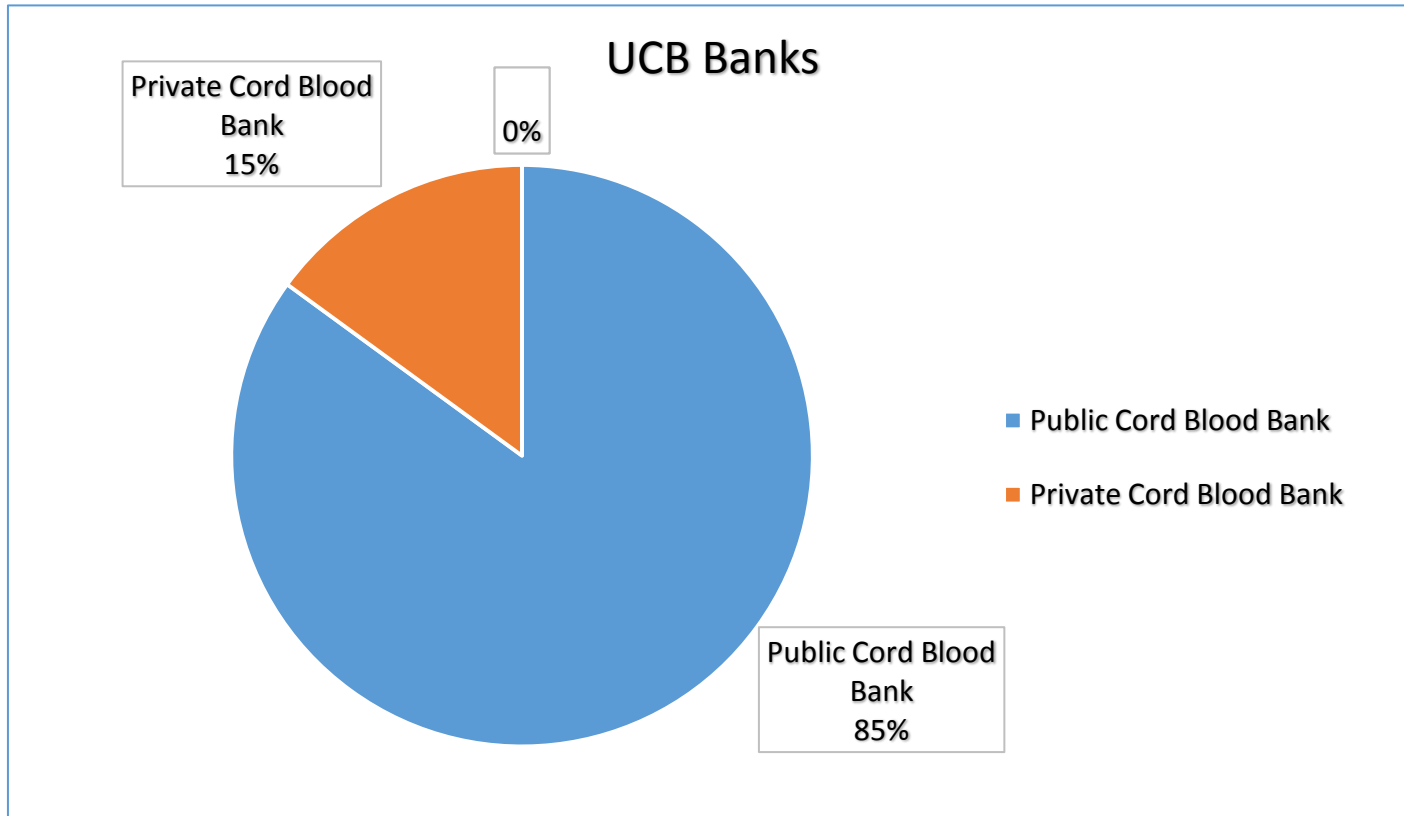
1. Gluckman E, Broxmeyer HA, Auerbach AD, Friedman HS, Douglas GW, Devergie A, et al. (1989) Hematopoietic reconstitution in a patient with Fanconi's anemia by means of umbilical-cord blood from an HLA-identical sibling. N Engl J Med 321(17):1174-8

STATISTICS OF CORD BLOOD TRANSPLANT

- More recently cord blood has also been used as a stem cell source for patients without a donor and more than **2000 Cord blood Haematopoietic Stem Cell Transplants** are performed annually.¹
- To date, more than **35,000** patients worldwide have received an UCB transplant.²

1. Ref: <http://www.who.int/transplantation/en/>
2. Ref: <http://www.nationalcordbloodprogram.org/>

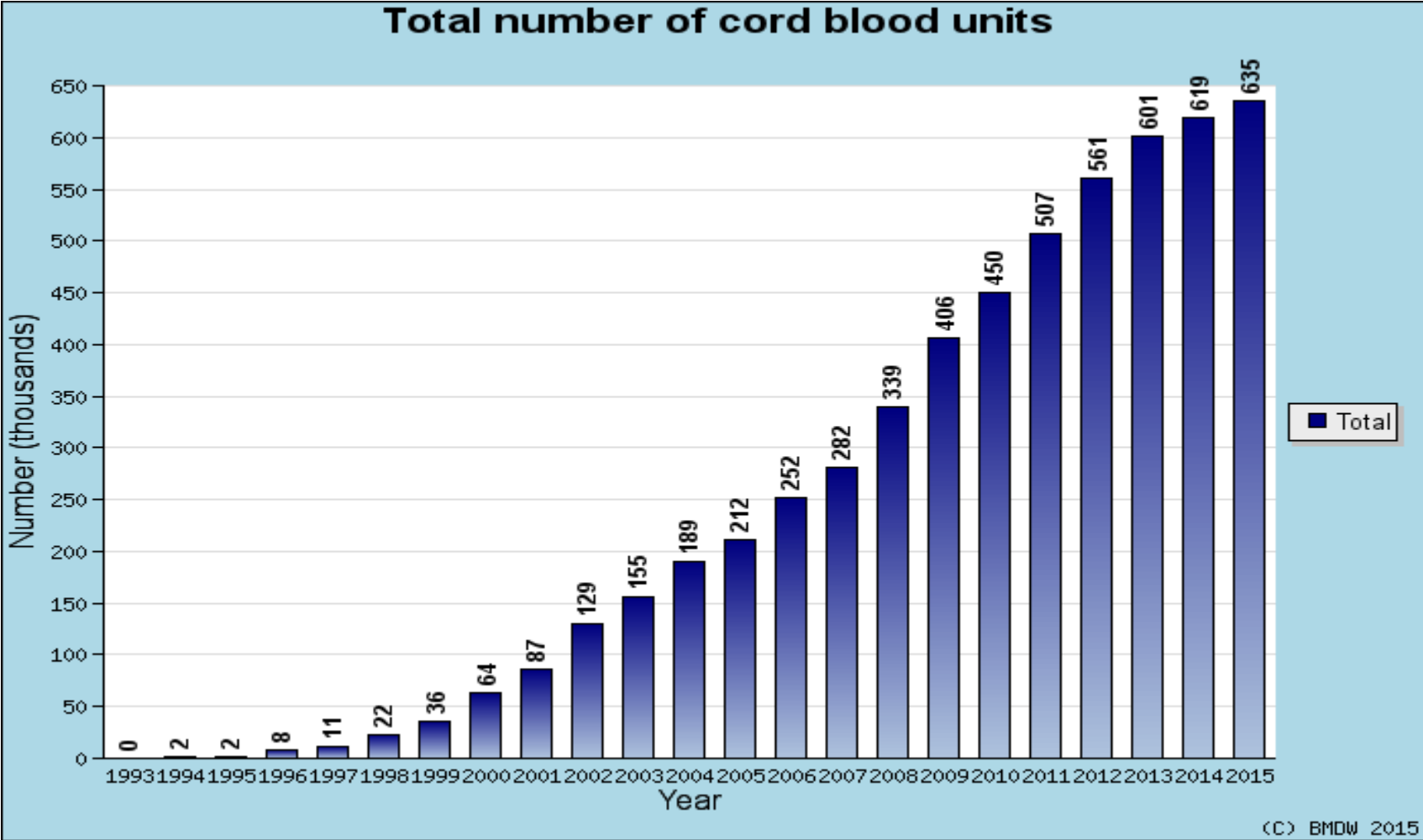
PUBLIC AND PRIVATE UCB BANKS



CORD BLOOD BANK INDIA (PUBLIC & PRIVATE)

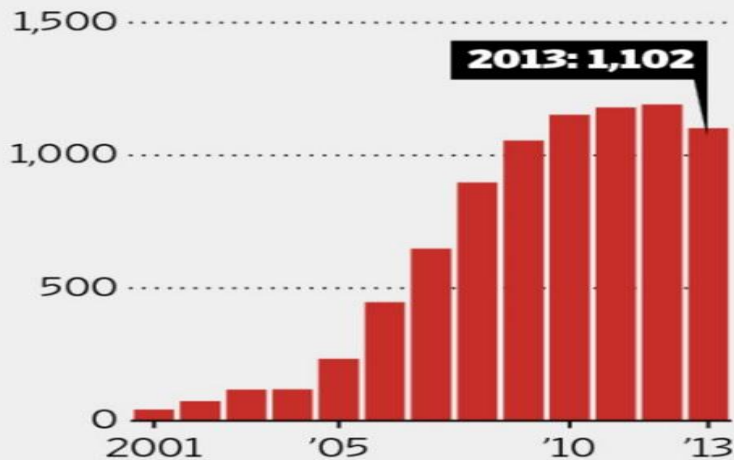
- At present there are at least **3 public** and **7 private** cord blood bank in India.
- BabyCell TM founded in 2009 as the first Indian biotechnology company to introduce cutting edge technology platform for regenerative medicine in India.
- It has achieved ISO 13485 in the very first year of operations and certified with GMP, GLP and GCP in its 2nd year of operations.

UCB UNITS INCREASING CONTINUOUSLY



New Treatment

U.S. cord-blood transplants
from public banks



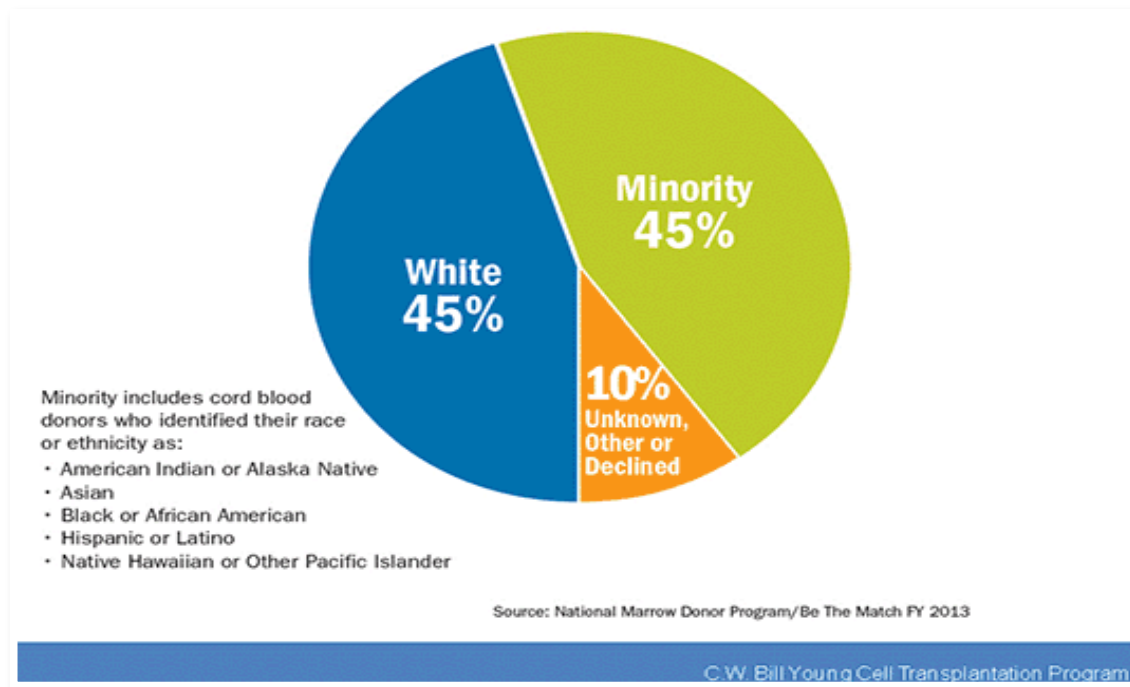
Source: Dept. of Health and Human Services
The Wall Street Journal

Out of total stored samples, 30 000 units distributed worldwide to treat children and adults with severe malignant and non-malignant haematological diseases.

In US only, more than 5000 umbilical cord blood transplant performed since 2009.

DIVERSITY OF CORD BLOOD UNITS

- Despite 13 million registered volunteer donors are presently accessible worldwide, asian patients needing HLA matched donors are unable to get one. About 5 out of 10 Caucasians who need stem cell transplant may find a perfect match. This drops to about 1 out of 10 people for Asian population especially Indian patients, mostly because their HLA types are more diverse .¹



1. Ref: CDC National office of public health genomics, www.cdc.gov/genomics & American Cancer Society. <http://www.cancer.org/treatment/treatmentsandsideeffects/treatmenttypes/bonemarrowandperipheralbloodstemcelltransplant/stem-cell-transplant-allogeneic-transplant>

RATES AND PROBABILITY

- *Nietfeld et al.* predicted the probability of a child, up to 20 years of age, receiving an autologous stem cell transplant to be **1 in 5,000** and increasing to **1 in 450 by age 70**.¹
- The HLA tissue type is inherited from the child's parents making the likelihood of a sibling match on 6/6 antigens 25% and the likelihood of a 4/6 match 39%.²
- Family history is one of the strong influencing factors on developing life threatening diseases and disorders.
- Scientists predict that there would be an increase in complex diseases and rare disorders in India.

1. Nietfeld JJ, Pasquini MC, Logan BR, Verter F, Horowitz MM. Lifetime probabilities of hematopoietic stem cell transplantation in the US. *Biol Blood Marrow Transplant.* 2008;14:316-22.

2. Fisk NM, Roberts IAG, Markwald R, Mironov V (2005) Can Routine Commercial Cord Blood Banking Be Scientifically and Ethically Justified? *PLoS Med* 2(2): e44

doi:10.1371/journal.pmed.002004

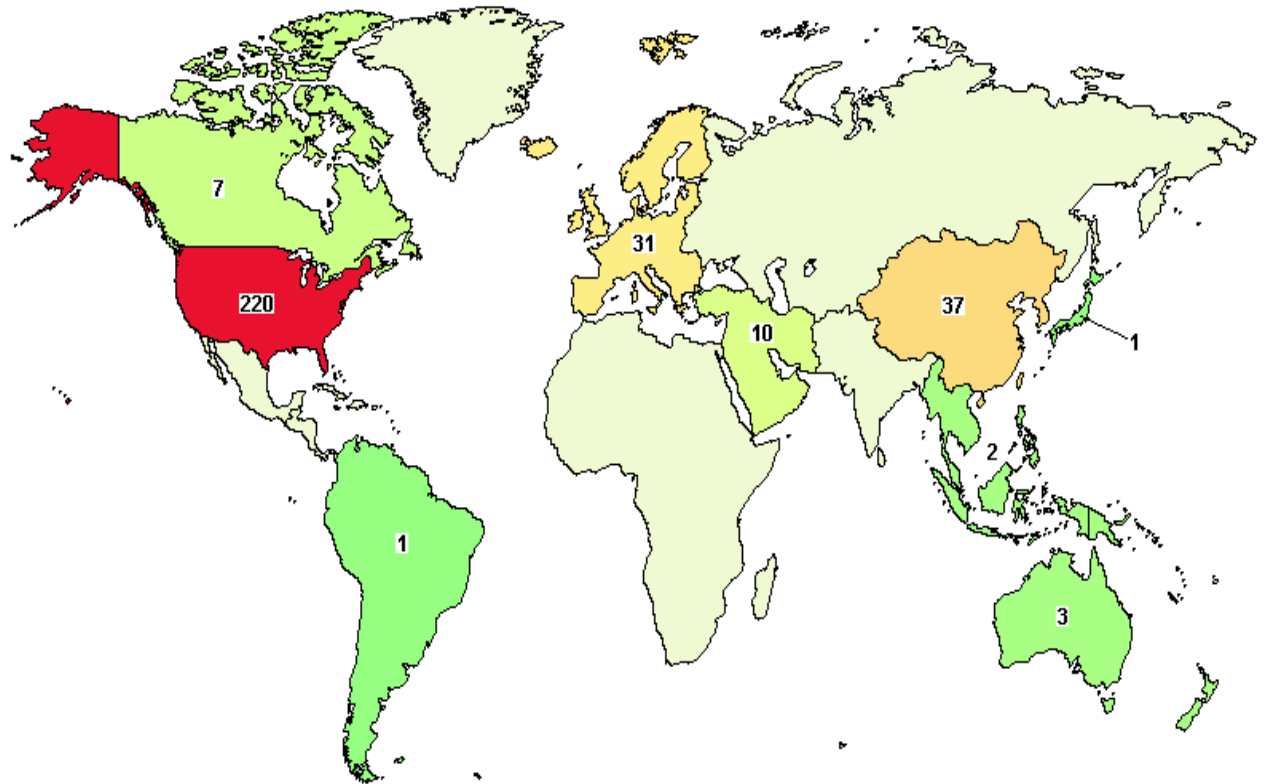
ODDS OF USING CORD BLOOD STEM CELLS ^{1,2}

| Odds | Indication |
|-----------------------------|---|
| 1 in 2,500 | Stem Cell Transplant by age 20 in USA |
| 1 in 2,000 | Thalassemia births in all of India, up to 10% of children have Thalassemia in some castes |
| 1 in 500 | Cerebral Palsy among full term births |
| 1 in 4 premies under 1500gm | Premature Lungs (BPD) |
| 1.7 per 1000 | Type 1 Diabetes diagnosis rate |

1. Statistics By Indian caste/ethnic group from Mohanty D et al. 2013; J Community Genet. 4(1):33-42 [PMC3537975](#)
2. Statistics on cumulative probability that a person In US will have some type of stem cell transplant by age 70, based on 2001-2003 national databases of diagnoses from [SEER](#) and transplants from [CIBMTR](#)

UCB TRANSPLANT CLINICAL TRIALS WORLDWIDE¹

| Region Name | Number of Studies |
|-----------------------|-------------------|
| World | 307 |
| East Asia | 37 |
| Japan | 1 |
| Europe | 31 |
| Middle East | 10 |
| North America | 222 |
| Canada | 7 |
| United States | 220 |
| Pacifica | 3 |
| South America | 1 |
| Southeast Asia | 2 |

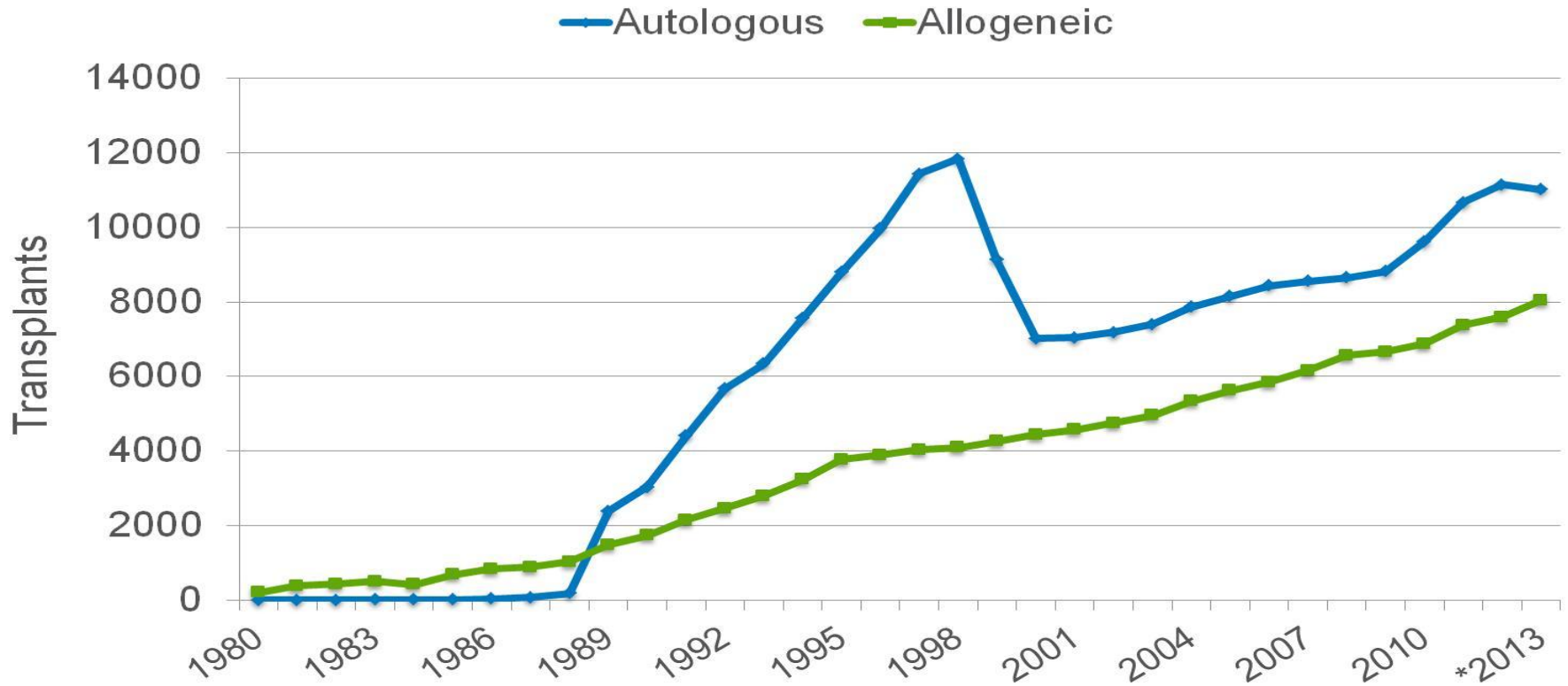


1. <https://clinicaltrials.gov/ct2/results/map?term=umbilical+cord+blood+transplantation&brwse-force=true>

UCB TRANSPLANT CLINICAL TRIALS-INDICATIONS

- Acute Lymphoblastic Leukemia
- Acute Monoblastic Leukemia
- Anemia
- Anemia, Sickle Cell
- Aplastic Anemia
- Beta-Thalassemia
- Diabetes Mellitus, Type 1
- Kidney Diseases
- Liver Diseases
- Lung Diseases
- Sickle Cell Anemia
- Skin Diseases
- Spinal Cord Injuries

Annual Number of Transplant Recipients in the US by Transplant Type



PEDIATRIC VS ADULT UCB TRANSPLANT ^{1,2}

- 28% of the cord blood transplants have been used to treat genetic diseases. The most common genetic disease treated is Severe Combined Immune Deficiency, closely followed by aplastic anemia.
- 27% of the cord blood recipients fall into the 18+ age category. One-third of this age demographic is above the age of 40.
- The children who received matched cord blood had a 20% higher survival rate than those children who received matched bone marrow stem cells.
- Adults in a Minnesota study on cord blood transplants appeared to have better than 60% survival at 2 years.

1. Statistics By Indian caste/ethnic group from Mohanty D et al. 2013; J Community Genet. 4(1):33-42 [PMC3537975](#)

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PEDIATRIC UNRELATED CORD BLOOD TRANSPLANT RESULTS

| Investigator | No. of patients | Diseases | Median follow up (months) | Disease free survival (%) |
|------------------------|-----------------|--------------------|---------------------------|---------------------------|
| Kurtzberg ¹ | 25 | Leukaemia / others | 13 | 48 |
| Locatelli ² | 60 | Leukaemia | 14 | 34 |
| Gluckman ³ | 65 | Leukaemia / others | 10 | 29 |
| Wagner ⁴ | 102 | Leukaemia / others | 32 | 47 |
| Michel ⁵ | 95 | AML | 31 | 41 |
| Staba ⁶ | 20 | Hurler Syndrome | 30 | 85 |

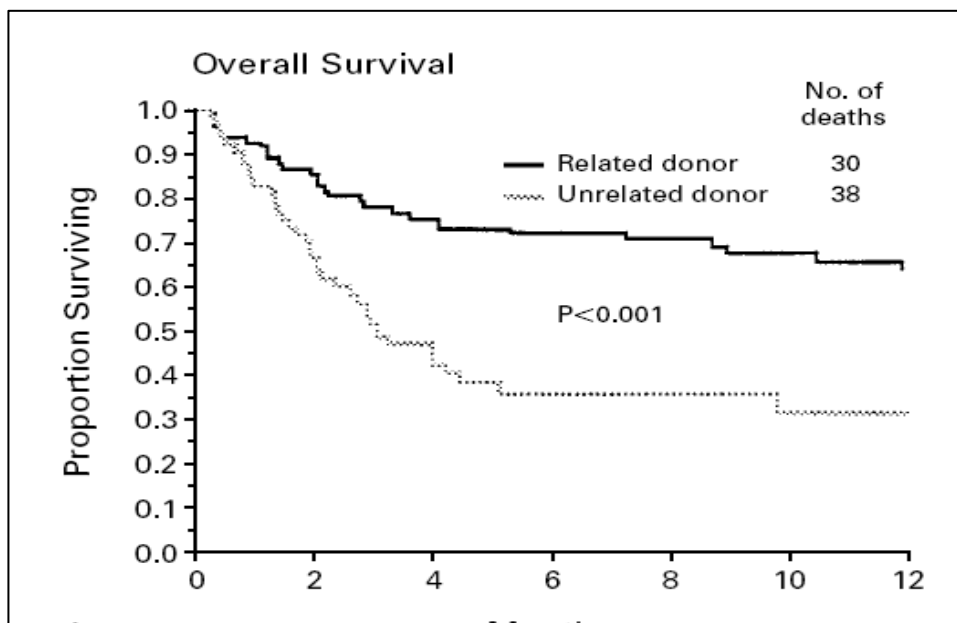
1. Locatelli F, Rocha V, Chastang C, *et al.* Factors associated with outcome after cord blood transplantation in children with acute leukaemia. Euro-cord-Cord Blood Transplant Group. *Blood* 1999;93:3662-71.
2. Kurtzberg J, Laughlin M, Graham ML, *et al.* Placental blood as a source of hematopoietic stem cell for transplantation into unrelated recipients. *N Engl J Med* 1996;335:157-66.
3. Gluckman E, Rocha V, Boyer-Chammand A, *et al.* Outcome of cord blood transplantation from related and unrelated donors. Eurocord Transplant Group and the European Blood and Marrow Transplantation Group. *N Engl J Med* 1997;337:373-81.
4. Wagner JE, Barker JN, DeFor TE, *et al.* Transplantation of unrelated donor umbilical cord blood in 102 patients with malignant and non-malignant diseases, influence of CD34 cell dose and HLA disparity on treatment related mortality and survival. *Blood* 2002;100:1611-18.
5. Michel G, Rocha V, Chevret S, *et al.* Unrelated cord blood transplantation for childhood acute myeloid leukaemia : a Eurocord Group analysis. *Blood* 2003;102:4290-97.
6. Staba SL, Escolar ML, Poe M, *et al.* Cord blood transplants from unrelated donors in patients with Hurler's syndrome. *N Engl J Med* 2004;350:1960-69.

ADULT UNRELATED CORD BLOOD TRANSPLANTATION

- Although initial studies were in children, during last few years, several investigators have published the results of cord blood transplantations in adult subjects.
- The disorders have included leukemia, lymphoma and myelodysplasia.
- Majority have received units which were mismatched at two or more HLA antigens.
- Grade III to IV acute GVHD occurred in 20% and chronic GVHD in 30%.
- Transplant-related mortality has been high - almost 50% by day-100 (infection being the leading cause followed by regimen-related toxicity).
- Twenty five percent of recipients are alive and disease-free by the end of two years. ¹

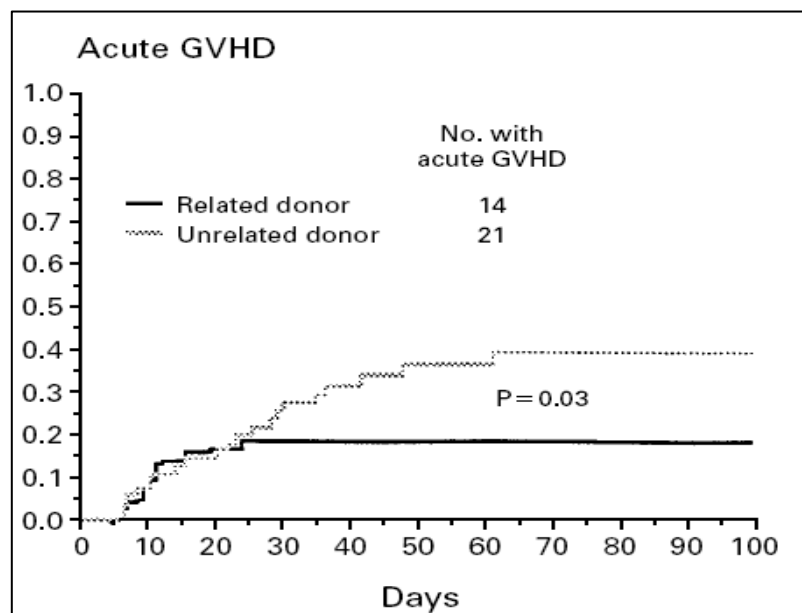
RELATED AND UNRELATED CORD BLOOD TRANSPLANTATION

- In one of the study by *Eliane Gluckman et al*; **recipients of cord blood from related donors, one-year survival was 63 percent**, and for recipients of cord blood from unrelated donors, it was 29 percent only. ¹



RELATED AND UNRELATED CORD BLOOD TRANSPLANTATION

- In one of the study, Among the recipients of cord blood from **related donors**, acute GVHD of at least grade II was observed in **14 patients**
- Among the recipients of cord blood from **unrelated donors**, acute GVHD was observed in **21 patients.**¹



DIFFERENCE BETWEEN RELATED AND UNRELATED TRANSPLANTS

- The vast majority of UCB transplants are from unrelated donors.
- Despite the fact that related UCB transplant was largely replaced by unrelated donor transplant, the former source of stem cells still remains a reality in a minority with not having access to suitable donors. ¹
- Hence, preserving the cord blood can be a good source of stem cells for related cord blood transplantation.

UCB TRANSPLANTS IN INDIA

- In India, more than **1000 cord blood transfusions** were done in children and adults for various indications, in an apparently safe and efficient manner.¹
- Indications for Cord Blood Transplant are Acute Myelogenous Leukemia, Juvenile CML, Thalassemia, Sickle cell disease, Wiskott Aldrich Syndrome, Hurler syndrome, Familial erythro/hemophagocytic lymphohistiocytosis.²
- Median age who underwent Cord Blood Transplant is 1-26 years.

1. Ref: Eliane Gluckman; Umbilical cord blood transfusions in low-income countries; The Lancet Haematology, Volume 2, Issue 3, March 2015, Pages e85–e86
2. Ref: www. CIBMTR. org

UCB TRANSPLANT CENTERS IN INDIA ^{1,2}

- | | |
|--|--|
| 1. Christian Medical College, Vellore | 10. Indian Institute of Science, Bangalore |
| 2. Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow | 11. Sir Ganga Ram Hospital, New Delhi |
| 3. Post Graduate Institute of Medical Education & Research, Chandigarh | 12. Gujarat Cancer and Research Institute, Ahmedabad |
| 4. Manipal Hospital, Bangalore | 13. Fortis Memorial Research Institute, Haryana |
| 5. All India Institute of Medical Sciences, New Delhi | 14. Tata Memorial Hospital, Mumbai |
| 6. National Centre for cell science, Pune | 15. Apollo Cancer/ Speciality Hospital, Tamil Nadu |
| 7. National Institute of Immunology, New Delhi | 16. Dr. B L Kapur Memorial Hospital, New Delhi |
| 8. Indian Institute of Technology, Chennai | 17. Apollo Hospital International Ltd., Gujarat |
| 9. Research & Referral Hospital, New Delhi | 18. Rajiv Gandhi Cancer Institute and Research Centre, New Delhi |

UNIQUE ISSUES RELATED TO CORD BLOOD TRANSPLANTATION ¹

| Feature | Cord blood | Unmanipulated BMT/ PBSCT |
|----------------------|---------------|-----------------------------|
| Availability | Limitless | Limited |
| Waiting period | Small | Large |
| Donor attrition | None | Significant |
| Matching | 4/6 or better | 10/10 or 9/10 |
| Collection procedure | Simple | Complicated |
| Risk of collection | Negligible | More |
| GVHD | Less | More |

Recent advances in understanding the unique biology of cord blood will further expand indications for its use in different settings, including those beyond hematopoietic stem cells transplantation (HSCT).

Thank you

