RESEARCH BRIEF

Public Cord Blood Banks

Worthy of National Investment

Transplanted stem cells from umbilical cord blood can be a lifeline for people who have certain disorders, like leukemia. Billions of stem cells reside in just a few ounces of cord blood, which is collected painlessly from the umbilical cord after birth. Cord blood banks then test, process, and store the units of cord blood, which are frozen and ready to use when needed.

The U.S. government began a federal cord blood program in 2005 to help create a nationwide inventory of high-quality and genetically diverse units of cord blood. However, the proportion of cord blood stem cell transplants relative to transplants using other types of stem cells—such as those from bone marrow—has been falling in recent years. Because of declining demand and increasing costs, some of the 19 public banks, which are nonprofit entities, have been struggling to make ends meet.

After more than 15 years of supporting the national cord blood system, the U.S. Department of Health and Human Services asked the RAND Corporation to evaluate the economics of the system and what could be done to improve its sustainability.

RAND researchers studied trends affecting public cord blood banks and the strategic decisions they make, and they considered ways in which the federal cord blood program might be changed to buttress banks' financial stability. Researchers found a system valuable to society and worthy of public investment, especially if such investment helps public banks to further improve the genetic diversity and quality of the national inventory.

Key findings:

- **A national program has significantly increased the publicly available cord blood inventory, but the proportion of stem cell transplants using cord blood has been declining.**
- **Future demand for cord blood is uncertain, and stagnating demand may force some public cord blood banks to close.**
- **Cord blood transplantation is not a panacea stem cell treatment, but it is important for certain populations.**
- **The RAND research team's calculations found that the value of having a public bank system far outweighs its operational costs.**

Cord Blood Fills a Critical Need

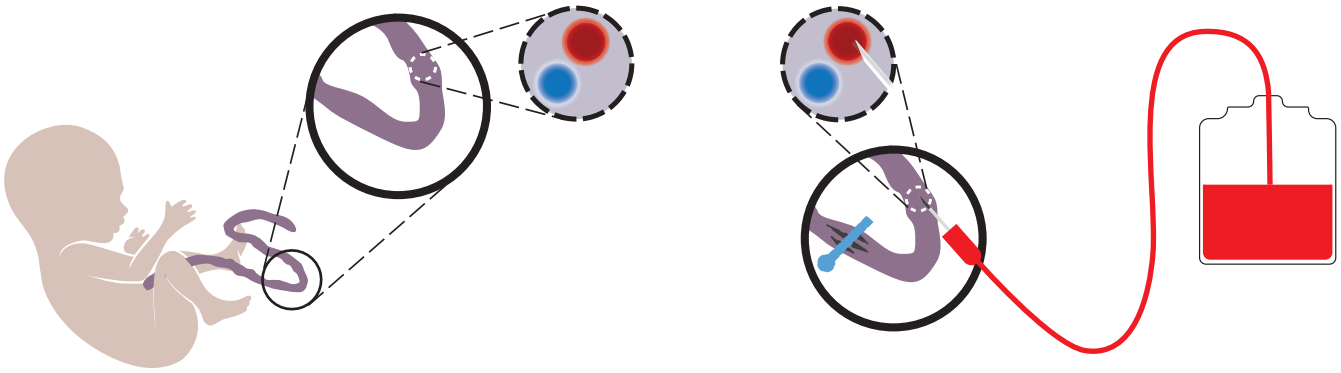
Stem cells collected from cord blood and from adult sources (e.g., bone marrow or peripheral blood) can be used to treat people with cancers and blood diseases such as leukemia, severe aplastic anemia, and sickle cell disease. Although these and other conditions for which stem cell transplants may be used are somewhat rare, they have relatively high mortality rates. Stem cell transplantation is often the last treatment option for these patients.

Different sources of stem cells have advantages and disadvantages, and no one source fits all patients' needs. Cord blood stem cells are less *differentiated* than stem cells from adult sources, meaning that they are better able to develop into various cell types as they mature. This quality is an asset for transplantation because it means that cord blood stem cells require less-stringent donor-recipient matching than adult stem cells and carry a lower risk that the recipient's body will reject them. (Rejection is a serious complication of a transplant that puts the recipient's life at further risk.) This less-strict matching also implicitly increases access to stem cells as a treatment source for those unable to find suitable matches among other sources.

Cord blood collection takes only minutes and inflicts no pain on the mother or baby (see Figure 1), but there are some disadvantages, too. The volume of collectible blood is small in comparison to that from an adult donor's bone marrow or peripheral blood. Fewer stem cells means that it takes a relatively long time—about 10–15 days longer than other sources—for the stem cells to establish themselves when introduced in the recipient's bone marrow. By extension, this means longer recovery time in the hospital for the recipient and a greater chance of infection.

Bone marrow and peripheral blood stem cell collection have their own disadvantages. Preparations for collection of bone marrow or peripheral blood, such as donor-recipient matching to minimize the chance of rejection, can take several

Figure 1. Cord Blood Extraction Process



weeks to complete. Collection itself requires the donor to undergo a procedure requiring sedation, typically done in an operating room, or take medication to stimulate stem cell production, both of which can be painful and can require recovery in the hospital. But because bone marrow and peripheral blood can provide more stem cells per donation, the cells usually *engraft*—incorporate themselves into the recipient—more quickly in the recipient's bone marrow, so the recipient typically has a shorter recovery period.

Doctors and patients balance these trade-offs when choosing a suitable stem cell donation for transplant. In some cases, the urgency to perform the transplant makes cord blood stem cells the preferred choice because they are usually available for overnight transport once a suitable match is identified. Other factors to consider include time to acquire the donation and quality of the potential stem cell sources, as well as the patient's age and disease.

National Inventory Has Grown, But Usable Inventory Is Still Low

The National Cord Blood Inventory (NCBI) program establishes individualized contracts with each public bank that provides cord blood units to the national inventory. As part of their contracts, the public banks receive subsidies every time they store an eligible cord blood unit and register it with the Be The Match® Registry, operated by the National Marrow Donor Program.

The federal government created the NCBI program to increase the number of high-quality cord blood units available through public banks so that anyone needing a stem cell transplant would have a chance to find one. The legislation authorizing the program set a goal of banking 150,000 publicly available cord blood units. Fifteen years after the start of the program, the goal has been surpassed, with more than 200,000 units currently stored.

Among other things, the initial testing of a new donation reveals its total nucleated cell (TNC) count, a measure of quality. Previous studies have shown that units with larger TNC counts result in better patient health outcomes. To some extent, a unit with a high TNC count can even offset some of the negative effects of mismatching between the donor and the recipient. Not surprisingly, cord blood units with high TNC counts are more likely to be selected for transplant than those with low TNC counts.

NCBI units must meet a minimum TNC threshold to collect an NCBI subsidy. That minimum is currently set at 0.9 billion cells per cord blood unit, which would translate to a dosage sufficient for a child who weighs approximately 80 pounds or less. Average-size adults would need a unit with a much higher TNC count, in the range of 1.8 to 2.3 billion cells. However, only about 15 percent of units in public banks' inventories have TNC counts above 1.75 billion. Demand for those units is high—accounting for nearly 60 percent of cord blood transplants between 2010 and 2016.

A second high priority of the NCBI program is to increase the genetic diversity of cord blood units available in public banks and therefore increase the odds that anyone needing a transplant will be able to find a suitable match. Minorities, in particular, often have a difficult time finding a suitable match among adult stem cell donors in The Registry. On average, the TNC counts of the minority units tend to be lower as well.

The current structure of the NCBI program implicitly creates competing demands for cord blood banks because the goal of increasing the *quantity* of units in the inventory is often at odds with increasing the average *quality* (TNC count) of the units. Thus, although the overall size of the national inventory has increased over time, the number of high-quality usable units is still relatively small. This also matters for increasing the genetic diversity because banks can increase access for racial and ethnic minorities by collecting

more units from a larger number of minorities and/or collecting more units with high TNC counts.

Demand for Cord Blood Units Is Falling

Although the national program to develop a comprehensive cord blood inventory has created a much larger inventory, the market for stem cells from cord blood may be in peril. Overall, stem cell transplants have been on the rise for several years. Almost 8,700 stem cell transplants were performed in fiscal year 2015 alone; this is up from 7,100 in 2010. However, the number of transplants using cord blood has declined over time from about 12 percent (822) of all stem cell transplants in 2010 to about 8 percent (718) in 2015.

Transplants using stem cells from first-degree relatives—or *haploidentical transplants*—almost tripled over the same period, from about 361 in 2010 to 1,045 in 2015. The innovation in haploidentical transplants comes from the use of high doses of a drug called Cytoxan, which reduces the risk of rejection enough to make this option attractive to doctors and patients. However, not everyone will have a haploidentical donor available to them.

Other factors may contribute to the declining demand for cord blood, such as higher procurement and treatment costs or provider preferences. In our interviews with stem cell transplantation doctors, some shared that cord blood units are used only as a last resort, whereas others mentioned a preference for cord blood, particularly for certain types of patients.

Over the short term, treatment costs are clearly higher for cord blood transplants relative to other stem cell transplants. This is primarily driven by longer engraftment periods, which translate into longer hospital stays. Further research is needed to determine whether cord blood recipients stay healthier over the long term than recipients of other stem cell types. The majority of the literature to date follows patients for only a short time period. Because cord blood transplants take longer to engraft, a short follow-up period will bias results and suggest more-favorable outcomes for other stem cell sources. Differences in collection costs are also unclear, as previous studies have tended to ignore the cost of harvesting adult stem cell sources, which can be significant.

Public Banks Are Struggling

Qualitative evidence from RAND researchers' interviews with stakeholders in the cord blood system (e.g., representatives of public and private banks, doctors, researchers, suppliers, and government regulators) suggests that the nonprofit public cord blood banks may be experiencing more-intense competition among banks, both in the United States and abroad.

Competition among public banks has increased as the net supply of cord blood units has grown. Private banks, in which individuals store cord blood for their own family use, also provide some competition because their units may not be released to the national inventory, keeping that segment of the market off-limits for most patients. In addition, international cord blood banks now supply about 24 percent of units used in the United States, up from 13 percent in 2004. Similarly, U.S. banks have been shipping fewer units to other countries: 16 percent of all cord blood units shipped in 2016 went to foreign locales, down from 24 percent in 2010.

The fee that a bank charges a transplant center for a cord blood unit tends to be the same (about $36,000) regardless of the unit's TNC count or genetic rarity. Banks could charge a premium on units with higher TNC counts, for example, if they were in the market to maximize profits, but it is unclear whether the market would bear it.

The current market environment for public banks makes it difficult to break even. Costs for public banks include processing, testing, and storage costs; licensure by the U.S. Food and Drug Administration; and overhead costs. The total expenses vary widely, ranging from $1 million to $6 million, depending on the size of the operation. On the other side of the ledger, revenue comes primarily from fees, but also from the NCBI subsidies for registered units, donations, grants, or in-kind donations of services.

Banks collect, on average, 8,500 units annually but ultimately store only 5 to 40 percent of those collections. Among units that have been banked, a low–TNC-count unit has only about a 0.1-percent chance of being used in a given year, as opposed to a 3-percent chance for larger units. Because banks collect fees only on units that are used, banks that store low–TNC-count units are more likely to lose money.

Banks have had to get creative with how they structure their businesses in order to remain viable. Some banks have adopted hybrid models, offering private family banking to cross-subsidize the nonprofit public banking operations under NCBI. Some have also improved their financial situation by selling their processing or testing services to private banks. Others are part of larger organizations, such as whole blood centers or hospitals, which can offer cheaper transportation and lab work.

Some stakeholders speculated that the NCBI program encouraged too many public banks in the first place. Some banks have already shut down collection sites, and others have closed altogether. Further consolidation of public banks appears likely in the near future if demand for cord blood continues to stagnate.

The RAND Research Team's Recommendations

Beyond evaluating the costs and benefits of public cord blood banks from both the bank and patient perspectives, the RAND team calculated the societal value of the public banking system. Publicly available cord blood units provide

potential treatment for all people, whether or not they end up developing a stem cell–treatable disease—or have the resources to bank cord blood privately. Transplant recipients clearly benefit directly from cord blood through healthier, longer lives. The RAND team calculated that the average annual value of having a national public bank system ranges from $883 million to $1.7 billion, far outweighing the aggregate industry operational costs of $60 million to $70 million to maintain the current system.

Given that the system is worthy of continued investment as a public good, the research team compiled a series of recommendations for the NCBI program and for the system as a whole.

NCBI Program Structure

The Health Resources and Services Administration, which oversees the NCBI program (see Figure 2), should

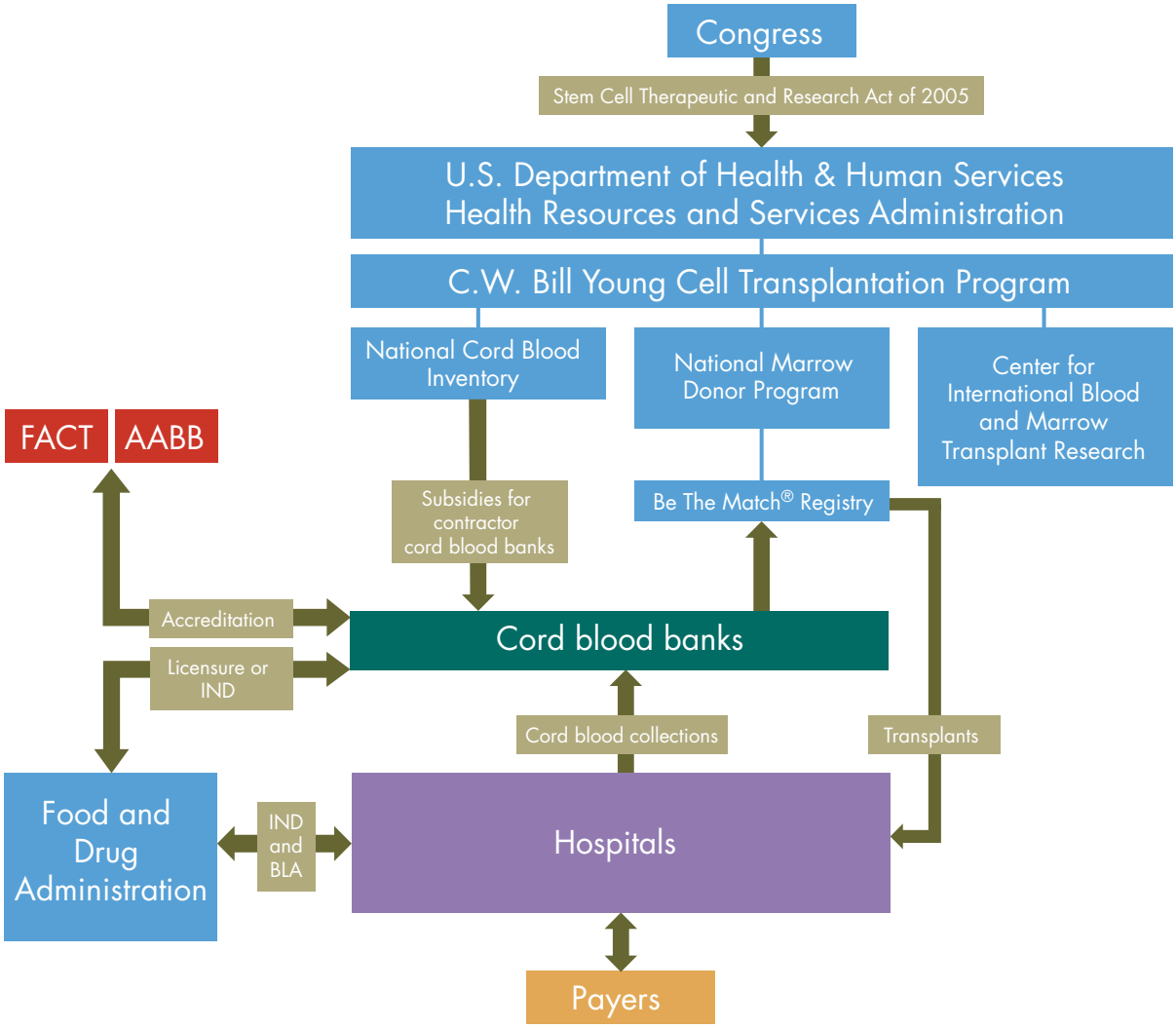
- **increase the diversity of the national inventory** by providing funding that encourages banks to add collection sites where more minority units can be collected; by increasing subsidies for minority units; and by increasing the minimum TNC-count threshold, especially for nonminority units.
- **standardize and consistently fund the NCBI contracts to the extent possible** because the uncertainty over contract funding and renewal makes it difficult for public banks to plan for the future.
- **prepare contingency plans** that would secure the fate of cord blood units stored at banks, should they go out of business if the market consolidates; currently, no such written plans are in place.

Cord Blood Banking System Operations

Several changes to the cord blood system could help it operate more smoothly.

- CMS should consider changes to reimbursement for stem cell transplants so that acquisition costs can be reimbursed separately.
- Federal funding could encourage knowledge sharing across banks and mentoring for centers and physicians with less cord blood experience.
- Giving banks the option to release smaller subsidized cord blood units to research endeavors could help advance scientists' understanding of cord blood and expand its use for transplantation or other uses in the future.

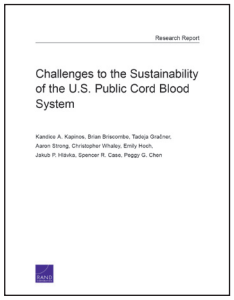
Figure 2. Federal Cord Blood Bank Support and Oversight



NOTES: AABB = American Association of Blood Banks. BLA = Biologics License Application. FACT = Foundation for the Accreditation of Cellular Therapy. IND = Investigational New Drug (application). Boxes in blue denote U.S. government agencies or programs. Payers include both private and public payers.

The Stem Cell Therapeutic and Research Act of 2005 established the C.W. Bill Young Transplantation Program to collect, maintain, and make available 150,000 new units of high-quality cord blood. Congress has reauthorized the act twice, in 2010 and 2015, each time increasing the authorized appropriation from $15 million for fiscal years 2007 through 2010 to $30 million for fiscal years 2016 through 2020. These funds cover NCBI subsidies and the program's administrative costs.

The Health Resources and Services Administration (HRSA) oversees the program, which, in turn, oversees NCBI, the National Marrow Donor Program, and the Center for International Blood and Marrow Transplant Research. NCBI interacts directly with public cord blood banks to help cover collection, storage, and processing costs and addresses certain needs of the inventory, such as minority or ethnic donors, through contracts. The National Marrow Donor Program links HRSA, physicians, and banks through its Be The Match® Registry, which serves as a logistic and financial intermediary between banks and transplant centers (usually hospitals), and as an educational resource for patients and clinicians.



This brief describes work done in RAND Health documented in *Challenges to the Sustainability of the U.S. Public Cord Blood System*, by Kandice A. Kapinos, Brian Briscombe, Tadeja Gračner, Aaron Strong, Christopher Whaley, Emily Hoch, Jakub P. Hlávka, Spencer R. Case, and Peggy G. Chen, RR-1898-DHHS, 2017 (available at www.rand.org/t/RR1898). To view this brief online, visit www.rand.org/t/RB9977. The RAND Corporation is a research organization that develops solutions to public policy challenges to help make communities throughout the world safer and more secure, healthier and more prosperous. RAND is nonprofit, nonpartisan, and committed to the public interest. RAND's publications do not necessarily reflect the opinions of its research clients and sponsors. **RAND**® is a registered trademark.

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