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FINANCING CHINA'S FIRST NATIONAL CORD BLOOD BANK

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ABSTRACT

China's National Hygiene and Health Commission began construction of its first National Cord Blood Bank (NCBB) in the spring of 2019. NCBBs bank cord blood units, which are used for hematopoietic stem cell therapy, a life-saving therapy indicated for over eighty diseases. Investment in a NCBB will lower the costs of purchasing cord blood units and is a response to the significant need for improved access to this therapy for Chinese citizens. However, a NCBB faces two major cost problems: the upfront costs of financing a centralized NCBB are enormous, and NCBBs, on their own, are not fiscally solvent and risk closure over the long run. This paper conducts a review of the literature for comparative models of financing NCBBs around the world and applies those lessons to China. I conduct a cost-benefit analysis to determine the ideal number of stored cord blood units and illuminate how post-transplant hospitalization costs arising from complications affect the cost model. Finally, I provide a number of policy recommendations for a fiscally sustainable NCBB.

Keywords: Chinese, cord blood banking, umbilical cord, hematopoietic, stem cell therapy, blood cancer, transplantation, stem cell transplants, stem cell transplantation, hematopoietic stem cell therapy, allogeneic banking, autologous banking, allogeneic, autologous, cord blood donation, cord blood units, public cord blood bank, private cord blood bank, CBUs, comparative bioeconomy, cost effectiveness, cost benefit analysis, health economics

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Table of Contents

I. Introduction

The Chinese National Hygiene and Health Commission (NHHC) began construction of its first National Cord Blood Bank (NCBB) in the spring of 2019. The NCBB is a joint venture between the NHHC and the private sector, and will act as a centralized public cord blood banking facility and national cord blood banking registry. The NHHC hopes that building a NCBB will reduce the costs of cord blood banking (CBB), and therefore the cost of hematopoietic stem cell transplants (HSCT) which use cord blood units (CBUs), by streamlining their existing blood banking system. This is supported by the experience of other countries such as Mexico, in which public CBB has become successful and cost-efficient enough so that the local availability of cord blood units (CBUs) is preferred in HSCTs despite the existence of a bone marrow donor registry (Navarrete and Contreras, 2009).

At this point in time, HSCT is unrealistic for most Chinese citizens because of the prohibitive costs that accompany treatment and hospitalization. HSCT therapy from cord blood tissue ranges from 235,00 RMB - 1,036,000 RMB (Tan et al., 2015). The average Chinese household income is 3,000 RMB - 36,000 RMB (Statista, 2017). In other words, the cost of cord blood transplants is nearly 30 to 80 times more than a family's annual household income, remaining unaffordable to most. The high cost of CBUs, and the hospital complications resulting from low-quality or poorly-matched CBUs, is a major contributor to the cost of HSCTs.

Yet the Chinese government remains interested in making HSCT accessible to its citizens because the need for HSCT in China is significant. The Chinese Red Cross found that almost two-thirds of children who require HSCT for leukemia (the leading cause of death among Chinese children) did not finish the treatment for financial reasons (The New York Times, 2011).

Leukemia, thalassemia, and HIV, the most prevalent diseases indicated for HSCT in China, constitute a disease burden of about 14,000,000 cases annually (Fang et al., 2010).

However, the upfront costs of financing a centralized NCBB are enormous. Authorities must build systems to procure cord blood and build specialized facilities – often with stringent temperature and cleanliness requirements – to store collected cord blood units for years. They must also pay for personnel to keep the NCBB in order and to ensure that collected cord blood units remain viable until they are released to patients. Ensuring that China builds a fiscally sustainable NCBB is the foundation to making HSCT accessible to all Chinese citizens.

This thesis examines how China can build a fiscally sustainable NCBB and provides policy recommendations for doing so. I first review the literature to explore international models for financing CBBs, including a comparison of public and private CBBs. Then, I contextualize China's approach to cord blood banking. Finally, I conduct a cost-benefit analysis and model how post-transplant complications change the financial expectations of a NCBB.

II. Literature Review: Financing Public Cord Blood Banks

IIa. Background

Since the first successful cord blood transplant in 1988 (Gluckman et al., 1989), umbilical cord blood has become the widely accepted alternative to bone marrow as the source of stem cell units, because it is a less-invasive, more forgiving, and more easily cultured source of stem cells (Gluckman and Wagner, 2010). Other benefits of cord blood as a stem cell source include its higher concentration of hematopoietic stem cells than is normally found in adult blood, meaning that fewer units of cord blood are needed for transplant. Cord blood derived stem cells are also substantially more viable for individuals without genetically identical counterparts and who come from minority or mixed-race backgrounds. Successful cord blood transplants require only 4 out of 6 human leukocyte antigen (HLA) matches between donors and patients, while traditional bone marrow transplants require all 6 HLA sites to match, making cord blood stem cell units are a good choice for individuals with fewer match options (Katz, 2015). Requiring less antigen-matching sites further reduces the chance of serious, life-threatening complications arising from post-transplant graft-versus-host-disease (GVHD) (Fasouliotis and Schenker, 2000).

HSCT therapy is of particular interest to clinicians, patients, and policymakers because HSCT therapy has cured over 80 life-threatening hematological diseases and is indicated for up to 240 diseases in total. Cancers of the blood and bone marrow, leukemia, lymphoma, thalassemia, aplastic anemia, and even HIV are all indications for HSCT (see Figure 1). With about 10% of all cancers diagnosed as leukemia each year (Leukemia Research Foundation, 2020) leukemia the leading cause of death for Chinese children (Liu et al., 2020), and global spending on cancer drugs rising to over $133 billion in 2017, up from $96 billion in 2013 (IQVIA, 2018), the burden of diseases indicated for HSCT continues to rise.

Table 1. *Diseases Treated by Cord Blood Transplantation**

Malignant diseases
Acute lymphocytic leukemia
Acute myelocytic leukemia
Chronic myelogeneous leukemia
Juvenile chronic myelogeneous leukemia
Myelodysplastic syndrome
Neuroblastoma
Nonmalignant Diseases
Adrenoleukodystrophy
Amegakaryocytic thrombocytopenia
Blackfan-Diamond syndrome
Dyskeratosis congenita
Fanconi's anemia
Globoid cell leukodystrophy
Gunther disease
Hunter syndrome
Hurler syndrome
Idiopathic aplastic anemia
Kostman syndrome
Lesch-Nyhan syndrome
Osteopetrosis
Severe combined immune deficiency
Thalassemia
X-linked lymphoproliferative syndrome

*Adapted from Fasouliotis and Schenker, 2000.

Cord blood is frozen in cord blood banks (CBBs) to preserve stem cells for future use in treatments. At birth, a newborn's cord blood can be donated to public CBBs for allogeneic transplants, or stored in private banks for autologous applications. Allogeneic refers to other donors providing CBUs, while auotologous refers to one's own self as the source of CBUs (American Cancer Society, 2020).

The financing of CBBs has been a source of global debate since the development of public and private CBBs. Similar to the practices surrounding blood donation as a voluntary and ethical gift to others in the tissue economy, donating umbilical cord blood to public banks is seen as a laudatory act of citizenship in mutually beneficial participation in a globally connected society (Rose, 2007). However, the existence of CBBs propelled biological tissues into a tissue economy, in which tissues are monetized and exchanged like products. Thus, private banks operating for profit are often able to generate revenue while public banks are vulnerable to competitive fiscal pressures in the marketplace.

This literature review first examines the public-private dichotomy and the natural tensions arising from this dichotomy. Second, I examine the broader gift-giving economy and tissue economy that CBBs reside in. Third, I explore various financing models of public CBBs.

Despite unanimous agreement that sustainable financing of CBBs are crucial to the existence of public CBBs (Katz and Mills, 2010), the continued existence of public CBBs as a crucial public good (Aznar Lucia, 2012; Katz, 2015), and numerous calls to action to better finance public CBBs (Petrini, 2014), there has been little literature reviewing various models of financing public CBBs. To the best of my knowledge, this paper is one of the few papers to conduct such a review.

IIb. Methodology

I used the key words "financing public cord blood banks" in Google Scholar and PubMed to search the literature. I then conducted a manual abstract review, and discarded articles if they failed to mention or evaluate financing, cost-effectiveness, or budget balancing. I drew from literature around the world as long as they were accessible to me, meaning that articles that could not be translated to English were discarded.

A note on ethical issues: There are numerous ethical issues related to the existence of allogeneic public CBBs and autologous private CBBs. Though I examine one aspect of the ethical dilemma in cord blood (gift giving in a tissue economy), most of these issues are outside the scope of this paper. For an overview of some forerunning ethical questions autologous private banking raises, see Katz, 2015.

IIc. The Cord Blood Bank Landscape

After the first successful treatment of Fanconi's anemia using stem cell units derived from cord blood, the United States was the first country in the world to establish a public cord blood bank in New York in 1992 (Rubenstein, 2006). Various states and countries followed suit, eventually giving rise to three types of cord blood banks: public banks, private banks, and hybrid banks.

Public banks characteristically accept CBUs as donations without charge or compensation. They process, store, and distribute allogeneic stem cells, list their banked units in national or international registries, and charge a fee when they release their units for transplant. Released CBUs are the only source of revenue for public banks, and often must cover the cost of procuring the CBU until its release. Public banks are financially backed by their released CBUs and government or philanthropic grants, funding, or subsidies (Katz, 2015).

Private banks store autologous stem cells for directed use, meaning that families bank their newborn's stem cells for future use if their child or their child's sibling gets sick later in life (Chen, 2011). Private banks charge a fee for this initial procurement and processing of cord blood, as well as an annual fee for the continued storage of the family's CBUs (Denburg, 2016). Unlike public banks, however, private banks do not receive any form of revenue when they release CBUs back to their donors. Private banks follow a commercial model, in which more clients, and therefore, more units banked, means more revenue.

Hybrid banks are a mix of public and private banking models. Often, hybrid banks refer to banks that have a public bank that is financed by its private counterpart. Though countries such as China (Chen, 2011) and the UK (Hauskeller, 2016) have implemented hybrid banking as a means of improving the fiscal sustainability of public banks, the literature appears unconvinced of hybrid banking's potential to resolve the fiscal, quality, or inclusivity issues that arise from public or private cord blood banking (Hauskeller, 2016). Consequently, this review does not explore hybrid banking in further detail, as it remains outside the scope of discussion.

It is important to note that there exists a distinction between banking and funding. For example, public banks may include a mix of private and public funding (through philanthropic grants and government subsidies, for example). This paper aims to examine the fiscal sustainability of public banks, regardless of whether that money is privately or publicly acquired.

IId. Tensions in the Public-Private Cord Blood Bank Dichotomy

After restricting the cord blood banking landscape to public and private banks, I examined the points of tension between these two types of banks. I found a variety of factors that may contribute to public CBB's financing problems, such as scarce resources, the persistence of private banks despite lack of clinical evidence for their efficacy, and the substantial upfront costs needed to fund public banks.

Scarce Resources: The private-public cord blood banking dichotomy illuminates unique tensions, one of which is resource allocation. From a public health perspective, there is the worry that private autologous banking might contribute to depleting public allogeneic banking efforts (Katz, 2011). Naturally, private CBBs divert resources from public CBBs. If families choose to donate their baby's cord blood to private banks, then public banks lose out on a potential donor

(Petrini, 2014). By definition, public banks and recipients outside the family will never have access to privately-banked CBUs.

This trade-off may be false if public banks only need to bank a smaller number of CBUs to meet the demand for indicated diseases relative to the number of potential donors. Theoretically, this is true. U.S. researchers estimated that banking150,000 CBUs would meet over 90% of patient needs (H.R. 2520, 2005 - 2006). Querol et al. calculated that the optimal U.K. bank size is 50,000 CBUs, allowing 80% to 98% of patients to find at least one matching donor (Querol, 2009). Singaporean authorities estimated that a target of 10,000 CBUs would provide its 5 million person population an 80% chance of finding a match (Koh, 2008). Of the 828,000 annual births in France, Fève and Florens estimated that just 5.6% of those (46,737 CBUs) would provide patients an 83% chance of finding a match (Feve, 2009). Figure 1 presents the target number of CBUs discussed here and compares them with annual births in the country and number of units currently banked.

Country	Annual live births per year	Target CBUs	Percent of target banked units (Target CBUs / Live Births)
France	828,000	46,373	5.6%
Singapore	39,279[1]	10,000	25.5%
U.K.	640,370[2]	50,000	7.8%
U.S.A.	3,790,000[3]	150,000	4.0%

Figure 1. Comparative chart of annual live births and target CBUs. The percent of target banked units in the far right does not include the average discard rate during procurement and assumes that banks will need to replenish their CBUs annually. The literature estimates 30% of collected umbilical cords are ultimately banked as CBUs, and banks release 1 to 2% every year of their total collected units. *Source: Author.*

Why, then, is there such worry about private banks diverting the number of CBUs available? For one, despite the large numbers of annual births in each country, cord blood is still

[1] Singapore Department of Statistics. “Births and Fertility - Total Live-Births, 2019.” Last updated 2019. Accessed July 2020.

routinely incinerated as medical waste around the world (Katz, 2015), as the infrastructure for donating cord blood to public banks remains underdeveloped. For example, of the 343 hospitals in the state of California in the U.S., only 14 hospitals accept cord blood donations (Katz et al., 2011) despite a 24-year history of public cord blood donations. For another, autologous banks appear to be thriving, as confirmed by the commercial success of private banks worldwide, which disclose enormous financial profit – often in the hundreds of millions to billions in revenue – each year (Katz et al., 2011). Even in countries such as France, where only allogeneic public banking is legalized, a growing number of parents choose to export their newborn's cord blood to commercial banks in nearby countries (Katz, 2015).

It appears that trade-offs manifest in a very real way when it comes to empirical data. My interpretation of the literature is that it is more accurate to say these tradeoffs exist because despite the large number of potential donors, the cord blood donor pool remains finite. Further limiting the potential donor pool are the institutional barriers to ubiquitous collection of cord blood in the U.S. and abroad.

Clinical evidence: One of the major sources of tension arise from the fact that there remains no clinical evidence on the therapeutic benefits of autologous transplants (Sullivan, 2008; WMDA, 2006). A Eurocord study found that out of over 3,300 cord blood transplants performed in 43 countries between 1988 and 2007, only three were autologous (Cairo, 2008). Taken in context of the 1 million autologous banked CBUs over the past 20 years, the literature remains sparse not only on the clinical outcomes of autologous treatments but also on the utilization of autologous CBUs (Katz-Benichou et al., 2007).

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[2] Office for National Statistics. "Live Births - 2018." Last updated 2018. Accessed July 2020.
[3] Elflein, J. "Births in the US – Statistics and Facts." Last updated 2018 on Statista. Accessed July 2020.

Of published autologous outcomes, clinical data indicate that allogeneic transplants have notably superior medical applications and outcomes. One reason for this is because autologous transplants are not indicated for all of the treatments that allogeneic transplants are indicated for (ie, chronic or acute leukemias) (Troeger, 2007). Another reason is because cord blood obtained from newborns who eventually go on to develop leukemia may contain DNA mutations, contra-indicating re-infusing the sick child with their own cord blood in case of re-introducing the disease (American Academy of Pediatrics, 2007). Finally, the slow turnover of CBUs in private banks (some studies estimate as low as 0.009%) (Kaimal et al., 2009) relative to allogeneic banks (about 1 – 2%) (Katz, 2015) may compromise the quality of the CBU following long-term cryopreservation (Katz and Mills, 2010).

Despite paltry clinical evidence of the efficacy of autologous private banking, private banks continue to financially outperform public banks. The literature largely points to the marketing employed by commercial banks as a form of "bioinsurance," in which families are led to believe that by banking their newborn's stem cells, they are securing their child's, and possibly their child's siblings, against future diseases (Katz, 2015). Purely based on evidence, such marketing is misleading at best: the likelihood that the child will develop diseases indicated for CBUs is slim, and the likelihood of the child benefitting from his or her own stem cells is slimmer, and most likely contraindicated. Furthermore, publicly-donated UCBs are always traceable. As the possibility of a CBU being released over a period of 11 years is about 4% in a public bank, there is a high probability that if the donor needed a transplant, their stem cells would still be available to them (Bart, 2012).

The donor pool's misunderstanding of the clinical evidence contributes to the tensions underlying the private-public cord blood banking dichotomy. These tensions remain entrenched, so much so that some papers have even raised the question of whether private banks should continue to be legal (Katz and Mills, 2010). Conversely, of course, taking away the option of autologous private banking may also raise legal and ethical concerns.

Substantial upfront costs of a public bank: The success of public cord blood banks depend largely on government support, and government authorities often have a hard time justifying the enormous upfront costs associated with establishing a public bank. Put another way, from the taxpayer's point of view, should public money finance hospital efforts to deliver information about public banking? Furthermore, should public banking of stem cells be regarded as a public health good?

One perspective the literature presents is that a public CBB is not a medical necessity (Chima, 2011). This view is persuasive because public CBBs tend to be available in higher income countries, (Argentina, China, and Mexico are exceptions) (Flegel, 2009) and are considered more of an ideal rather than a norm (Jain, 2007). The costs of establishing and maintaining a public CBB are enormous: a released CBU from public banks in the U.S. range from $30,000 to $50,000, which is calculated to cover the procurement, processing, and storage of the CBU as well as the maintenance of the bank (Bart et al., 2013). It is also important to note that these public banks are already often receiving some sort of governmental assistance – the U.S. authorized a Stem Cell Therapeutic and Research Act in 2005 that allocated nearly $80 million over 5 years – to maintain public banks. Funding public banks is a doubly expensive endeavor when we take into account the actual therapeutic value provided by these banks, as an average of 1- 2% of these banked units are released annually (Ruff et al., 2008).

Thus, for countries considering establishing a public CBB, it may be a fruitful exercise to conduct a cost-benefit analysis before building a public CBB. Authorities should also realize that, in general, the upfront costs can be recovered if the bank is committed to selling CBUs on a cost-recovery basis.

IIe. The Tissue Economy

The uncompensated donations of CBUs to public banks, which are consequently re-sold for thousands of dollars, has been an ethical issue of much debate in the literature (Petrini, 2014). Relevant to our discussion about financing CBBs is acknowledging that their existence propels the tissue economy forward (Waldby and Mitchell, 2006). Petrini describes each cord blood unit as "represent[ing] a full-fledged immune system that carries power to save a life…a biological currency." This representation is what allows CBUs to be capitalized in "banks" and sold as "bioinsurance" (Petrini, 2014). It becomes normal for biological products like cord blood to become an importable and exportable good, one that responds to pricing logic based on factors such as quality and compatibility. The twenty-first century has reversed the blood economy, in which cord blood, like blood, was considered a gift to the community and therefore a shared public good. The tissue economy is a new form of capitalization that creates both a demand and a marketplace for cord blood (Waldby and Mitchell, 2006).

IIf. Financing Public Cord Blood Banks

While the literature establishes public CBBs as an unequivocal public health good, many public CBBs have struggled to remain financially viable. In 2013, the World Marrow Donor Association (WMDA) revealed that only 16 of 139 public cord blood banks operating worldwide were financially sustainable (WMDA, 2013). In 2016, France shut down half of its operating public CBBs just two years after launching its national development plan to sustain public banking (Magalon et al., 2015). Private banks, on the other hand, report no such issues.

One of the major reasons for why this is the case is because the economic models of each type of bank is distinct. Public banks bear the full cost of procuring, storing, maintaining, and releasing the CBU to a transplant center. Private banks charge for these costs up front. However, private banks do not generate any revenue when they release a CBU, while public banks need to generate enough revenue to recoup most of their upfront costs. In other words, public banks generate 70% to 89% of their revenue from 1% to 2% of their stored units which are released, whereas commercial banks generate 100% of their revenue from 100% of their stored units (Katz, 2015). Thus, commercial bank models are both stable and highly profitable, while public banks often depend on public funding or some sort of government support to stay open. For illustrative purposes, Figure 2 presents international prices of allogeneic CBUs.

COUNTRY	Rate per CBU
GERMANY	
Düsseldorf	21,000 EUR
ZKRD	-
BELGIUM	22,450 EUR
SPAIN	
Redmo	23,500 EUR
BCB Barcelona	23,000 EUR
FINLAND	22,491 EUR
ITALY	17,461 EUR
NETHERLANDS	22,450 EUR
SWIZERLAND	27,049 EUR
UNITED KINGDOM	
Nolan Trust	21,000 GBP
BBMR	19,623 GBP
AUSTRALIA	39,000 AUD
ISRAEL	
Hadassah	26,000 USD
Sheba	22,000 USD
TAIWAN	
Healthbanks Biotech	10,000 USD
Bionet Corp	4,500 USD

NB: an additional charge of 1,950 USD for shipment of CBU from NMDP banks

NMDP Banks (USA)	City	Rateper CBU (USD)
LifeCord	Gainesville	43,250
Belle Bonfils Memorial Blood Center	Denver	32,750
San Diego Blood Bank	San Diego	38,000
St Louis Cord Blood Bank	St Louis	37,160
ITxM Clinical Services Cord Blood Lab	Rosemont	34,850
Texas Cord Blood Bank	San Antonio	34,850
Children's Hospital of Orange County	Orange	32,750
New Jersey Cord Blood Bank	Camden	43,250
Michigan Cord Blood Bank	Grand Rapids	38,000
Puget Sound Blood Center & Program	Seattle	38,000
StemCyte International Cord Blood Center	Covina	37,615
J.P. McCarthy Cord Stem Cell Bank	Detroit	38,000
Carolinas Cord Blood Bank	Durham	40,100
COBLT Units – Carolinas Cord Blood Bank	Durham	21,335
Lifeforce Cryobanks	Altamonte Springs	37,475
New Jersey Cord Blood Bank	Allendale	43,250
M.D. Anderson Cord Blood Bank	Houston	36,425
Puget Sound Blood Center (ARC Units)	Seattle	38,000
ITxM Cord Blood Services (ARC Units)	Glenview	34,850
Carolinas Cord Blood Bank (ARC Units)	Durham	40,100
CORD:USE Cord Blood Bank	Orlando	40,100
Gift of Life Bone Marrow Foundation	Boca Raton	24,350
University of Colorado Cord Blood Bank	Aurora	41,150
SemCyte Taiwan National Cord Blood Center	Taipei – Taiwan	34,150
New York Blood Center	New-York	41,190
Cleveland Cord Blood Center	Warrensville Heights	41,845
Celgene Cellular Therapeutics / Lifebank USA	Cedar Knolls	47,450

Figure 2. Prices of allogeneic CBUs in 2013. *Source: Katz, G. Ch 24.*

It appears that the annual release rate of 1% to 2% of public CBB's total CBUs is an empirical threshold for public CBBs to meet their break-even targets. The literature has reported that some public CBBs with release rates below 2% have filed for bankruptcy, such as the US Memorial Medical Center in Worcester, USA (Kapinos et al., 2017) and the public CBB of the Saint-Louis Hospital in Paris, located on the same campus where the first successful cord blood transplant was performed in 1988. Both hospitals had to stop their activities in the early 2000s and were out of operation until they were refinanced by other public health entities or acquired by commercial banks (O' Connor et al., 2012).

Though public banks are not-for-profit, they participate in the competitive logic of the tissue economy by making their CBUs more appealing to transplant physicians, who select which CBU to use by comparing the quality of grafts that will result (Bart et al., 2013). To meet this demand, public banks have raised their selectivity standards of which CBUs to bank and which to discard. Since their revenue comes from successfully releasing CBUs – we'll call this the "utilization rate" of CBUs – banks are moving towards increasing their fiscal sustainability by increasing the number of CBUs released. That entails selecting CBUs on a range of quality criteria, such Human Leukocyte Antigens (HLAs), of which ethnic diversity profiles matter for better outcomes, and the number of total nucleated cells (TNCs). Increasing rare haplotypes and cell concentration increases banks' probability of releasing more CBUs and growing their revenue.

Public CBBs face a variety of cost factors. First, banks must collect donated cord blood and process them for use in transplants, an extremely costly endeavor. To illustrate the costs of procurement, in registered USA and Swiss public banks the average cost of each unit that was actually stored was $1,524. This includes the indirect expenses for units that were collected but not banked (Petrini, 2014). An estimated 67% (Bart et al., 2013) up to 80% (Katz, 2015) are discarded for a variety of reasons, such as failure of testing, below a bankable size, insufficient volume, insufficient cell count, biological anomalies, bacterial contamination, and technical incidents (ie, consent withdrawal). Thus, the average percent of banked CBUs from donated umbilical cord blood hovers around 30% - 33% (average selectivity) (Katz and Mills, 2010; Katz, 2011). Then, banks must store the UCB for any number of years before it is released. Bart et al estimates that the direct cost of volunteer recruitment is $206; direct cost to recruit and process cord blood is $1,092; annual storage cost of a CBU is $27; and the net profit per released

CBU is $29,237 (Bart, 2012). The annual operating costs of the US Memorial Medical Center in Worcester, USA mentioned above were around $750,000.

The literature has even proposed a composite scoring system that could score the quality of CBUs based on these parameters and others that impact the price and costs of banks. Such a scoring system could help authorities determine which banks to keep open based on their cost-effectiveness (Katz and Mills, 2010).

Some papers measured the cost-effectiveness of CBUs themselves against other stem cell units. Bart estimated that over the 12-year period from 1997 to 2009 in a healthcare-system setting such as the US, cord blood stem cells cost $318,890 to $1.19 million per CBU. Other adult stem cells (bone marrow and peripheral stem cells) cost $47,638 to $65,681 per stem cell unit. The staggering cost differential may be due to the small number of CBUs used relative to the number of CBUs stored (Bart, 2012). Other studies have argued that stem cells would be more cost-effective relative to bone marrow registries and traditional stem cell sources if banks were able to scale up by a significant factor, although it has a relatively low cost-effectiveness ratio (Feve and Florens, 2009; Tennvall and Fasth, 2017).

It appears that the tissue economy is pushing public CBBs to maximize the quality of their CBU products while minimizing the operating costs of the bank. However, private banks remain immune as ever to these pressures – a paper found that over the 2009 – 2012 period (during the global economic crisis), the average gross profit margin of private banks was nearly 70%, with only 1.1% of that revenue invested in research and development. The inventory of the four leading private autologous CBBs was 1.58 times larger than the combined inventories of all 137 public banks worldwide, yet the released number of CBUs – their therapeutic benefit – was 269 times lower (Katz, 2015).

One study modeled the strategy of public CBBs discussed above to see whether they could help banks remain financially sustainable in the long run. The authors considered various quality standards of CBUs – ethnic haplotype diversity, TNC and CD34+ (a marker found on the surface of stem cells) cell counts – as input, and CBU utilization rate and bank economic profit as output. They concluded that in the best-case scenario, public CBBs would indeed be able to finance itself over the long-term. However, the best-case scenario would still incur a deficit, albeit a limited one ($0.98 million) that could be overcome with fundraising or public grants (Katz and Mills, 2010). Raising quality standards by increasing the pre-freezing TNC level to 18 x 10^8 would be the most cost-effective strategy for maximizing both therapeutic value and economic profit.

Besides simply maximizing output and minimizing operating costs, what else can public banks do to ensure financial sustainability? One paper examining the French CBB system suggests that increasing bank sizes through a regionally centralized, nationally structured network of banks would provide economies of scale (Sirchia et al., 2002). However, studies commissioned by government authorities have not discussed increasing banked CBUs to economies of scale in their policy approaches.

Many papers stated their belief that no country can realistically reach self-sufficiency alone, and pointed to the import-export of cord blood as empirical evidence (Katz et al., 2011). Spain, France, and the US are all major importers of cord blood. The 247 CBU imported by France during 2008 made up 64% of all its utilized CBUs that year, and cost the national healthcare system €4.94 million. As importation is a significant indicator of a short-term response to unmet medical needs (Katz and Mills, 2010), the thriving import-export tissue economy might suggest that building up the cord blood marketplace is indeed the right direction to go. Until public CBBs become financially self-sufficient, the literature calls for cooperation among an international coalition of public CBBs, such as the Netcord model (Querol, 2012), to promote quality control guidelines for safe collection, storage, and export.

III. The Chinese Market

China provides an extraordinary market study for cord blood and tissue banking. First, the benefits of cord blood have prompted the development of “cord blood banks” to store umbilical cord blood for future medical use. China has built these cord blood banks on an unprecedented scale, with facilities in Beijing and Guangdong storing half a million to 1.5 million units of umbilical cord blood, respectively (Chang, 2017). Second, the Chinese government only supports one cord blood banking license in each province (Hildreth, 2018). China’s blood banking system is composed of seven primary banks that have obtained government operating licenses from the Chinese Ministry of Health. Though these banks can only accept regional donations, they can sell cord blood across all provinces to increase their consumer network. Third, the banks function as a hybrid public-private model: the private, for-profit sector of the bank is expected to make a profit to fund the public, donation-based sector of the bank (Chen, 2011). Under this model, “banks [are] used to pay for banks,” a policy that has resulted in public banks setting up private cord-blood banks on the same physical premise as their public banks, using profits from the private banks to support the public one (Zhao and Li, 2008). Similar to attitudes worldwide, donations to public allogenic banks are considered “gift relations” (Titmuss, 1970) and contributions to public good in China (Waldby, 2006).

The 2008 Shanghai Cord Blood Bank scandal illuminated the ongoing local and global debate over hybrid banks. After more than 200 CBUs tested positive for anaerobic bacteria, these CBUs were accepted for storage at the hybrid Shanghai Cord Blood Bank. The ensuing investigation found that the bank’s controlling shareholder was a private shareholder, with only 30% of the holdings held by a public shareholder. The investigation further revealed that there was competition between the private and public sectors of the bank. The bank encouraged families to store CBUs for autologous use (a vital source of revenue) while limiting its development of public sector use, which would generate expenses but not profits (Guo, 2008).

The hybrid bank largely persists because the government pushed for public cord blood banks as a means of working towards common public good while relying on private enterprises to help address the financial shortfalls of public banks. In a case study of Tianjin Cord Blood Bank, one of the seven blood banks awarded a government license, employees and experts at the bank pointed out that it is difficult to run public cord-blood banks on their own without full government support. According to a team member at Tianjin:

> In China there was a problem with the rate of use. Over the last two years, about one hundred units have been used for transplants every year. One reason [for the low use] is the financial situation of Chinese patients. Now, Japan has done well with cord-blood banking, but most of its banks are private. It has been difficult to get money from the Chinese central government, and the revenues of public cord-blood banks have not been covering their basic expenditures. The Guangzhou Cord Blood Bank is the only one that has had full government support, but it is facing a dilemma: in the future, it will merge with the Beijing Cord Blood Bank. (Interview, as told to Haidan Chen, Tianjin, 5 December 2008)

It is, of course, possible that Chinese authorities will choose to build their centralized NCBB as a hybrid bank. However, both the literature review and historical experience would suggest that authorities move towards another model of CBB, and in particular, a financially sustainable model of a public CBB.

Establishing a centralized national cord blood bank in China is thought to be more feasible than in the United States. Because of China's large population size and relatively homogenous ethnic makeup, there exists a higher possibility of matching at the clinically acceptable threshold of 4, 5, or 6 leukocyte antigen sites out of 6 possible sites relative to a diverse heterogeneous population like that of the United States.[4] A cord blood donor base of only 100,000 - 500,000 units would serve a majority of the Chinese population.

Typing donors, processing, and storing cord blood units have already eaten up most of the NHHC budget allocated for HSCT. Despite NHHC fronting costs, HSCT is unrealistic for most Chinese citizens because prohibitive costs remain: patients must pay for treatment and hospitalization themselves. HSCT therapy from cord blood tissue ranges from 235,00 RMB up to 1,036,000 RMB if post-transplant complications arise (Tan, 2015). Considering that the average Chinese household income is 13,000 RMB to 36,000 RMB (Statista, 2017), the cost of cord blood transplants remains unaffordable for all except the wealthiest Chinese. A report from the Chinese Red Cross showed that almost two-thirds of children who require HSCT for leukemia, the leading cause of death among Chinese children, did not finish the treatment for financial reasons (The New York Times, 2011). Leukemia, thalassemia, and HIV, the most prevalent diseases indicated for HSCT in China, add up to a disease burden of about 14,000,000 cases annually, even as the 2010 recorded cord blood transplant rate was less than 1% in thalassemia cases alone (Fang, 2010). In countries such as China where health insurance does not cover HSCT fees, it is common to forgo treatment because of cost.

China faces three unique pressures that add to its urgency for bringing down the costs of CBUs and HSCTs. For one, catastrophic illnesses continue to be a major driving cause of

[4]Personal communication with Dr. Robert Chow, Chief Scientist to the NHHC for China's first National Cord Blood Bank.

poverty. For another, hospitalization costs for illnesses indicated for HSCT continues to rise. Finally, China's history with its one-child policy has effectively eliminated sibling donors.

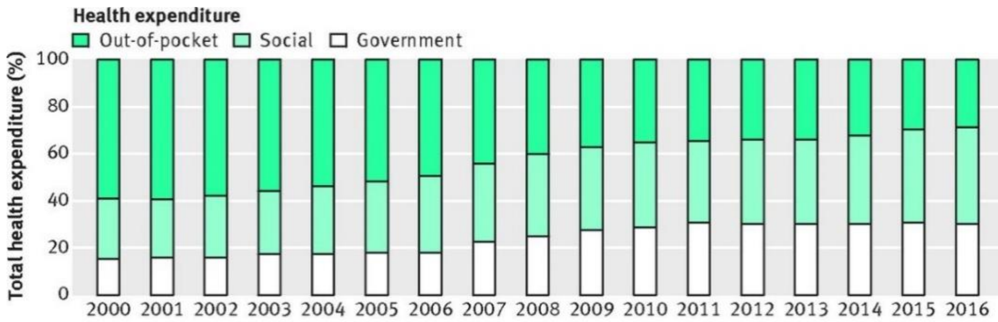

Figure 3. Total health expenditures by source of spending, 2000 – 2016.
Source: Tan et al., 2015.

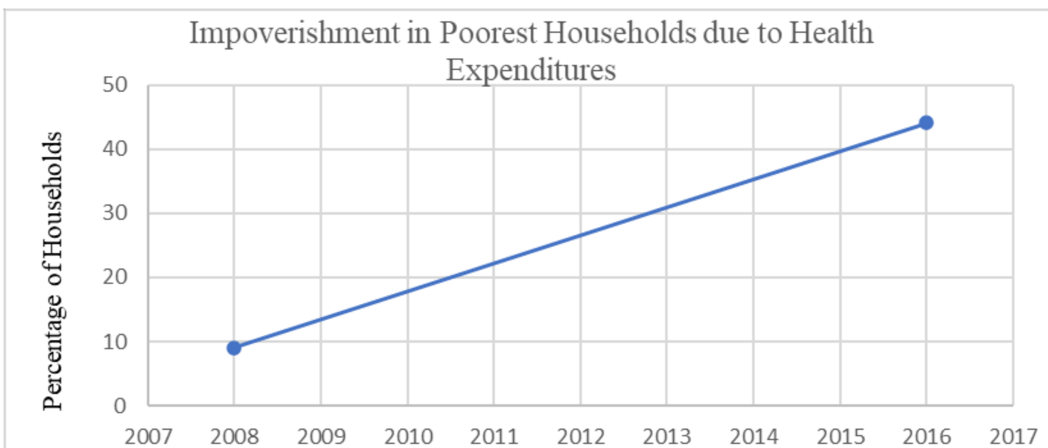

Figure 4. Impoverishment in poorest households due to health expenditures, 2007 – 2017.
Source: Tan et al., 2015.

The percentage of out-of-pocket payments in total health expenditures declined from 60% to less than 30% from 2001 to 2016, with researchers attributing this trend to China's implementation of universal health coverage (Figure 3). Despite this, the percentage of underprivileged households who became impoverished because of costs related to catastrophic illness burden jumped from 9% in 2008 to 44.1% in 2015 (Figure 4). Hospitalization costs for illnesses like leukemia, widely treated by cord blood HSCT, continue to rise (Figure 5). And despite the government officially discontinuing China's one-child policy in 2015, three decades under the policy has effectively eliminated sibling donors in China. Since cord blood can deliver successful transplant outcomes even if patients are not able to find exact antigen leukocyte match rates, the lack of sibling donors means that more units need to be banked to meet patient needs. Building a NCBB is one way to ensure a consistent supply of clinically ready CBUs.

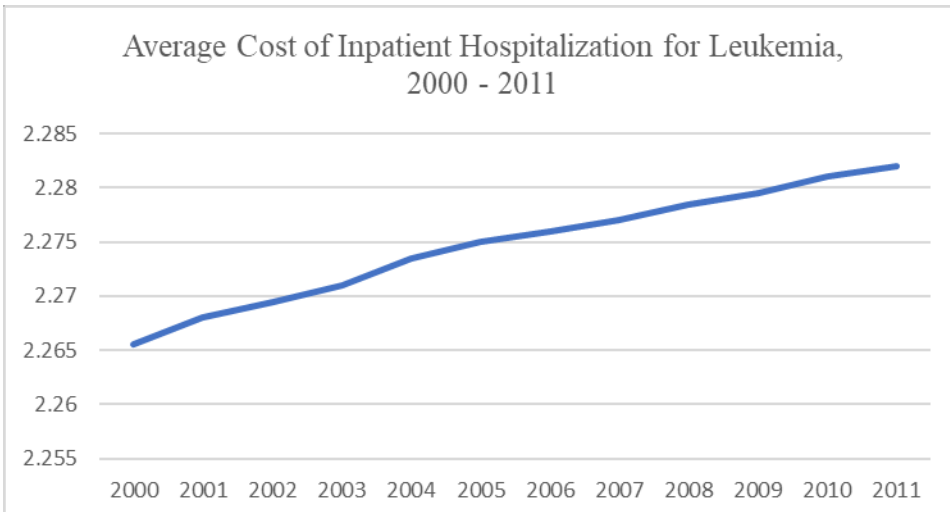

Figure 5. Average cost of inpatient hospitalization for leukemia, 2000 – 2011. In billions of RMB. Trendline was obtained by averaging the low bound and high bound inpatient hospitalization costs for males with acute leukemia, using the 6.5:1 conversion rate for CNY:USD. I assumed that all patients who eventually died received inpatient hospitalization. *Source: American Cancer Society Report, 2020.*

IV. Cost Benefit Analysis

I conducted a cost-benefit analysis (CBA) to determine what will need to be charged per CBU released for China's first National Cord Blood Bank to break even. This "break-even cord blood unit fee" is represented as *f*. In my analysis, I included the post-transplantation costs of HSCT, such as the costs of hospitalization, because the Chinese government is interested in whether the NCBB can subsidize the cost of HSCT therapy.[5] I assumed that each patient needs only one CBU for a successful HSCT transplant, though double CBU transplants are not uncommon for larger individuals (Katz, 2015). CBA calculations are based on the U.S. Institute of Medicine's Committee on Establishing a National Cord Blood Stem Cell Bank Program Cost-Benefit Analysis, commissioned by the National Academies of Sciences (Howard et al., 2005).

My access to data was limited, as I was unable to conduct the fieldwork I had planned beyond my conversations with Dr. Chow. As a result, I used numbers in the literature to help me conduct my CBA. China's average number of HSCT transplants has hovered around 40 to 50 annually.Therefore, I assumed T, the target transplant number, is 50 at status quo. Based on discussions with Dr. Robert Chow, the NCBB's Chief Scientist, a reasonable policy goal for China is to double the number of transplants annually to T = 100. For speculative reasons, I also calculated the break-even fee if T = 3,110, the number of cord blood HSCTs performed worldwide annually, and T = 14 million, the number of transplants indicated based on annual end-of-life fatality numbers for thalassemia, leukemia, and HIV combined (the three most prevalent diseases in China indicated for cord blood HSCT). N is our inventory size of clinically ready cord blood units. Table 1 displays these variables and their estimates to the nearest thousand RMB.

[5] In personal communications with Dr. Robert Chow.

	Break Even Fee f *(in nearest thousand RMB)*			
Target Transplant Number "T"	N=100,000; Case 1	N=100,000; Case 2	N=500,000; Case 1	N=500,000; Case 2
50 transplants	120	164	198	244
100 transplants	220	310	298	388
3110 transplants	6,250	9,048	6,328	9,128
14,044,800 transplants	28,133,200	40,773,600	28,133,400	40,773,600

Table 1. Break Even Fee *f*. Case 1 is without post-transplant complications, Case 2 is with complications. See Appendix A for CBA calculations and additional tables.

The CBA calculations show that much of the costs of HSCT are driven by post-transplant complications. For 100,000 banked CBUs (N) with 100 transplants annually (T) without complications (Case 1), the break-even fee is approximately 220,000 RMB. Should complications arise, that cost shoots up to 310,000 RMB per HSCT, almost 100,000 RMB more. Having a larger inventory size appears to do little to offset the costs if complications arise. For the same scenario with complications (T = 100, Case 2) but five times the number of banked CBUs (N = 500,000), the government should expect to pay an additional 90,000 RMB per HSCT. This suggests that simply banking more units is not enough – it is important to have as many quality and antigen leukocyte matching CBUs as possible available to patients.

As more transplants are performed annually, *f* per HSCT appears to rise proportionally. This makes sense, because my CBA, based on Howard et al.'s CBA, mostly accounts for cost savings in the reduction of administrative costs and typing, banking, and processing CBUs over time. As China uniquely banks a large number of cord blood units already, its NCBB will not benefit from these cost-saving mechanisms, making the *f* per HSCT appear to rise more linearly. However, because the number of cord blood units is less of an issue for China, it may be possible that economies of scale for HSCT therapy would occur at some threshold and start to bring down the costs of transplant, if not the costs of post-transplant hospitalization.

	RMB (in nearest thousands)			
T	N=100,000; Prob = 0.56	N=100,000; Prob = 0.2	N=500,000; Prob = 0.56	N=500,000; Prob = 0.20
50 transplants	2,143	8,200	3,536	12,200
100 transplants	3,929	15,500	5,321	19,400
3110 transplants	111,607	452,400	113,000	456,400
14,044,800 transplants	$502*10^9$	$2,039*10^9$	$502*10^9$	$2,038*10^9$

Table 2. ICER. Based on survival probability to 5 years. The probability of survival to 5 years ranges from 0.56 (best case) to 0.2 (worst case).

The incremental cost effectiveness ratio (ICER) in Table 2 shows that the government currently pays about 2.1 to 3.5 million RMB (or $304,000 to $506,000 USD) per additional life year gained in the best case scenario (probability of survival is 0.56). Should the government and NHHC double the number of transplants T performed annually, they would pay 3.9 to 5.3 million RMB ($564,000 to $767,000) per additional life year gained. International assessments for ICER's cost-effectiveness threshold range recommends staying between $100,000 up to $175,000 (Institute for Clinical and Economic Review, 2019). Though the numbers presented in Table 2 are large, international threshold guidelines suggest that though cord blood HSCT treatment remains above the ICER cost-effectiveness threshold, treatment is not a grossly expensive decision by international standards (consider America’s widespread use of ventricular assist devices as a bridge to heart transplants for adults and children, which range $138,000 to $398,000) (Sutcliffe et al., 2013).

Life Years Gained				
T	**Best Case (probability = 0.56)**		**Worst Case (probability = 0.20)**	
50	140		50	
100	280		100	
3110	8,708		3,110	
14,044,800	39,325,440		14,044,800	
Income Gained (in millions of RMB)				
T	**Urban, Best Case**	**Rural, Best Case**	**Urban, Worst Case**	**Rural, Worst Case**
50	25.2	91.0	9.0	3.3
100	50.4	18.2	18.0	6.5
3,110	1,567.4	566.0	559.8	202.2
14,044,800	$7.0*10^{10}$	$2.5*10^{10}$	$2.5*10^{10}$	$9.1*10^{10}$
Non-Monetary Benefits				
Greater trust among citizens regarding government capability to care for its population				
Counteracting demographic and population decimation				
Soft power respect from international medical community				
Reproducible global model for HSCT cost reduction				

Table 3. Projected Benefits.

Table 3 presents the projected benefits in both the best case scenarios (survival probability = 0.56) and worst case scenarios (survival probability = 0.20). Purely in terms of monetary income, the numbers show that it is worth doubling the annual transplant rate (T=100) in the best-case scenario. The break-even cord blood fee ranges from 220,000 to 298,000 RMB in the best case scenario for doubling the number of current transplants. In context of life-years gained, urban individuals will make 50.4 million RMB or about 504,000 RMB per person, while rural individuals make 182,000 RMB in the best case scenario. Benefits largely come from urban earnings.

In the worst-case scenario, HSCT costs 310,000 to 388,000 RMB per individual while income returns are expected to be 180,000 RMB for urban residents and 65,000 RMB for rural residents for T = 100. Though costs exceed income benefits in the worst case survival probability, it is important to consider the non-monetary benefits of expanding HSCT treatment. In particular, considering that China's population is predicted to decline precipitously by the year 2027 as another unintended effect of the one-child policy, and the workforce is predicted to drop 35% (The New York Times, 2019), it may be important for the longevity of China's workforce and national productivity to invest in cord blood HSCT if productive lives become more valued over time.

V. Policy Recommendations

Recommendation 1. The NHHC should work with the Chinese government to compile a task force to determine whether economies of scale and size exist in the cord blood HSCT market.

To the best of my knowledge, a review of the literature does not yield any discussion of whether cord blood-derived HSCT experiences cost reductions due to economies of scale. Therefore, I looked into the parallel blood market. The literature was sparse, with few researchers asking this question. Most papers seemed to assume that economies of scale would exist. I did find one paper that discussed economies of scale explicitly: Pereira conducted data envelopment analysis of 71 blood centers in the U.S. and found that expanding the level of operations beyond a certain threshold actually led to decreasing returns to scale (DRS). Blood centers did exhibit increasing returns to scale below 75,000 blood units before they made the transition to constant returns to scale and then to DRS (Pereira, 2006). Interestingly, Pereira pointed to blood centers' technical inefficiency (such as processing and storing blood units) as a contributor to DRS. If blood donation centers parallel cord blood institutions, it is possible that expanding the number of banked units (N) beyond a certain threshold will also lead to the Chinese NCBB to DRS.

Because the cost of HSCT is largely driven by treatment and hospitalization costs, I also looked into whether economies of scale existed in medical treatment literature. The literature was similarly sparse. However, I found an interesting article by Gaynor et al. that examined the volume-to-outcomes relationship in coronary arterial bypass graft (CABG) procedures. They found that increases in scale economies reduced mortality in patients by 25% (Gaynor et al., 2007).

Taken together, these papers suggest that economies of scale might play a cost-saving role only in the sense that more HSCTs performed means better outcomes in life-years gained and reduction in mortality, while economies of size can only happen if long-run average cost curves are decreasing (the cost per unit of output decreases when production increases) (Rassmussen, 2012).

Based on the absence of economies of scale or size, I cannot recommend the Chinese government to increase its annual cord blood transplant rate beyond a target transplant rate of T = 100. However, I do think the literature remains incomplete. Thus, I urge the Chinese government, the NHHC, and the NCBB to compile a task force that collects data from its existing transplant centers to determine whether economies of size and scale exist.

Recommendation 2. Catastrophic disease insurance should offer a "transplant bundle" that includes HSCT along with kidney, liver, and heart transplants.

China has already achieved universal healthcare coverage for over 95% of its population, and is on target to cover 100% of its population by 2020. Despite its impressive coverage efforts, China has struggled with providing high-quality and consistent coverage to its citizens. In particular, urban and rural residents receive vastly different service quality when it comes to care. The NRCMS caters to rural residents while URBMI covers urban residents. NRCMS, introduced about 10 years later than URBMI, provides coverage at the county level and hence has a much larger risk pool and less government and quality oversight when it comes to care. Much of the universal healthcare coverage offered goes towards coverage of chronic diseases: one in four Chinese has high blood pressure, China accounts for a third of the world's smokers, and diabetes affects over one-tenth of the Chinese population. Even for universal basic insurance, out-of-pocket expenditures continue to rise, and coupled with income inequality, advanced medical treatment and drugs are still out of reach for many citizens.

In light of the shortcomings of universal basic insurance, the Chinese government has introduced catastrophic disease insurance (CDI) to protect against catastrophic illnesses for its most vulnerable populations. It is possible that CDI might look different for urban and rural residents, especially if rural insurance continues to have gaps in healthcare coverage that makes rural post-transplant hospitalization costlier. CDI has traditionally been used to cover terminal illnesses such as cancer. The government should consider adding a "transplant bundle" to its CDI coverage. This transplant bundle should include HSCT and other transplant procedures, including liver, kidney, and heart transplants, to make the bundle more attractive to a larger group of individuals. Though offering a transplant bundle is unlikely to save money in the sense that bundling transplant costs will mean that the NHHC will have to balance a line item that includes more than just HSCT costs, offering coverage for a bundle of transplant costs as opposed to HSCT makes opt-in to insurance more likely and spreads the risk pool beyond potential HSCT patients to those who think they might need transplant services.

Recommendation 3. The Chinese government needs to address the cultural barriers to buying into catastrophic disease insurance in order to pool insurance risk.

Chinese citizens appear to be frugal with their spending, especially in rural areas. A study on spending habits found that most elderly Chinese spent money on living necessities, housing, and saved the rest for their children and grandchildren. Very little is spent on personal costs like vacations or travel. Therefore, despite rising income inequality, many Chinese citizens continue to pay for care by personal savings and receiving money gifts from family and friends. The culture of personal frugality and generosity in money gifts contribute to Chinese suspicion of insurance risk pooling – few individuals want to participate in an insurance scheme where payout is not guaranteed.

Considering expansion of CDI is incomplete without considering these demand-side incentives for insurance risk pooling. One way the NHHC can address this is to partner with local media on education campaigns about the benefits of purchasing add-on insurance like CDI. The WHO ran a similar education program to target smokers in China by pairing with young celebrities on an anti-smoking campaign, with the educational program reaching over 10 million users on WeChat (China's most popular social media platform).

Managing cultural expectations is critical and can make a big difference in how patients experience care. For example, because Chinese patients expect providers to oversee every aspect of care, reflected in the way existing insurance schemes reimburse extensive episodes of hospitalization and reimburse care that could be administered at home, such as palliative care, patients stay in hospitals much longer than their international counterparts. For example, the average length of stay at Peking University First Hospital in Beijing averaged2 weeks for cardiac disease. By contrast, the average post-hospitalization stay for US seniors fell to 4 days by 2014, with comparable health outcomes. The NHHC should take seriously the importance of realigning cultural barriers to purchasing catastrophic insurance.

VI. Conclusion

Interest in HSCT is global. Canada, Taiwan, the UK, and the US have all built national cord blood inventories or banks in the hopes of making HSCT more affordable to patients. However, without further government support, the availability of public and national cord blood units has done little to increase HSCT around the world, and costs have remained sky-high. The Chinese government can learn from the shortcomings of existing inventories and address the real drivers of cost so that in the coming decade, China can model to other countries how to make subsidized HSCT fiscally sustainable. Solving fiscal barriers of HSCT will make China a leader in cancer therapy in the upcoming decade.

VII. APPENDIX A. Methodology: A Cost-Benefit Analysis of China's National Cord Blood Bank

CBA calculations are based on the U.S. Institute of Medicine's Committee on Establishing a National Cord Blood Stem Cell Bank Program Cost-Benefit Analysis, commissioned by the National Academies of Sciences (Howard et al., 2005).

Units Needing to Be Collected

$$U = [(1/y) * N + T] / 1 – \text{lambda}$$

Where U is the number of units needing to be collected; y is the expiration date of the unit (for my purposes, I conservatively estimate y = 20 years, though most private banks tend to discard in the range of 20 - 30 years), N is the stable inventory size amount, T is the number of units transplanted, and lambda is the number of units discarded during the collection process due to subquality of the cord blood, which we conservatively estimate at ⅓.

Annual Cost

$$C = U*[(1 - \text{lambda})*c^{PS} + \text{lambda}*c^{PD}] + N*c^{S} + A$$

Where C is the annual cost; c^{PS} is the cost of processing a stored unit, c^{PD} is the cost of processing a unit that will be discarded prior to storage for quality reasons; c^{S} is the annual cost of storing a unit, and A is the annual cost of administration.

One-time Cost of Bringing Inventory N_0 up to Target Inventory N

0

Though Howard et al. calculated the one-time cost of bringing up the United State's existing inventory of banked units N_0 to a target inventory size N, I assume that China faces a cost of 0 RMB to bring its inventory up to size. This is because cord blood banking has uniquely taken off in China – Beijing's regional bank alone boasts 1 million - 1.5 million banked cord blood units. With seven regional banks in China, I assume a conservative estimate of 7 million banked cord blood units, far above the number of our target inventory size of 100,000 - 500,000 quality cord blood units. Like Howard et al, I also assume that collection occurs instantly, and that administrative costs are negligible here.

Total Cost

$$TC(N) = C + r*C_0 + T*c^T$$

This leads me to calculate the total cost of inventory size N, where C is the annual cost, r is the discount rate 0.03, C_0 is our one-time cost of bringing up inventory to size; T is the number of units transplanted; and c^T is the direct cost of treatment. There are two possible ways to measure the direct cost of treatment:

1. By equation:

$$c^T = p + (m*c^{RX} + (1 - m)* c^{1-RX}) + c^H)$$

   a. Where p is the cord blood procurement cost; m is the probability of matching at 6 out of 6 possible leukocyte antigen sites and (1-m) is the probability of matching at 4 or 5 out of 6 possible sites; c^{RX} is the treatment cost of a 6 out of 6 match and c^{1-RX} is the treatment cost of a 4 or 5 out of 6 match; and c^H is the post-transplant hospitalization cost.
   b. Where c^H has two cases:
      i. Case I: no complications post-transplant

ii. Case II: complications post-transplant (for the sake of simplification, we assume all complication costs come from graft-versus-host disease (GVHD), the most common HSCT complication)

2. By literature:
    a. costs range from 235,00 RMB (no post-transplant complications) up to 1,036,000 RMB (complications from GVHD)

Break Even Fee

$$[(f^*T) / r] + E - C_0 - C / r = 0$$

To calculate the break even fee per cord blood unit, I subtract the net present value of revenue from the net present value of costs. I am solving for *f*, where *f* is the break even fee; T is the number of units transplanted, E is the initial endowment from NHHC and the Chinese government, which I assume to be 0 because of sunk costs, as the national CBB is already being built; C_0 is the one-time startup cost of bringing inventory up to size, and C/r is the discounted net present value of costs.

Incremental Cost Effectiveness Ratio (ICER)

$$ICER = TC(N) / LY(N)$$

I calculate our ICER using TC(N), the total cost of having inventory size N, divided by LY(N), the number of life-years gained from having inventory size N.

Table I: Cost Model Parameters

Notation	Description	Value	Unit	Reference
N_0	initial inventory	7,000,000	cord units	Hildreth, 2018.
lambda	discard rate	0.33	proportion	Robert Chow, MD.
y	length of storage before discard	20	years	Howard et al., 2005.
c^{PS}	cost of initial processing, stored unit	6,900	RMB	Robert Chow, MD.
c^{PD}	cost of initial processing, discarded unit	17,500	RMB	Global Cord Blood Corporation, 2018.
c^{S}	cost of storage, annual	69	RMB	Chen et al., 2010.
c^{T}	cost of transplantation	235,000 to 1,036,000	RMB	Tan et al., 2015.
E	endowment	0	RMB	Assumption
A	annual administrative cost	243,500	RMB	Global Cord Blood Corporation, 2018.
p	procurement cost, cord blood unit	14,968	RMB	Global Cord Blood Corporation, 2018.

c^{RX}	treatment cost, 6/6 matching	247,144	RMB	Tan et al., 2015.
$c^{1\text{-}RX}$	treatment cost, 4 or 5/6 matching	364,120	RMB	Tan et al., 2015.
c^{H}	post-transplant hospitalization cost, no complications	307,374	RMB	Tan et al., 2015.
c^{H}	post-transplant hospitalization cost, complications	441,138	RMB	Tan et al., 2015.
m	matching at 6 out of 6 antigen sites	0.1	proportion	Howard et al., 2005.
r	discount rate	0.03	proportion	Howard et al., 2005.

Table I. Units Needing to Be Collected

Target Annual Transplant Number "T"	Stable inventory size; N = 100,000 quality units	Stable inventory size; N = 500,000 quality units	T estimated from:
50 transplants	7,575 units	37,575 units	CIMBTR-associated hospitals in China
100 transplants	7,659 units	37,650 units	Client (Dr. Robert Chow and NHHC)
3,110 transplants	2,165 units	42,165 units	Worldwide demand for CB-derived HSCT
14,044,800 transplants	21.074 million units	21.105 million units	Lower-bound incidence of AML (Acute Myeloid Leukemia), thalassemia, and HIV in China

Table III. Annual Cost. In nearest millions of RMB.

T	N = 100,000 (lower-bound)	N = 100,000 (upper-bound)	N=500,000 (lower-bound)	N=500,000 (upper-bound)
50 transplants	33.1	33.3	164.2	164.4
100 transplants	33.4	33.6	164.5	164.6
3110 transplants	49.0	49.1	180.1	180.2
14,044,800 transplants	72,714.7	72,714.9	72,845.8	72,846.0

Table IVb. Total cost, using literature. In nearest millions RMB.

T	N=100,000; 235,000 RMB	N=100,000; 1,036,000 RMB	N=500,000, all 235,000 RMB	N=500,000, 1,036,000 RMB
50 transplants	6.0	8.2	9.9	12.2
100 transplants	11.0	15.5	14.9	19.4
3110 transplants	312.5	452.4	316.4	456.4
14,044,800 transplants	1,406,660	2,038,680	1,406,670	2,038,680

Table V. Break Even Fee. (Based on literature assumptions of direct cost)

T	N=100,000; Case 1	N=100,000; Case 2	N=500,000; Case 1	N=500,000; Case 2
50 transplants	120,000	164,000	198,000	244,000
100 transplants	220,000	310,000	298,000	388,000

3110 transplants	6,250,000	9,048,000	6,328,000	9,128,000
14,044,800 transplants	28,133,200,000	40,773,600,000	28,133,400,000	40,773,600,000

Table VI. ICER. Based on survival probability to 5 years, in nearest RMB.

T	N=100,000; Prob = 0.56	N=100,000; Prob = 0.2	N=500,000; Prob = 0.56	N=500,000; Prob = 0.20
50 transplants	2,142,857.143	8,200,000	3,535,714.286	12,200,000
100 transplants	3,928,571.429	15,500,000	5,321,428.571	19,400,000
3110 transplants	111,607,142.9	452,400,000	113,000,000	456,400,000
14,044,800 transplants	502,378,571,429	2,038,680,000,000	502,382,142,857	2,038,680,000,000

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