A cost analysis of public cord blood banks belonging to the Italian Cord Blood Network

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Background. Public cord blood banking is currently managed in Italy by a network of 19 regional cord blood banks coordinated by the National Blood Centre and the National Transplant Centre. A cost analysis was carried out within the Italian network to determine the relationship between cost of cord blood collection and banking and size of the bank inventory, which ranged from 106 to 9,341 units on December 31st, 2012.

Materials and methods. The 19 banks were invited to report costs incurred in 2012 related to cord blood unit collection, transportation, biological validation, characterisation, manipulation, cryopreservation, storage, data management, and general costs. Missing information on selected items was replaced with standardised costs represented by average data obtained from the reporting banks. Eight banks (52%) participated in the study. Average costs were determined in the three banks with inventories of >3,000 units *vs* the three banks with inventories of <1,000 units.

Results. Both cord blood collection and cord blood banking costs per unit were lower in the larger banks than in the smaller banks (average collection costs: € 119.25 and € 151.31, respectively; average banking costs: € 3,614.15 and € 8,158.37, respectively).

Discussion. The study outlined an inverse relationship between the costs of cord blood collection and banking and the size of the bank inventory, suggesting that scale economies could be obtained through centralisation of banking activities.

Keywords: cord blood, banking, stem cell transplantation, costs, cost analysis.

Introduction

Since the first allogeneic cord blood (CB) transplantation performed in France in 1988[1], the use of CB units as a source of haematopoietic stem cells in paediatric and adult patients has risen steadily. The advantages of this technique include the ready availability of cryopreserved units and the possibility to perform transplantation even when there is a mismatch (i.e. a low degree of compatibility between donor and recipient), thanks to the fact that these cells are relatively immature. The possibility of storing CB units as a source of haematopoietic stem cells and the early successes of haematopoietic stem cell transplantation triggered the setting up of cord blood banks (CBB). The first public CBB were established in New York (1991), Düsseldorf (1992), Milan (1993) and London (1996).

In Italy, CBB are an integral part of and run by the National Health Service, which is responsible for all the banking activities, from donor selection to the release of CB units for clinical use. Despite the aforementioned advantages of CB transplantation, it is common knowledge that only a small proportion of cryopreserved CB stored in CBB is used for its intended purpose. According to World Marrow Donor Association (WMDA) figures (Annual Report 2015), the global rate of CB units shipped for transplantation decreased from 1.24% in 2007 to 0.45% in 2015. In 2015, CB transplantation represented about 17% of all haematopoietic stem cell unrelated transplants. Despite the relevant decrease of transplants with CB, there is currently no justification for discontinuing CB banking activities mainly for two reasons: (i) CB units are still a source of haematopoietic stem cells for many patients belonging to ethnic minorities who are unable to find a compatible adult donor enrolled in international registers[2,3]; and (ii) there is still no scientific evidence to support that the long-term outcome of transplantation from a haploidentical donor is better than that of a CB transplantation[4,5].

Nonetheless, the limited number of units actually used for transplantation is forcing a rethink regarding both the costs of maintaining and running CBB and the sustainability of this activity in a public healthcare context.

Since 2009, in Italy all CBB have been part of the Italian Cord Blood Network (ITCBN) under the coordination of the National Blood Centre (CNS, *Centro Nazionale Sangue*), and the National Transplant Centre (CNT, *Centro Nazionale Trapianti*) in their respective fields of expertise. Donor selection, CB procurement, manipulation, cryopreservation, storage and distribution activities are carried out by 19 CBB (Online Supplementary Table SI) that avail themselves of 320 collection centres. At the end of December 2015, 39,662 CB units for unrelated allogeneic transplantation were available in Italy (National Blood Centre figures, April 2016). The target of a national inventory of about 60,000 units was agreed upon by the competent regional authorities, the National Blood Centre, the National Transplant Centre, the Italian Bone Marrow Donor Registry and the ITCBN in 2009, the year in which the Italian network was established.

In this study, we present the results of a cost analysis of all the activities regarding the collection and banking of CB units performed by eight out of 19 CBB belonging to the ITCBN.

Materials and methods

A cost analysis of CB units collected in 2012 in Italy was performed to define the average standard production cost. In 2012, an investigation was conducted on the costs of each activity involved in the collection and banking processes performed in CBB (Online Supplementary Table SI) belonging to the ITCBN, in collaboration with the Management Control Offices of the Health Care Facilities in question.

Data matrix models

The process in question was analysed and the activities identified: the related health aspects as well as those of an economic-management nature were analysed. Banks with CB inventories >3,000 units, between 1,000 and 3,000 units, and <1,000 units were considered large, medium and small, respectively.

The banks participating in the study were asked to provide quantitative information on 19 cost items (in Euro) linked to banking activities pursuant to the legislation in force.

It was decided to analyse the costs for each phase of the production separately in terms of staff, technological fixed assets, disposables and other related costs. The costs regarding CB biological characterisation and qualification testing were added if not performed by the CBB itself.

General costs, including certification/accreditation programmes, donor awareness-raising campaigns and other items such as utilities, were also taken into account.

Subsequently the data collection forms were processed. Due to the complexity and the large data set involved, data were collected using an application specifically created for the ITCBN (https://cns.sanita.it/ITCBN) on the National Blood Information System (*Sistema Informativo dei Servizi TRAsfusionali*, SISTRA).

Data collection

Each bank was provided with an account to insert their data into the dedicated app. The costs of CBB activities were determined for the five phases of the process as follows:

- *Phase 1.* Transportation from the collection centre: data regarding the type and cost of transportation of CB units from the collection centre (delivery room) to the CBB were collected.
- *Phase 2.* Biological validation and characterisation of the units: the data collected regarded the type, number and cost of tests performed on CB units and maternal blood when the units were banked. Data on laboratory equipment and materials used were also collected.
- *Phase 3.* Manipulation and freezing: data regarding the type, number and cost of the laboratory equipment and materials used for the manipulation and freezing of suitable CB units were collected.
- *Phase 4.* Cryopreservation and storage: data regarding the type, number and cost of the laboratory equipment and materials used for the cryopreservation and storage of CB units were collected.
- *Phase 5.* Data entry into the Italian CB Registry and release: data regarding the type, number and cost linked to the tests performed on CB units and maternal blood when the unit was released were collected. Data on laboratory equipment and materials used were also recorded.
- *General costs.* Costs deriving from the utilities and liquid nitrogen supplies, certification and accreditation, donor awareness-raising campaigns, and from software management and training, were also taken into account.

A separate form was given to each CB collection centre to report data regarding the type, number and costs of equipment and materials used for CB collection. The data related to staff (type, number and cost) were recorded for each phase and the percentage of time the operator/s dedicated to each of them was specified. The CBB analysed were identified with a letter code.

Data analysis

The analysis was carried out starting from the data related to costs and activities provided by the CBB.

The participating CBB did not provide data for all the required items, such as in the case of HLA typing costs. The costs related to staff were recorded for each phase according to the percentage of time the operator/s dedicated to each of them. In phase 2 (Biological validation and characterisation of the CB units), the tests performed on CB and maternal blood were subdivided into two categories: mandatory, i.e. pursuant to the legislation in force, and discretional, i.e. performed by the CBB according to internal procedures, and their costs are specified in euros and as a percentage of the overall costs. The general costs were calculated separately. The total cost of each CBB (in the year data were collected), is equal to the sum of the costs of each phase plus the general costs.

In order to homogenise the data of the various CBB, the following integrations were applied during the standardisation phase:

1) *Transportation costs*. The average cost was calculated for each collection centre. The figure was obtained by dividing the total transport costs by the number of collection centres.
2) *Collection costs*. As it was not possible to calculate the collection costs based on real data provided by each collection centre, a standard cost was estimated and subdivided as follows:
   - selection of donor couples: € 20.70, according to the Italian National Health Service charge for the clinical examination;
   - device used for the collection of a CB unit: average cost € 18.00, calculated by averaging out the data provided by the CBB;
   - test tubes (five) for the collection of maternal blood samples for the biological qualification of the unit: average cost € 0.09 for a total of € 0.45, calculated by averaging out the data supplied by the CBB;
   - collection activities carried out by obstetric staff: € 19.50, a cost based on the supposition that on average it takes a midwife 30 minutes to collect one unit of CB [30 minutes × (€ 0.65 − cost/minute)]. The average cost per minute of 7th level healthcare providers (nurses, obstetricians, midwives, and biomedical laboratory technicians) is € 0.65, in compliance with the national collective labour agreement.

     The standard cost obtained was € 58.65 per unit collected.
3) *Staff costs*. When a CBB was unable to provide data regarding staff costs, the average cost of each separate role was used, based on the data provided by the other CBB.
4) *Costs of the laboratory tests performed on CB for biological characterisation and on maternal blood for the biological qualification of each unit.* In this phase only the costs of the tests stated by the legislation in force (State-Regions Agreement n. 75 of 20th April 2011), as shown in Online Supplementary Table SII were taken into consideration. Screening the CB unit for haemoglobinopathies, and determining the presence of antibodies to hepatitis B core antigen and of immunoglobulin G (IgG) and M (IgM) anti-cytomegalovirua antibodies, and searching for human T-lymphotropic virus type I and II in maternal blood were attributed to the banking phase, as this modality, although not adopted by all the CBB, provides more exhaustive information regarding the units made available for transplantation.
5) *Costs of fixed assets*. When a CBB was unable to provide data regarding the purchase of equipment, an average cost was calculated for equipment with similar technical characteristics and a comparable degree of wear and tear. An 8-year amortisation period was calculated for the scientific equipment and a 5-year period for information technology systems and accessories (printers, etc.). In order to be able to take into account existing equipment (beyond the amortisation period) as well as considering their average technological complexity, ordinary and extraordinary maintenance was estimated to be 5% of the total cost of the equipment regardless of the year it was purchased.
6) *General costs*. These were estimated to be 20% of the calculated costs from phase 1 (transportation) to phase 5 (insertion into the Italian CB Registry and release of CB units). Training costs were included in the general costs.

For each CBB, the calculation of the cost per unit was based on the number of units collected and banked in 2012. For the collection phase the cost of phase 1 (collection and transportation) was divided by the number of units collected; for the banking phase the collection and transportation costs (phase 1), the biological validation and characterisation costs (phase 2), the manipulation and freezing costs (phase 3) and the cryopreservation and storage costs (phase 4) were divided by the number of units banked in 2012.

The weighted average cost for each phase was also calculated. Given the varying sizes of the inventories of the eight CBB analysed, weighted average cost was calculated for the three CBB with inventories of >3,000 units, for the two CBB with medium-sized inventories (1,000-3,000 units) and for the three CBB with inventories of <1,000 units.

Results

Data collection terminated in 2013. The analysis was carried out on data obtained from eight (42%) of the 19

CBB belonging to the ITCBN. These eight CBB represent 59.7% of the national inventory of CB units available for allogeneic transplantations; according to the size of their inventories three of them are considered large CBB (>3,000 CB units), two medium-sized (1,000-3,000 CB units) and three small (<1,000 CB units). Currently, they are all located in transfusion services in public hospitals, apart from one that is in a partly state-owned hospital accredited with the Italian National Health System. At the time the data were collected one CBB was located in the Haematology Unit of a public hospital. The characteristics of the banks are shown in Table I.

The costs obtained after standardisation are shown in Tables IIA-C. The costs originally provided by each CBB for each phase are shown in the Online Supplementary Table SIII.

Table I - Characteristics of the Italian cord blood banks included in the study and data relative to 2012.

	CBB-A	CBB-B	CBB-C	CBB-D	CBB-E	CBB-F	CBB-G	CBB-H
Year of foundation	1993	1997	1996	2001	1999	2005	2008	2008
CB units entered in registry as of 31/12/2012	9,341	3,767	1,057	3,761	300	663	106	1,346
CB units collected	2,751	1,383	282	2,230	491	950	306	1,953
CB units banked	350	151	31	260	51	118	17	93
CB units released	26	7	3	21	0	2	0	0

CBB: cord blood bank; CB: cord blood.

Table IIA - Costs (in Euro) of the Italian cord blood banks included in the study in 2012 (phases 1 and 2).

In registry as of 31/12/2012		9,341	3,767	1,057	3,761	300	663	106	1,346
Collected CB units		2,751	1,383	282	2,230	491	950	306	1,953
Banked CB units		350	151	31	260	51	118	17	93
Banking rate*		12.7%	10.9%	11.0%	11.7%	10.4%	12.4%	5.6%	4.8%
CB units released		26	7	3	21	0	2	0	0
N. of collection centres		39	13	10	29	5	15	6	14
N. of operators		13	8	5	10	7	7	9	8
Total cost		*590,853.39*	*204,562.00*	*123,417.46*	*435,284.70*	*149,731.33*	*383,587.17*	*157,307.08*	*453,373.48*
Collection		*161,346.15*	*81,112.95*	*16,539.30*	*130,789.50*	*28,797.15*	*55,717.50*	*17,946.90*	*114,543.45*
Phase 1 - Transportation		185,681.97	61,893.99	47,610.76	138,071.21	23,805.38	71,416.14	28,566.46	66,655.07
Phase 2 Biological validation and characterisation	Staff	165,875.80	79,535.08	39,725.49	160,127.70	86,238.74	100,156.92	39,326.77	113,343.37
	Staff (n. operators/ phase)	13	8	5	9	7	7	9	8
	CB testing	413,880.90	150,331.87	6,184.67	85,383.70	36,759.78	78,030.51	22,275.10	32,816.20
	Mandatory	413,880.90	150,331.87	6,184.67	84,611.50	32,016.78	78,030.51	22,275.10	32,816.20
	Discretional	np	np	np	772.20	4,743.00	np	np	np
	Mandatory tests on mother	30,575.00	25,528.05	4,639.45	83,187.00	17,885.70	17,622.72	2,367.76	10,988.30
	Mandatory	30,575.00	25,528.05	4,639.45	83,187.00	17,885.70	17,622.72	2,367.76	10,988.30
	Total fixed assets	3,443.43	9,573.04	2,113.80	1,677.08	407.65	5,664.70	19,424.30	5,056.40
	Amortisation	1,704.33	893.63	75.00	632.38	91.65	3,453.80	2,796.00	3,504.00
	Rental fees	0.00	7,503.21	0.00	0.00	0.00	0.00	15,000.00	0.00
	Maintenance	1,739.10	1,176.20	2,038.80	1,044.70	316.00	2,210.90	1,628.30	1,552.40
	Net disposables**	2,169.20	2,098.64	1,162.05	0.00	371.45	3,849.00	887.80	9,920.00
	Disposables	77,196.20	8,996.33	1,162.05	12,305.07	371.45	20,657.00	887.80	9,920.00
	CB collection bags	54,027.00	na	na	na	na	16,808.00	na	na
	Laboratory kits	21,000.00	6897.69	na	12,305.07	na	na	na	na
	Total phase 2	*615,944.33*	*267,066.68*	*53,825.46*	*330,375.48*	*141,663.32*	*205,323.85*	*84,281.73*	*172,124.27*

All figures indicated have been standardised. *The banking rate is obtained from the banked units/collected units ratio. **The "Net disposables" field indicates the cost of disposables less the cost of collection and laboratory kits if used. CBB: cord blood bank; CB: cord blood; np: not performed; na: not applicable for cost standardisation (costs included in others fields).

Table IIB - Costs (in Euro) of the Italian cord blood banks included in the study in 2012 (phases 3 and 4).

	CB Bank	CBB-A	CBB-B	CBB-C	CBB-D	CBB-E	CBB-F	CBB-G	CBB-H
Phase 3 Manipulation and freezing	Staff	210,332.65	31,360.88	50,257.64	144,164.00	26,310.57	164,945.99	39,326.77	113,343.37
	Staff (n. operators/ phase)	11	8	5	9	5	6	9	8
	Total fixed assets	9,789.72	14,247.90	2,045.41	20,691.73	5,663.92	18,677.69	10,833.79	15,183.26
	Amortisation	4,325.00	10,058.50	512.01	12,118.60	1,100.00	12,698.35	7,738.42	10,845.00
	Maintenance	5,464.72	4,189.40	1,533.40	8,573.13	4,563.92	5,979.34	3,095.37	4,338.26
	Net disposables	87,872.40	14,726.40	4,785.04	51,909.27	2,612.91	15,245.88	7,968.10	7,124.00
	Disposables	83,660.40	14,726.40	4,785.04	159,012.77	2,612.91	15,245.88	7,968.10	7,124.00
	Fractionation kits	4,212.00	na	na	46,718.00	na	na	na	na
	CB collection bags	na	na	na	60,385.50	na	na	na	na
	Total phase 3	*307,994.77*	*60,335.18*	*57,088.09*	*216,765.00*	*34,587.40*	*198,869.56*	*58,128.66*	*135,650.63*
Phase 4 Cryopreservation and storage	Staff	53,910.75	29,005.72	12,517.59	58,305.25	13,949.46	36,654.67	39,326.77	113,343.37
	Staff (n. operators/ phase)	11	5	5	9	5	6	9	8
	Total fixed assets	115,520.00	10,645.80	14,002.08	38,776.20	3,493.60	29,709.45	35,580.02	42,665.00
	Amortisation	71,716.00	1,162.00	8,135.02	23,327.50	11.50	20,596.25	25,414.32	30,475.00
	Maintenance	43,804.00	9,483.80	5,867.06	15,448.70	3,482.10	9,113.20	10,165.70	12,190.00
	Total phase 4	*169,430.75*	*39,651.52*	*26,519.67*	*97,081.45*	*17,443.06*	*66,364.12*	*74,906.79*	*156,008.37*

All figures indicated have been standardised. CBB: cord blood bank; CB: cord blood; na: not applicable for cost standardisation (costs included in others fields).

Table IIC - Costs (in Euro) of the Italian cord blood banks included in the study in 2012 (phase 5 and general costs).

	CB Bank	CBB-A	CBB-B	CBB-C	CBB-D	CBB-E	CBB-F	CBB-G	CBB-H
Phase 5 Entry into registry and release	Staff	160,734.20	64,660.32	20,916.74	51,939.75	23,232.56	81,829.59	39,326.77	113,343.37
	Staff (n. operators/phase)	12	8	5	10	4	7	9	8
	FU tests on mother	10,112.05	4,849.80	485.68	8,892.00	1,978.80	4,182.10	635.50	2,730.00
	Maternal tests at release	7,915.44	2,131.08	913.32	6,393.24	na	608,.88	na	na
	CB tests at release	30,341.64	6,193.39	544.17	5,369.07	na	1,711,.47	na	na
	Fixed assets	2,795.35	1,285.20	2,237.39	na	2,006.10	7,746.48	2,343.00	1,575.00
	Amortisation	1,740.00	918.00	753.90	na	981.25	5,524.63	1,673.57	1,125.00
	Maintenance	1,055.35	367.20	1,483.49	na	1,024.85	2,221.85	669.43	450.00
	Disposables	1,447.54	na	190.35	na	na	67.55	2,600.00	na
	Total phase 5	*213,346.22*	*79,119.79*	*25,287.65*	*72,594.06*	*27,217.46*	*96,146.07*	*44,905.27*	*117,648.37*
General costs	Costs up to phase 5	1,653,744.18	589,180.11	226,870.93	985,676.70	273,513.77	693,837.25	308,735.81	762,630.15
	+20%*	330,748.84	117,836.02	45,374.19	197,135.34	54,702.75	138,767.45	61,747.16	152,526.03
	Total	*1,984,493.02*	*707,016.13*	*272,245.12*	*1,182,812.04*	*328,216.53*	*832,604.70*	*370,482.97*	*915,156.19*

All figures indicated have been standardised. *The cost obtained by calculating 20% of the total costs from the collection phase to phase 5. NB: Maintenance includes both ordinary and extraordinary maintenance. CBB: cord blood bank; CB: cord blood; FU, follow up; na: not applicable for cost standardisation (costs included in others fields).

Table III shows the total costs provided by the CBB and those obtained after standardisation. The overall standardised annual costs ranged from about € 270,000 to more than € 1,900,000 depending mainly on the size of the CBB inventory. Table IV shows total collection and banking costs, as well as the costs of each unit of CB collected and banked in 2012. Table V presents the average weighted cost based on the data obtained from the eight evaluable CBB. Of these eight CBB, the average weighted costs are indicated for the three large, two medium-sized and three small CBB. The average weighted cost of collection for all CBB was € 118.93, ranging from € 151.31 in banks with inventories of <1,000 units to € 119.25 in banks with inventories of >3,000 units. An even more marked difference was observed when banking activity was considered. The average weighted cost of banking for all CBB was € 4,375.60, ranging from € 8,158.37 in banks with inventories of <1,000 units to € 6,827.14 in medium-sized CBB (1,000-3,000 units) and € 3,614.15 in banks with inventories >3,000 units.

Discussion

We have performed the first cost analysis of public CBB belonging to the ITCBN since the institution of the network. The data analysis revealed a broad variation between the CBB in terms of total costs (determined by different volumes of activities) and in terms of costs per banked CB unit.

The comparative analysis of the costs per unit in each phase of the process showed a great difference in the banking costs (Table V). This difference was mainly caused by the costs of the biological characterisation and qualification of CB units and those related to freezing and preservation, which are strongly affected by the costs of cold chain maintenance and running cryogenic areas. The difference was relevant when CBB with inventories of 1,000-3,000 units were compared with those with inventories of <1,000 units and very marked when CBB with large inventories were compared with those with inventories of <1,000 units. In fact, the weighted average costs of the banking phase decreased by 17.4% in CBB

Table III - Costs (in Euro) of the Italian cord blood banks included in the study in 2012.

CB Bank	CBB-A	CBB-B	CBB-C	CBB-D	CBB-E	CBB-F	CBB-G	CBB-H
Total A	1,682,826.66	788,071.44	293,893.64	1,075,819.00	287,682.20	702,386.31	38,117.40	292,394.08
Total B	1,984,493.02	707,016.13	272,245.12	1,182,812.04	328,216.53	832,604.70	370,482.97	915,156.19
Difference B-A (Δ)	+301,666.36*	−81,055.31**	−21,648.52¥	+106,993.04#	+40,534.33$	+130,218.39¤	+332,365.57§	+622,762.11°

The total costs, as provided by the cord blood banks, are indicated (Total A), as are those obtained after standardisation (Total B). The difference B-A indicates the increase/decrease of the costs following standardisation. *CBB-A (D + € 301,666.36) had lower costs in phase 2 (tests performed on CB and mother, disposables) and general costs, but higher costs in phase 1 (transportation), phase 3 (manipulation and freezing) and phase 4 (cryopreservation and storage) that depended on the fixed assets item, due to the calculation of the amortisation of scientific equipment, and in phase 5 (entry into the Italian CB registry). Furthermore, the costs of staff after standardisation had an impact on every phase. In fact, CBB-A had a percentage of non-permanent staff (5 operators out of 13) but the CBB itself did not take their costs into account. **CBB-B (Δ − € 81,055.31) had lower costs in phases 2 and 5 and in general costs, but higher costs in phases 1, 3 and 4 (amortisation of scientific equipment). ¥CBB-C (Δ − € 21,648.52) had lower costs in all phases except phases 3 and 4 (amortisation of scientific equipment). #CBB-D (Δ + € 106,993.04) had lower costs in phases 1, 2 and 5, but higher costs in phases 3 and 4 (amortisation of scientific equipment). $CBB-E (Δ + € 40,534.33) had higher costs in all phases except phase 5, which derived from the cost of equipment not indicated by the CBB. ¤CBB-F (Δ + € 130,218.39) had lower general costs, but higher costs in all the other phases (amortisation of scientific equipment). Furthermore, the costs of staff after standardisation had an impact on every phase; in fact, CBB-F had a percentage of non-permanent staff (4 operators out of 7). §CBB-G (Δ + € 332,365.57) had higher costs in all phases as it did not indicate costs related to staff. °CBB-H (Δ + € 662,762.11) had higher costs in all phases as it did not indicate costs related to staff. CBB: cord blood bank; CB: cord blood.

Table IV - Costs (in Euro) of the Italian cord blood banks included in the study subdivided in phases.

CB Bank	CBB-A	CBB-B	CBB-C	CBB-D	CBB-E	CBB-F	CBB-G	CBB-H
Units collected 2012	2751	1383	282	2230	491	950	306	1953
Units banked 2012	350	151	31	260	51	118	17	93
Total collection costs	*347,028.12*	*143,006.94*	*64,150.06*	*268,860.71*	*52,602.53*	*127,133.64*	*46,513.36*	*181,198.52*
Total banking costs	*1,440,397.97*	*510,060.32*	*201,583.28*	*913,082.64*	*246,296.31*	*597,691.17*	*263,830.54*	*644,981.79*
Cost per one unit of CB (collection)	126.15	103.40	227.48	120.57	107.13	133.82	152.00	92.78
Cost per one unit of CB (banking)	5,060.42	4,158.25	7,966.37	4,270.07	5,901.94	6,241.17	19,151.63	8,575.35

For each CBB, the total number of units collected and banked, the total collection and banking costs, as well as the costs of each unit of CB collected and banked in 2012 are indicated. CBB: cord blood bank; CB: cord blood.

with inventories of >3,000 units compared to the weighted average cost calculated for all the CBB, and by 55.7% compared to those of CBB with inventories of <1,000 units (Table V). Our study outlined an inverse relation between the costs of CB banking and the size of the bank inventory, suggesting that scale economies could be obtained through centralisation of banking activities. The data are not in contrast with those reported in the international literature. In 1999, a study conducted by Sirchia *et al*. estimated three fees (US$ 15,061, US$ 12,666 and US$ 11,602) based on three different models[6]. The authors performed a cost simulation between a model composed of seven networked banks operating in Italy at the time of the study and two hypothetical bank models, one intermediate-sized and multiregional formed of two banks, and the other a single large national bank. This study suggested that with a single large central bank it would be possible to cut costs by about 30%, above all through staff reduction, but to the detriment of a major operating flexibility provided by the model with a higher number of banks. Another study performed in 2008 by Howard *et al*. hypothesized a number of scenarios based on increasing national CB inventory levels from 50,000 to 300,000 units[7]. They defined the costs after calculating a break-even point, i.e. the value that indicates the quantity, expressed in either production volume or turnover, necessary to cover previously sustained costs so the reference period closes with neither profit nor loss. With an inventory of 50,000 CB units, their calculation of the break-even point was a fee of US$ 15,336 per unit released.

As far as concerns the definition of an optimal national inventory, several studies[8-10] established the demand for CB as one unit per 1,000 inhabitants in order to ensure that more than 90% of patients from the same ethnic group (Caucasians) seeking a match to undergo an allogeneic transplantation find at least one unit with the lowest degree of compatibility. Considering that in Italy the optimal inventory, estimated to be about 60,000 units, has not yet been achieved, our data assume greater importance because they state our motivation for designing a more sustainable CBB network.

Nevertheless, the authors are aware of the limitations of this study, which depend mainly on: (i) the low response rate from the banks (10/19 responded, but only 8/19 i.e. 42% reported evaluable data), and (ii) the use of data which do not represent costs but rather "reimbursement fees" for which there is no evidence of their accuracy, such as in case of HLA typing cost. With regards to HLA typing (low resolution for A and B loci and high resolution for the DRB1 locus), as shown in Online Supplementary Table SIV, this has a highly variable impact on the cost of CB units (from 41.3 to 76.3%) because of the very different fees applied for the tests carried out at local/regional level which, in turn, range from € 78.60 to € 700.50.

Several CBB did not provide data regarding important cost items. In the case of staff costs, some CBB provided only partial data as they did not include the cost of non-permanent operators and this resulted in an underestimation of their current costs. Another factor that contributed to the variation between the costs of CBB costs was the use of different testing panels for the characterization of CB despite the specific legislation in force and national guidelines.

The missing or incomplete data were adjusted through standardisation so that the CBB had a positive or negative delta (Δ) value between current costs and standard costs (Table IV).

Despite the limitations of the study, the participating CBB represent more than 50% of the national inventory available for allogeneic transplantation and the evaluable data can be considered reliable for supporting the reorganisation of the IICBN.

A recent publication by Magalon *et al.*[11] suggested an organisational model to increase the sustainability of CBB by improving operational standards and quality of CB units. Their model hypothesises the introduction of a 18×10^8 threshold of nucleated cells for the banking of CB units in order to obtain a 12.9% utilisation rate. This strategy would save about US$ 1,000,000 against an increase in the units released for transplantation. Since July 2011, the ITCBN has adopted a collection threshold of 15×10^8 total nucleated cells and a banking threshold of 12×10^8 total nucleated cells; this has resulted in a 10% drop in the national average banking rate on the one hand, but an enhanced quality of inventoried CB units on the other. Initially, this strategy increased the release rate of certain CBB but now, as a result of the growing use of haematopoietic stem cells from haploidentical donors, there is an ongoing decrease in release rate.

Table V - Weighted average costs (in Euro) of the Italian cord blood banks included in the study.

CB Bank	All CBB	CBB with an inventory of >3,000 units	CBB with an inventory of 1,000-3,000 units	CBB with an inventory of <1,000 units
Collection	118.93	119.25	109.78	151.31
Banking	4,375.60	3,614.15	6,827.14	8,158.37

The average weighted cost based on the data obtained from the eight evaluable banks are indicated. Of these eight cord blood banks, the average weighted costs are indicated for the three with inventories >3,000 units, for the two with a medium-sized inventory (1,000-3,000 units) and for the three with inventories of <1,000 units. CBB: cord blood bank.

Conclusions

The ITCBN, as it stands today, is burdened by high costs that along with a drop in the number of CB units released over the last few years have made it barely sustainable. This trend should make us think carefully about the need to adopt strategies to rationalise the activities of the Italian CBB network with the aim of reducing running costs.

Among the initiatives aimed at improving the ITCBN inventory both in terms of quality and quantity, an increased effort to collect units of CB from members of the fast growing ethnic minority communities in our country, would appear to be a valid strategy if supported by a consolidated network of collection centres (delivery rooms).

The centralisation of HLA typing in a very limited number of laboratories that, thanks to the effect of adequate economies of scale, would be capable of providing widespread typing at highly competitive costs seems to be a viable proposition.

In recent years, the ITCBN CBB have committed themselves to research and to the development of new blood components[12-13] that can be obtained from CB. This potential use of CB supports the possibility of diversifying the activities within the ITCBN.

Nevertheless, it is essential to concentrate cost-consuming activities in no more than three to five CBB to maintain a sustainable CBB network in order to continue to offer our patients a chance of curative treatment.

Authorship contributions

SP designed the study, was responsible for study coordination and was the lead writer of this paper; MB and LL were responsible for data collection and helped to write the manuscript; AC, DC and AG designed and performed the economic analyses; GM and MF revised the manuscript; GG and GML were the guarantors of the study. All Authors saw and approved the final version of this manuscript.

Disclosure of conflicts of interest

GML is the Editor-in-Chief of Blood Transfusion and this manuscript has undergone additional external review as a result. The other Authors declare no conflicts of interest.

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