

# Introduction of principles of blood management to healthy donor bone marrow harvesting

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## Vox Sanguinis

**Background and Objectives** Patient blood (more accurately: haemoglobin, Hb) management (PBM) aims to optimize endogenous Hb production and to minimize iatrogenic Hb loss while maintaining patient safety and optimal effectiveness of medical interventions. PBM was adopted as policy for patients by the World Health Organization (WHO), and, all the more, should be applied to healthy donors.

**Materials and Methods** Observational data from 489 bone marrow (BM) donors were retrospectively analysed, and principles of patient blood management were applied to healthy volunteer BM donations.

**Results and Conclusion** We managed to render BM aspiration safe for donors, notably completely avoiding the collection of autologous blood units and blood transfusions through iron management, establishment and curation of high-yield aspiration technique, limitation of collection volume to 1.5% of donor body weight and development of volume prediction algorithms for the requested cell dose.

**Key words:** allogeneic donor, donor safety, patient blood management, stem cell transplantation.

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## Introduction

The WHO has identified PBM as a policy target [1]. Main building blocks are optimizing endogenous haemoglobin (Hb) synthesis, blood-sparing techniques and adherence to the professional societies' recommended conservative transfusion thresholds, while maintaining comfort, safety and efficacy of the related medical intervention. We applied principles of PBM to healthy BM donors, since, in contrast to patients, they do not benefit from the intervention which could offset risks associated with transfusion or anaemia. In difference to patients who benefit from the medical intervention themselves, the success of

BM harvests is gauged by recipient outcomes. Optimal BM products provide timely engraftment with a small collection volume. BM harvesting is currently resurging due to novel approaches for haplo-identical transplantation [2–5]. We addressed BM donor pre-donation Hb management by strictly foregoing autologous red blood cell (RBC) collection and by iron supplementation in hypoferritinemic individuals. We minimized intra-operative blood loss by curating a high-yield BM aspiration technique and limiting collections to algorithm-predicted volumes needed to achieve target cell dose. Transfusion thresholds were guided by the restrictive national guidelines [1,6,7]. The totality of this approach saved an average of 150 g of Hb/donation, maintained safe Hb levels and avoided transfusions. Donor PBM did not negatively impact recipient outcomes.

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## Methods

### Study and validation cohorts

Four hundred eighty-nine of 524 healthy adult donor BM harvests, performed from 2011–2013, served as study cohort, 88 harvests in 2014–2017 for validation. Pre-donation work-up was performed as described [8]. Eligibility assessment followed World Marrow Donor Association criteria [9]. As per internal guidelines, autologous blood was not collected. Marginally hypoferritinemic donors (<9/<18 µg/l for women/men, respectively) were offered oral iron. Four weeks after donation, donors provided written self-reported health information.

### Bone marrow donation

Bone marrow was aspirated under general anaesthesia from both pelvic bones. Collection volume was guided by target dose, using nomograms based on in-house benchmarking except that 15 ml of BM/kg donor weight or 1500 ml total could not be exceeded. TNC is not measured intra-operatively; collections are instead guided by dose:volume prediction algorithms. A calibrated tension spring balance is used to monitor the collected volume. In the laboratory, precision scales are used for product volume calculation (volume = weight corrected for haematocrit). Quality controls include infectious disease markers, sterility testing [10] and haemacytometry including CD34+ [11] and CD3+ cell enumeration. Donors were mobilized immediately after awaking but remained hospitalized overnight.

### Data collection

This is a concurrent/retrospective analysis of routine observational clinical data (product/process quality review) as required by laws and regulations. No data outside clinical routine were collected; for these anonymous observational analyses, specific consent was not required according to the Ethics Committee of Goethe University School of Medicine.

### Donor outcomes

Donor age, sex, height and weight as well as recipient weight were queried.

Complete blood cell count (CBC) with differential and clinical symptoms was assessed during the evaluation visit, on day 0 before BM donation, on the day of discharge (day 2, BM harvest being day 1) and >4 weeks after donation (FU), serum iron and ferritin only during work-up and FU. 'Donor blood volume (TBV)' was

calculated from the sex, height and weight using Nadler's formula:

Male:  $TBV (L) = 0.3669 \times \text{height (m)}^3 + 0.03219 \times \text{weight (kg)} + 0.6041$ .

Female:  $TBV (L) = 0.3561 \times \text{height (m)}^3 + 0.03308 \times \text{weight (kg)} + 0.1833$  [12].

### Product quality

Harvest volume, haematocrit, total nucleated cells (TNC) and CD34+ values were extracted from the laboratory information management system. TNC concentration in the product was corrected for dilution with anti-coagulant.

### Patient outcomes

Engraftment data (neutrophils, platelets) were extracted from day-100-reports [13] where available. Total neutrophil count >500/µl or platelets > 20 000/µl without transfusion within the last 7 days were defined as neutrophil or platelet engraftment.

### Statistical analysis

Differences between pre- and postoperative laboratory values were calculated by Student's *t*-test or Mann-Whitney's U-test, as appropriate. Pearson's or Spearman's correlation analysis was performed to estimate the correlation between BMV, TNC and CD34+ cell count in the product and the prediction formulae. Linear regression analysis was applied to determine predictors of TNC and CD34+ cell concentrations in the product. Variables with a *P*-value <0.1 in the univariate analysis were entered into a stepwise multiple regression model (forward selection). IBM SPSS statistics 24 was used for statistical analyses (IBM Corp., Armonk, NY). A *P*-value <0.05 was considered statistically significant.

## Results

Four hundred eighty-nine BMs were collected; epidemiology was typical for a stem cell donor cohort (Table 1; [8,14]). To test our hypothesis that women could be at greater risk to become anaemic from BM donation, we compared baseline data from female and male donors. The rationale for our hypothesis is the following: women have lower 'lower limits of normal' for ferritin and Hb, while the thresholds for defining anaemia severity are the same, that is women can afford to lose less Hb before they are anaemic. Moreover, in the normal population women are smaller than men, but donor selection could have skewed against smaller women. Indeed, in our

**Table 1** Donor characteristics

		Study cohort			<i>t</i> -test <i>f:m</i>	Validation cohort	
		Female	Male	All		All	<i>t</i> -test study: validation
<i>n</i>		180	309	489		88	
[%]		36.8	63.2				
Weight	Mean	69.8	85.1	79.5	<b>&lt;0.0001</b>	80.8	0.49
[kg]	Range	50–132	51–143	50–143		48–125	
Height	Mean	167.8	181.6	176.5	<b>&lt;0.0001</b>	176.8	0.78
[cm]	Range	152–188	163–200	152–200		162–198	
BMI	Mean	24.7	25.8	25.4	<b>0.017</b>	25.7	0.49
	Range	17.7–42.9	16.9–42.2	16.9–42.9		17.4–43.3	
Hb	Mean	13.46	15.59	14.8	<b>&lt;0.0001</b>	14.6	0.22
[g/l]	Range	11.2–16.8	11.9–18.3	11.2–18.3		11.8–16.8	
Ferritin	Mean	45.0	162.8	119.9	<b>&lt;0.0001</b>	n.d.	
[µg/l]	Range	3–354	7–710	3–710			
Total RBC mass	Mean	1.6	2.2	2.0	<b>&lt;0.0001</b>	2.0	0.57
[kg]	Range	1.2–2.8	1.4–3.5	1.2–3.5		1.3–3.0	

In the study cohort, female and male donors were compared (Student's *t*-test) to ascertain potential differences in terms of risk factors for postoperative anaemia. Study and validation cohort were tested for similarity to justify the use of the latter for validation purposes.

Statistically significant differences ( $P < 0.05$ ) are shown in bold script.

cohort women were smaller and had smaller iron stores and total RBC mass ( $P < 0.0001$  for all), yet donated, on average, relatively larger BM volume ( $P < 0.0014$ ).

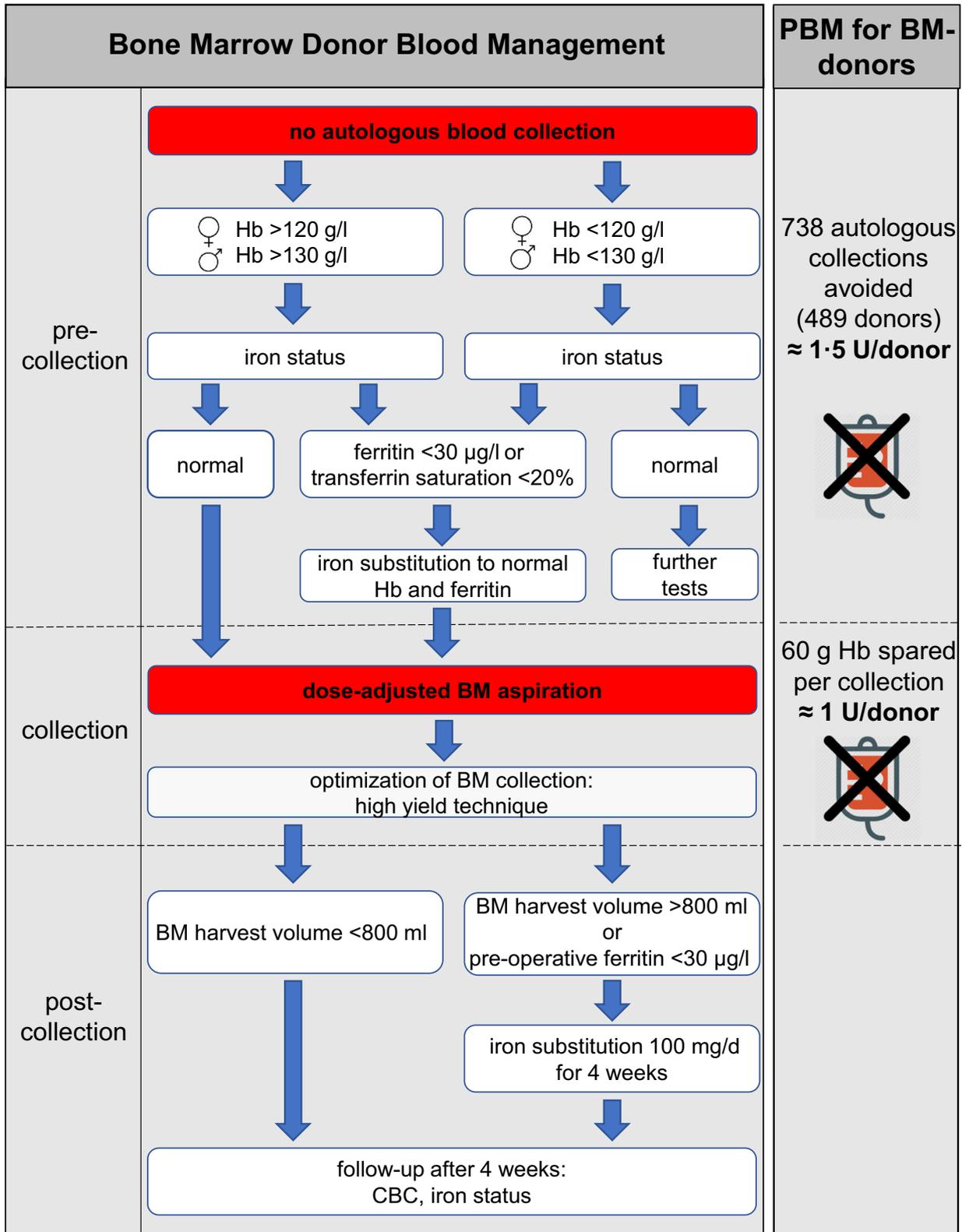
### Preoperative donor blood management: Autologous blood

Deviating from the National Marrow Donor Program (NMDP, 22nd edition) and JACIE guidelines valid at the time of data collection, we opted against collection of autologous blood. To validate this decision, we calculated theoretically collected RBC units, theoretical expiration of units because of re-scheduling, theoretically transfused units based on guideline-recommended transfusion triggers [6,7,15–17] and units which would have expired unused, by necessity ignoring potential exacerbation of anaemia due to generation of autologous units. 54.4% and 33.3% of donors were slated for collection volumes of 501–1000 ml and 1001–1500 ml, respectively, for a total of 592 autologous units which should have been collected according to above-referenced guidance. Re-scheduling of 115 BM harvests would have seen an additional 145 units exceed shelf life. Units of prospective donors whose donations were cancelled are not accounted for here. None of the donors lost enough Hb to qualify for a blood transfusion ( $\leq 70$  g/l). Thus, pre-donation autologous blood collection would have resulted in 738 non-used units of

autologous blood, that is 1.5 discarded autologous RBC units for each BM harvest (Fig. 1).

### Intra-operative blood management: Correlation of BM volume and Hb loss

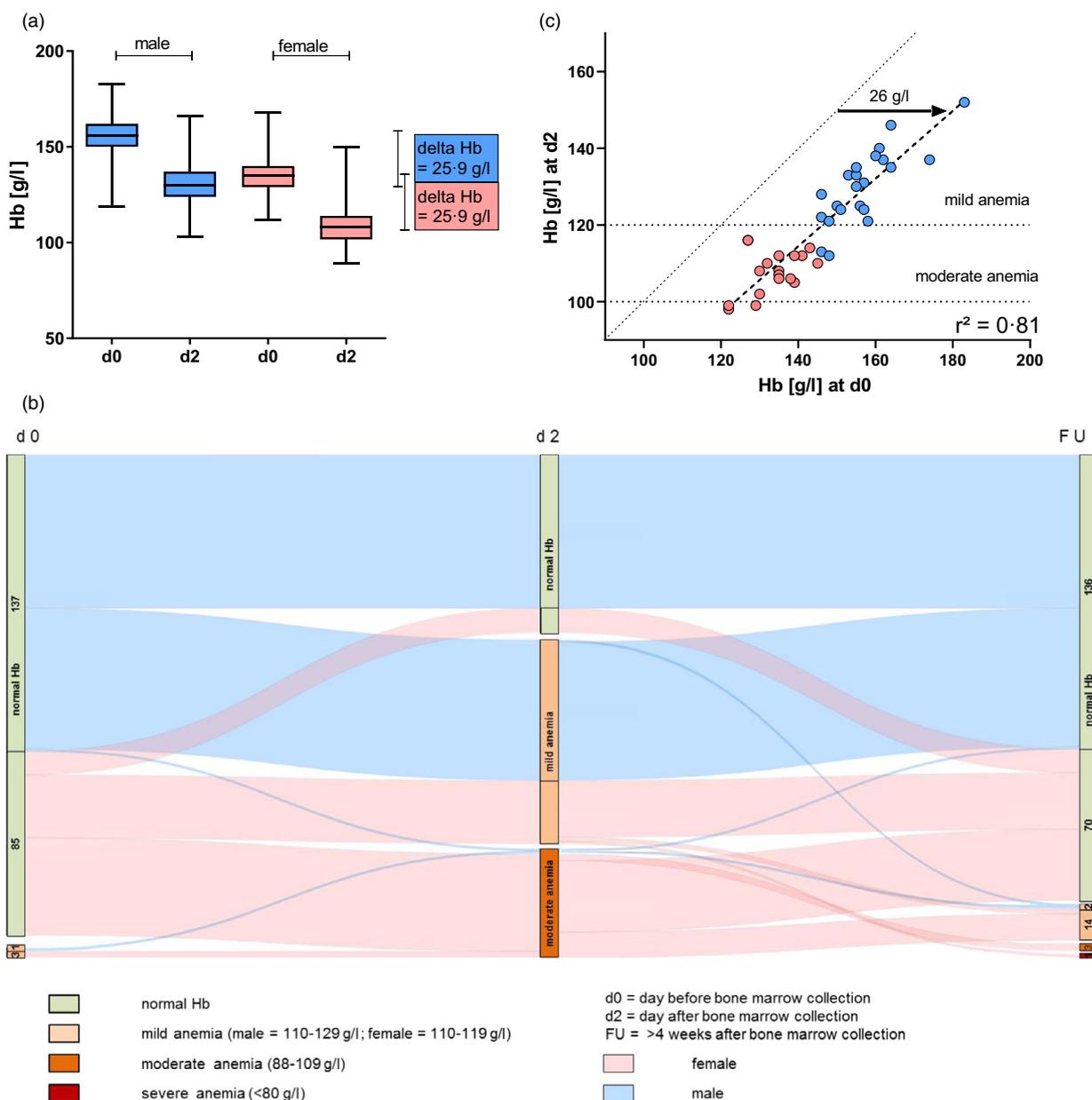
Pre- and postoperative CBC was available for analysis from 414 donors. Mean pre- and postoperative Hb levels in female ( $n = 150$ ) were significantly lower than in male donors ( $n = 264$ ), but the delta was the same, 26 g/l (pre/post,  $P < 0.0001$ ) (Fig. 2A). BM donation rendered half the male (129/264) and most female (131/150) donors anaemic by WHO definition [18]. Anaemia was mostly mild in men (128/129 anaemic men), but moderate in more than half (58%) of the women (Fig. 2b). At 89 g/l, even the lowest post-collection Hb remained markedly above transfusion triggers [6,7]. To address whether donors with pre-existing anaemia would suffer a greater decrease in Hb than non-anaemic donors, we generated a sub-cohort of donors of similar harvest volumes ( $925 \pm 25$  ml, to remove collection volume as a variable) and compared their pre- and post-collection Hb. We observed a strong correlation between pre- (d0) and post-collection Hb (d2) and risk for anaemia (linear regression,  $r^2 > 0.81$ ;  $P > 0.0001$ ) with a mean Hb loss of 26 g/l (Fig. 2c). Delta Hb was independent of pre-collection Hb, that is highly predictable and hence, occurrence of post-collection anaemia was predictable as well. 240 donors provided week 4 follow-up (FU) CBC,



**Fig. 1** Donor blood management. Introduction of blood management in healthy bone marrow (BM) donors is shown in a flow chart, with the actions in the middle and the associated blood savings in our cohort in the right column.

generating 226 complete data sets for Hb (d0, d2, FU) (Fig. 2b). In all but 18/2 female/male donors (8.3%), Hb had normalized at FU. Of these, two had initially presented

with Hb < 120 g/l and 11 with Hb < 130 g/l. Multivariate analysis identified sex, harvest volume and height as predictors of Hb loss (data not shown).



**Fig. 2** Effect of BM donation on Hb. (a) Hb levels (y-axis; g/l) are shown (mean, SD) for male (blue) and female (pink) donors at baseline (x-axis, d0) and 1 day after BM donation (x-axis, d2). The mean loss of Hb due to BM donation was the same for males and females, 26 g/l. (b) To assess Hb loss relative to preoperative Hb independently of BM collection volume, 40 donors with a collection volume of  $925 \pm 25$  ml were selected and preoperative Hb (x-axis; g/l) was plotted over postoperative Hb (y-axis; g/l). Hb loss was constant, 26 g/l (arrow), irrespective of preoperative Hb values ( $r^2 = 0.81$ ;  $P < 0.0001$ ). Pink and blue dots depict values from female/male donors. (c) Changes in Hb level from each donor between day 0 (d0), day 2 (d2) and follow-up (FU; >4 weeks) are plotted in a Sankey diagram. Female donors are marked in pink and male donors in blue. Time course is shown on the x-axis (not linear) at d0 (left bar), d2 (middle bar), FU (right bar), outcome (normal Hb = green, mild anaemia = orange, moderate anaemia = red, severe anaemia = dark red per WHO anaemia definition) on the y-axis. Length of bars equals relative size of the respective cohort, connecting lines (magnitude of) interchange between cohorts. Thus while almost all donors were non-anaemic before BM donation, the majority of female donors developed mild or, more frequently, moderate anaemia. Among male donors, by contrast, half each of the donors remained non-anaemic or became mildly anaemic with only one case of moderate anaemia after donation. By day 28, the vast majority had regenerated a normal Hb.

### Peri-operative donor iron management

Ferritin values at FU were available for 209 donors. Even though most had recovered normal Hb, in 62 (29.6%) ferritin remained below normal, 30 of whom had already presented with reduced ferritin during work-up. The mean drop in ferritin for the complete cohort was 61  $\mu\text{g/l}$ . In donors with high normal ferritin values at work-up, self-reported iron supplementation after collection significantly attenuated mean ferritin loss in donors with BM collection volumes  $>800$  ml with 66.6  $\mu\text{g/l}$  vs. 118.6  $\mu\text{g/l}$  in donors without iron supplementation ( $P < 0.0004$ ). Iron supplementation had no significant effect on ferritin loss where bone marrow collection volume was below 800 ml (Fig. 3). 118/170 donors reported taking iron at a dose of 50–100 mg/day for a median of 30 days (range: 2–100 days).

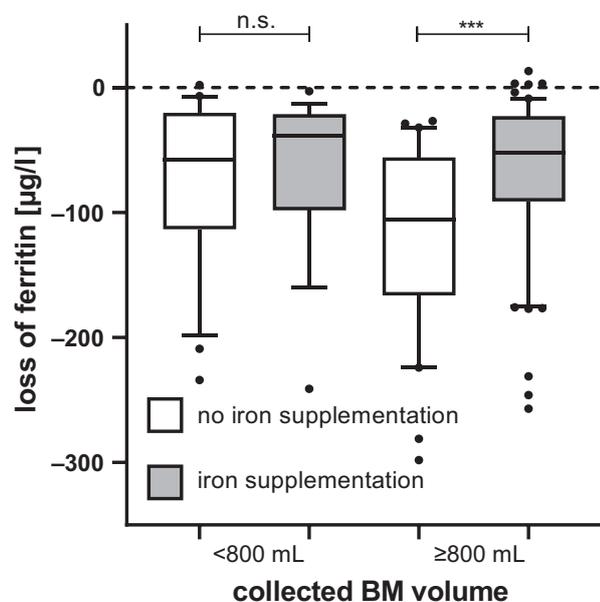
### Pharmacological graft quality: TNC and CD34 + cell yield

Collection volume ranged from 211 to 1576 ml (median: 872 ml). Lowest-to-highest TNC and CD34+ counts differed seven- and 20-fold, respectively, for means of  $26.5 \times 10^3/\mu\text{l}$  for TNC (range:  $11.3$ – $81.2 \times 10^3/\mu\text{l}$ ) and

$186.5/\mu\text{l}$  for CD34+ cells ( $44.6$ – $1075/\mu\text{l}$ ). Product characteristics are summarized in Table 2.

Fifteen transplants (3%) contained  $<2 \times 10^8$  TNC/kg recipient weight. In all 15 donors, the maximum permissible volume of 15 ml/kg donor weight was collected. Nine are explained by unfavourable weight disparity between donor and recipient, two additional donors weighing  $\leq 60$  kg. In four products with sub-par TNC dose, TNC concentration was below the 5th percentile. To estimate the quality of our products, we benchmarked against the totality of BMs harvested for the DKMS stem cell donor registry. Median TNC for DKMS was  $15.8 \times 10^3/\mu\text{L}$ , that is including the 5–5% harvests performed by us. By comparison, TNC was  $23.7 \times 10^3/\mu\text{l}$  for our centre; other product parameters similarly indicate very high cell counts harvested at our centre.

Total nucleated cells and CD34+ cells correlated (Spearman correlation;  $r^2 > 0.60$ ;  $P < 0.0001$ ), as did BM volume and TNC dose ( $r^2 > 0.72$ ,  $P > 0.0001$ ) or CD34+ cell dose ( $r^2 > 0.52$ ,  $P > 0.0001$ ). TNC and CD34+ cell concentrations were independent of collection volume (Fig. S1). Linear regression analysis was undertaken to identify routinely available pre-harvest data associating with collection outcomes but failed to find parameters useful for refining prediction algorithms (data not shown).



**Fig. 3** Loss of ferritin. Box and whisker plots with values for ferritin loss at FU compared to pre-harvest values (y-axis) are plotted for donors without iron supplementation (white) and donors taking iron supplementation (grey). The horizontal line marks the mean. Comparisons are done separately by BM collection volume,  $<800$  ml or  $\geq 800$  ml. Among the donors of  $\geq 800$  ml BM, loss of ferritin was less pronounced in those taking iron supplementation ( $P < 0.0004$ ).

**Table 2** BM product characteristics

Bone marrow products		489
TNC	Median	20.9
[ $\times 10^3/\mu\text{l}$ ]	Range	11.3–81.2
CD34 cells	Median	0.68
[% of TNC]	Range	0.27–1.9
Platelets	Median	131 000
[ $/\mu\text{l}$ ]	Range	44 000–360 000
Recipient weight	Median	60
[kg]	Range	4–160
TNC $\times 10^8/\text{kg}$	Median	4.2
per kg recipient weight	Range	1.4–45.1
$<2 \times 10^8/\text{kg}$	<i>n</i> [%]	15/488 [3.1]
$<3 \times 10^8/\text{kg}$	<i>n</i> [%]	151/488 [30.9]
CD34+ cells $\times 10^6/\text{kg}$	Median	2.8
per kg recipient weight	Range	0.5–27.3
$<2 \times 10^6$ CD34 + cells/kg	<i>n</i> [%]	151/488 [30.9]
$<1.5 \times 10^6$ CD34 + cells/kg	<i>n</i> [%]	70/488 [14.3]
TNC $\times 10^8/\text{kg}$	Median	2.8
per kg donor weight	Range	0.7–7.5
CD34+ cells $\times 10^6/\text{kg}$	Median	1.8
per kg donor weight	Range	0.3–6.4
BMV/TBV donor	Median	18
[%]	Range	3–31

BM, bone marrow; BMV, bone marrow product volume; TBV, total blood volume; TNC, total nucleated cell.

### Graft function: Engraftment

Median TNC and CD34+ cell doses per kg of the recipient were  $4.2 \times 10^8$  (range:  $1.4\text{--}45.1 \times 10^8$ ) and  $2.8 \times 10^6$  ( $0.52\text{--}27.3 \times 10^6$ ) (Fig. 4a). Engraftment data were obtained for 197 patients. Overall median time to neutrophil and platelet engraftment was 20 and 23 days (range: 4–61 and 8–121 days), in agreement with reported data [19,20]. Three (1.5%) patients failed to engraft, all despite TNC doses  $>5 \times 10^8/\text{kg}$ ; two partial engraftments occurred after transplantation of  $2.2 \times 10^8/\text{kg}$  and  $5.2 \times 10^8/\text{kg}$  TNC. Engraftment velocity for platelets or neutrophils was independent of TNC or CD34+ cell dose (Fig. 4b–d), that is the threshold dose for timely engraftment is markedly below typical transplant doses. 46% of grafts contained  $>3 \times 10^6$  CD34+/ $\text{kg}$ , 69%  $>2 \times 10^6$  CD34+/ $\text{kg}$  and 97%  $>1 \times 10^6$  CD34+/ $\text{kg}$  recipient weight. Median engraftment of the twenty patients with the lowest CD34+ cell doses (range:  $0.7\text{--}1.2 \times 10^6/\text{kg}$  recipient weight) was achieved after 23/24 days for neutrophils/platelets.

### Prediction tools for dose and collection volume

Other centres routinely collect 20 ml/kg of donor weight up to 1500 ml. According to that approach, the lowest collection volume in our cohort would have been 1000 ml, the mean 1500 ml. Instead, we individually calculated the BM volume required for each patient. Lowest collection volume thus was 211 ml, mean 914 ml. Our approach reduces the BM collection volume by an average of one unit of RBC. Where BM harvests are limited by donor weight, dose prediction can guide expectations of the transplant centre. For both cases, we developed formulae, based on an aggregate almost 500 donors. We here describe how the formulae were developed to facilitate similar benchmarking exercises in other collection centres:

–Identify formula describing the regression curve (here: linear)

–Identify 5th and 50th percentile for TNC concentration ( $16.8$  and  $25.6 \times 10^3/\mu\text{l}$ )

Thus, target volume is calculated as:

Target BM volume [ml] = requested TNC dose/ $16.8 \times 10^{-6}$  (95% probability).

Where collection volume is limited by donor weight, transplant centres can be informed of doses expected with, for example, 95% probability:

Expected TNC dose ( $\times 10^{-6}$ ) = permissible BM volume [ml]  $\times 16.8$  (95% probability).

The formulae were tested by plotting for each donor observed and calculated TNC dose (Spearman correlation,  $r^2 = 0.72$ ; 95% CI from 0.6747 to 0.7626,  $P < 0.0001$ )

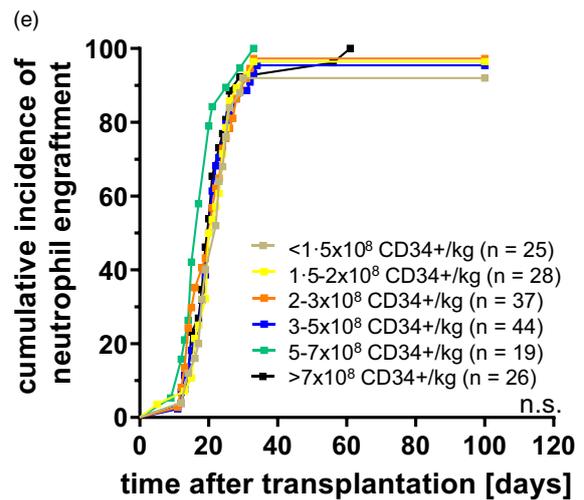
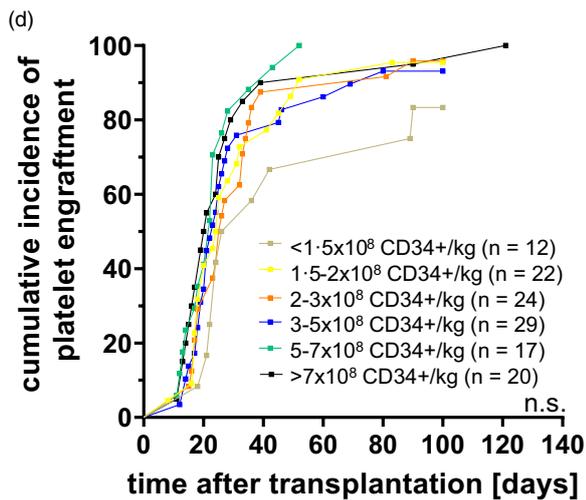
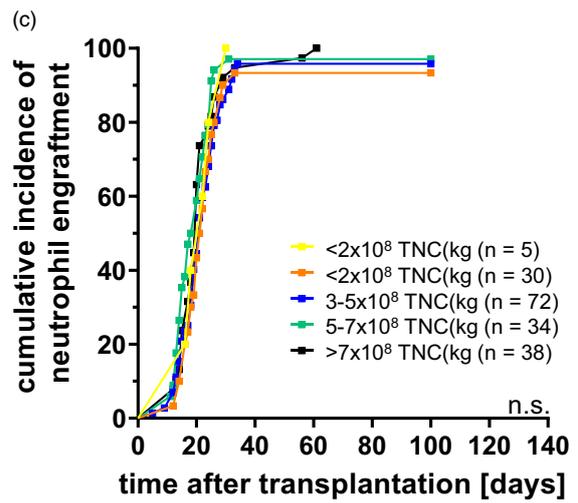
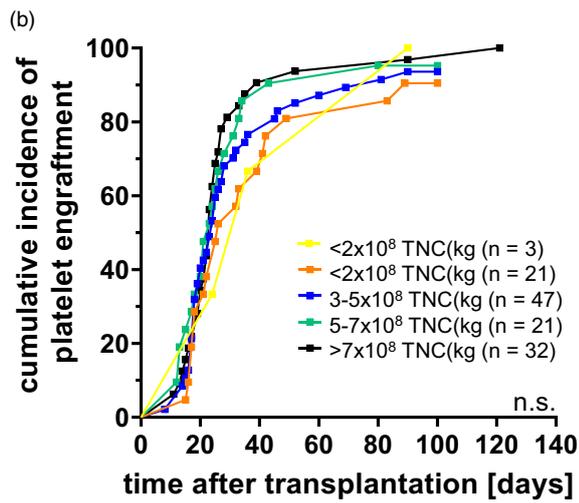
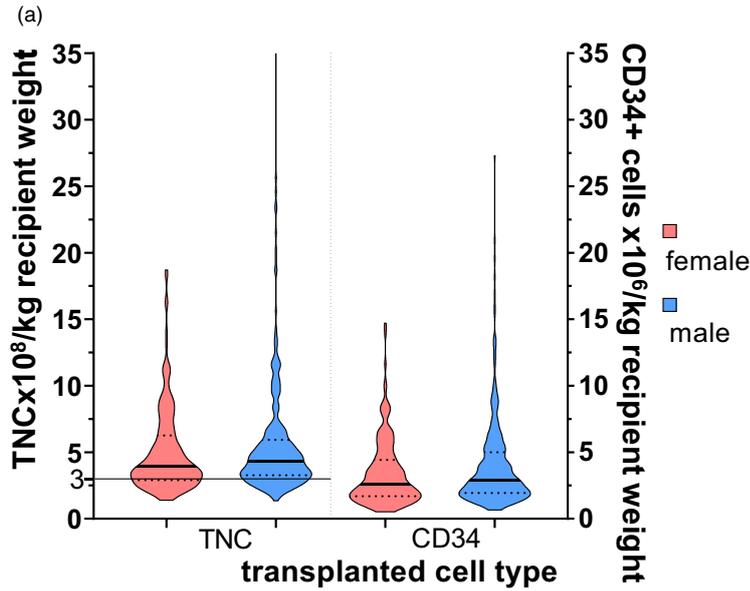
and further validated using an independent in-house validation cohort ( $n = 88$ ) (TNC median/range =  $21.1 \times 10^3/\mu\text{l}/11.5\text{--}43.9 \times 10^3/\mu\text{l}$ ; Pearson correlation  $r^2 = 0.65$ ; 95% CI from 0.5039 to 0.7583,  $P < 0.0001$ ).

### Discussion

Bone marrow grafts have regained importance due to the introduction of haplo-identical BM-post-transplant cyclophosphamide (PTCy)-based regimens [21–25], reflected in steeply increasing BM-PTCy transplantations [4,5]. Data suggesting at least equally good outcomes for haplo-identical first-degree relative PTCy as for MUD transplantation predict a continuing surge of BM harvesting [26]. BM donor blood management has not previously been addressed; guidelines for optimization and standardization of BM collection procedures are lacking. On a cohort of 489 BM donations, we assessed the applicability of PBM principles, that is the ability to maintain optimal graft quality while minimizing donor risks and avoiding RBC transfusions (Fig. 4).

Bone marrow harvests removed considerable amounts of RBCs which was not infrequently symptomatic. Despite an average Hb loss of 26 g/l, severe anaemia necessitating RBC transfusion was never observed. While iron supplementation was offered to all donors with harvest volumes  $>500$  ml, the degree of compliance is unknown but the decrease of ferritin was apparently attenuated by supplementation. Despite our efforts towards Hb-sparing BM collections, at FU one in twelve donors showed some degree of residual anaemia; all had already been mildly or marginally anaemic or hypoferritinemic at donor evaluation. This observation supports pro-active pre-collection Hb management and identifies our current activities as lacking. The missed opportunity to study in appropriate detail effects of iron supplementation on ferritin and Hb dynamics between donor assessment and BM harvest as well as on development and correction of anaemia limits this study.

Previous studies had reported somewhat greater decrease of Hb (29–35 g/L) and slower donor recoveries (2.3–3 weeks) [27–29]. Several factors likely contribute. In several series, in addition to BM, routinely 1–3 units of autologous blood were collected [27,28,30,31]. Foregoing autologous blood collection saves an average of 1.5 RBC units or 90 g of Hb per donor in our cohort, independently validating similar conclusions by others [32,33]. Furthermore, contributing to PBM is our policy of limiting collection volume to  $\leq 15$  ml/kg donor weight compared to 20 ml/kg used in previous reports [27,30,31] and use of individually calculated collection targets. Both together save, on average, another RBC unit =60 g of Hb for each donation. The basis of our



**Fig. 4** Transplant dose and engraftment. (a) Violin plots of transplanted TNC ( $\times 10^8$ ) and CD34+ cells ( $\times 10^6$ )/kg recipient's weight from female/male (pink/blue) donors. Solid and dashed lines mark median and quartiles, respectively. The horizontal line marks the typical target dose,  $3 \times 10^8$  TNC/kg recipient's weight. Cumulative incidences of engraftment data (days, x-axis) of (b, d) platelets ( $n = 134$ ) and (c, e) neutrophils ( $n = 179$ ) after stem cell transplantation of the recipients are plotted according to transplanted TNC (b, c) or CD34+ (D, E) doses. TNC doses are  $< 2 \times 10^8$ /kg (yellow),  $< 3 \times 10^8$ /kg (orange),  $3-5 \times 10^8$ /kg (blue),  $5-7 \times 10^8$ /kg (green) and  $< 7 \times 10^8$ /kg (black). CD34+ doses are  $< 1.5 \times 10^6$ /kg (brown),  $1.5-2 \times 10^6$ /kg (yellow),  $2-3 \times 10^6$ /kg (orange),  $3-5 \times 10^6$ /kg (blue),  $5-7 \times 10^6$ /kg (green) and  $< 7 \times 10^6$ /kg (black). Within the dose ranges applied, a marked dose effect is not apparent.

policy is to protect donor safety, as published reports demonstrate an excessive propensity for arterial hypotension and fainting in donors donating  $>1.5\%$  of body weight [30,31]. Strictly formalized aspiration technique yielding high [34,35] and volume-independently linear [36] TNC concentrations nevertheless ensured high, predictable product quality. TNC concentration is affected by harvesting technique, aspiration needle and physician experience [34,35,37], but also by donor variables such as WBC in blood. The linear volume:dose correlation allowed identification of a divisor,  $16.8 \times 10^{-6}$ , with which to calculate the collection volume which will, with 95% probability, contain at least the targeted TNC dose. Variation in cell yields among collection centres is high and may necessitate higher collection amounts elsewhere, especially in small-volume BM harvesting centres [38,39].

What constitutes an ideal dose of cells in a BM graft has been discussed [40–42]. Dose-independent engraftment data within the narrow range of transplanted doses are presented here solely to serve as evidence of adequate graft quality in light of the practiced donor blood management, not to add to that discussion. Given that donor

weight determines the maximum harvest volume and hence, total TNC dose, the patient:donor weight ratio will occasionally limit suitability of a given donor.

In summary, principles of PBM can be gainfully applied to BM donors. Autologous blood collection is dispensable. Limitation of collection volume to 15 ml/kg donor weight does not impair patient outcome. Target volume should be guided by the requested cell dose. Aggregate donor PBM efforts save, on average, 150 g Hb, equal to 2.5 RBC units, per BM donation.

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## Conflict of interests

The authors declare no conflict of interests.

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## Supporting Information

Additional Supporting Information may be found in the online version of this article:

Fig. S1. Correlation of BM collection volume with TNC and CD34+ cell dose. (a+b) Scatter plots of absolute TNC cell counts (TNCx10<sup>9</sup>, [a]) and CD34+ cell counts (CD34x10<sup>6</sup>, [b]) plotted over BM collection volume (ml), each dot representing one sample of a female (triangle) or a male (circle) donor. (C+D) TNC and CD34+ cell concentrations according to BM collection volume. Column bars (minimum, maximum and mean) for TNC (c) and CD34+ cell concentrations (d) plotted for different BM collection volume cohorts, as indicated. Cell concentration is constant across all harvest volumes.