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ORIGINAL ARTICLE

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The impact of donor type on resource utilisation and costs in allogeneic haematopoietic stem cell transplantation in the Netherlands

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Abstract

Background: Allogeneic haematopoietic stem cell transplantation (HSCT) is increasingly used, but this treatment is complex and costly. As clinical outcomes of HSCT with matched unrelated donor (MUD) and haploidentical donors are similar, costs could influence donor choice.

Method: We retrospectively compared resource utilisation and costs of HSCT using the three different donor types (matched related donor (MRD) ($n = 32$), haploidentical related ($n = 30$) and MUD ($n = 60$)) within the first year after transplantation. Costs were analysed through a bottom-up method. Non-parametric bootstrapping was applied to test for statistical differences in costs. Subgroup analyses were performed to identify predictors for costs.

Results: Cost pre-transplant for search and acquisition of the graft were significantly higher in MUD HSCT (€35 222) versus MRD and haploidentical HSCT (€15 356 and €16 097 respectively). The costs of haploidentical HSCT were the highest in the transplant phase. Main cost factors were inpatient days and medication. Overall, the costs for haploidentical and MUD HSCT were similar (€115 724 for MUD, €113 312 for haploidentical).

Conclusion: Our study suggests no difference in total transplantation costs between allogeneic HSCT using a MUD or a haploidentical donor. Since clinical outcomes seem similar as well, the choice of donor type might be based on availability, speed and logistics.

KEYWORDS
cost drivers, costs, donor type, hematopoietic stem cell transplantation, resource utilisation

Novelty statement:

1. What is the new aspect of your work? General overview of resource utilisation and costs in different donor types for allogeneic HSCT.

2. What is the central finding of your work? No difference of costs between MUD and haploidentical donor transplant.

3. What is (or could be) the specific clinical relevance of your work? Better understanding for clinicians of financial implications treatment choices in HSCT.

1 | INTRODUCTION

Allogeneic haematopoietic stem cell transplantation (HSCT) is an important curative treatment option for many, especially malignant, haematological disorders. Over the last decades, procedures have been changed to make HSCT possible in a larger group of patients and the incidence of HSCT is rising exponentially.[1] However, the treatment is complex, resource intense and thereby costly.[2-4] The most ideal donor is a human leucocyte antigen (HLA)-identical family donor, as it is often easily obtained and clinical results of HSCT with this type of donor are best.[5] Since families in our community are getting smaller, the availability of this type of donor is decreasing. In the last years, there is an increase in the use of alternative donors,[6] like HLA-identical matched unrelated donors (MUD), unrelated umbilical cord blood (UCB) or related haploidentical donors.

When looking for an alternative donor, in only 50%–60% of patients worldwide, an HLA-identical donor can be found in the extensive unrelated donor registries, and for patients from non-European descent, this percentage is even much lower.[7]

A haploidentical donor is a family donor that shares one haplotype with the patient, and differs with a variable number of HLA genes in the other, unshared haplotype. This means that every parent or child can be a suitable donor, and 50% of the siblings. Even second-degree family members still have 25% change to be a haploidentical match. This means that for almost all patients, a haploidentical family donor can be found.[8] This donor type is increasingly used worldwide since the introduction of post-transplantation cyclophosphamide (PTCY).[9,10] Traditionally, when using a haploidentical donor, there was higher incidence of graft-versus-host disease (GVHD) and infections and thereby poor outcomes. However, studies have shown that PTCY has overcome this problem and even though some studies give contradicting results and prospective studies on this subject are lacking, outcomes (especially the composite end-point GVHD-free relapse-free survival (GRFS)) of haploidentical HSCT + PTCY seem quite similar to the outcomes in MUD HSCT.[11-13]

Since outcomes are comparable, the choice between a MUD and haploidentical family donor is difficult and mostly based on local guidelines, or logistical aspects. Perhaps in this case, resource utilisation and thereby costs might be an important aspect in donor choice. Larger studies on costs of allogeneic HSCT are conducted based on insurance claims with limited clinical information and show that allogeneic HSCT, in general, is a very costly treatment with high healthcare resource utilisation, but provide no information about different donor types.[2,14] Smaller studies from hospital perspective are limited and also do not compare costs between MUD and haploidentical donors.[3,15]

As clinical outcomes of HSCT with MUD and haploidentical donors are similar and no other studies have been performed on this subject, we investigated if there was a difference in intervention and hospital care costs between different donor types.

Therefore, the study aims to gain insight into the differences in resource utilisation and costs among matched related donor (MRD), MUD and haploidentical donor HSCT from a hospital perspective looking in the time-period around the HSCT (pre, during and after transplant) and identify the main cost drivers.

2 | MATERIALS AND METHODS

2.1 | Design

We conducted a retrospective cohort study in a contemporary group of adult patients that received an allogeneic HSCT to describe the health resource utilisation and costs of transplantation from a hospital-based perspective.

2.2 | Study population

This retrospective cohort study included consecutive haematological patients treated with an allogeneic stem cell transplantation between January 2016 and September 2018 in the Maastricht University Medical Centre in the Netherlands. The clinical outcome has been published and shows comparable outcome on graft-versus-host free progression free survival in the different groups.[16] Patient characteristics, such as age, sex and diagnosis, were obtained. All patients signed consent forms allowing analysis and dissemination of their outcome data.

2.3 | Three phases of transplantation

We divided the transplantation into three phases: pre-transplantation, transplantation and post-transplantation. The pre-transplantation phase included the donor search and selection and the harvesting of stem cells. The transplantation phase began on the first hospital admission day for the stem cell transplantation procedure, including conditioning, until discharge. The post-transplantation phase was defined as the period from discharge to 1-year after the stem cell transplantation or death if it occurred earlier.

2.4 | Perspective, costs and resource utilisation

We took a hospital perspective and for the identification, all treatment-related hospital activities were incorporated. Data included all relevant treatment activities. In the pre-transplantation phase, only activities for the donor selection (including HLA typing of patient and potential donors, medical examination donors and all costs related to the MUD search and acquisition) and harvesting of stem cells (both peripheral blood as well as bone marrow) were seen as relevant. In the transplantation and post-transplantation phase,

the activities were subcategorised into six cost groups: inpatient days, outpatient visits (including day care), intensive care admission, medication, blood products, laboratory and other activities (e.g. endoscopy and radiation).

For the resource use measurement, data were obtained from the hospital information system provided by System Applications and Products (SAP) that included detailed information about all relevant inpatient treatment activities. In addition, we collected information from electronic patient documents (EPD). For the pre-transplant phase, we only collected data on the number of potential donors that we tested for HLA type for every patient to find a suitable match. We divided them in potential family donors and unrelated donors. For the transplant phase, we examined inpatient days, intensive care unit (ICU) admission and blood product use for all different donor types since these are activities are costly and also well registered in the information systems.

For the valuation, costs were calculated by multiplying recorded units of healthcare resources used with corresponding unit prices.[17] Most of the unit costs were taken from the Dutch Manual for Healthcare Costing Research.[17,18] For costs of medical procedures that were not available in this manual, the tariffs from the Dutch healthcare authority (NZa) were used. Medication costs were calculated per unit based on the price per dosage of the drug in the Netherlands (medicijnkosten.nl) and multiplied by the total dosage given.

The index year for the study is 2020, and all cost-prices are updated to this year using consumer prices indices.[19]

2.5 | Analysis

For baseline characteristics, categorical variables were expressed as number and proportion and continuous variables as median and range. Differences between baseline characteristics of the different groups were calculated using a Pearson's Chi-squared test for categorical variables and a one-way ANOVA for continuous variables. Mean transplantation costs per patient were calculated for each phase and per cost category. The 95% confidence interval (CI) was determined using non-parametric bootstrapping with 5000 iterations (resampling with replacement) and was used to test for statistical differences in costs between different donors.[20] If costs were not overlapping, they were considered significantly different. The main cost drivers for each type of SCT were identified by calculating the proportion of total costs of each cost group. Differences in resource utilisation between groups were calculated with one-way ANOVA. Multiple linear regression was used to investigate the association among baseline characteristics (disease risk index (low/intermediate versus high/very high), age (<40, 40–60, >60 years), stem cell source (peripheral blood versus bone marrow), myeloablative conditioning (MAC) (yes or no), the occurrence of clinical events (early death (within 100 days after transplantation), death 100 days to 1 year after transplantation, relapse, all grades of GVHD, acute GVHD grade III/IV, chronic GVHD, the occurrence of cytomegalovirus reactivation/disease and intensive care unit (ICU) admittance)) and total costs. For all analyses, a p-value under .05 was considered significant. The analyses were performed using Microsoft Excel 2016 and SPSS, version 25.

3 | RESULTS

A total of 122 patients receiving HSCT were included in the analysis; 32 with MRD, 60 with MUD and 30 haploidentical family donors. Patient characteristics are listed in Table 1 and are similar in all three groups.

The median age was around 60 years, and there was a slight male predominance. Acute myeloid leukaemia was the most common diagnosis in all groups; disease risk index (DRI) was most frequently intermediate. Besides donor type, there were more differences in transplantation strategy between the groups. All patients receiving a haploidentical stem cell transplantation received post-transplantation cyclophosphamide (PTCY) as part of the GVHD prophylactic therapy, and none of the patients in the other groups did. The main stem cell source in patients with a haploidentical donor was bone marrow (90%), in both other groups it was peripheral blood (97 and 95% respectively) ($p < .0001$). A variety of conditioning regimens was used during the study period based on donor, patient and disease type, but 93% of patients in the haploidentical cohort had myeloablative conditioning, versus 13% in MRD and 23% in MUD ($p < .0001$). Furthermore, significantly more patients with a MRD and a MUD donor received TBI as part of the conditioning regimen (MRD 78%, MUD 80% and haploidentical 10%; $p < .0001$).

3.1 | Costs and healthcare resource utilisation

3.1.1 | Pre-transplantation phase

Table 2 presents the mean costs and health resource utilisation for the pre-transplantation phase for all donor types. The mean costs for a MUD were significantly higher than for the other types of donors (€35 222 versus €15 356 for MRD and €16 097 for haploidentical donor). The mean costs for graft acquisition in MUD were €19 050. To identify an appropriate haploidentical donor, HLA typing was done on average only one extra family member. However, the total amount of potential donors that were HLA typed was similar in each group.

3.1.2 | Transplantation phase

Table 3 presents the mean costs for the transplantation phase for all donor types. The mean costs for a haploidentical HSCT were significantly higher than for a MRD and MUD HSCT (€59 568, €35 874 and €42 154 respectively). Inpatient days are the largest cost category in all groups. In haploidentical HSCT, the second

TABLE 1 Patient and transplantation characteristics

Characteristic	MRD ($n = 32$) No. (%)	MUD ($n = =60$) No. (%)	Haplo ($n = =30$) No. (%)	p value
Median age (range) (years)	60.0 (23–71)	58.5 (21–76)	60.3 (19–74)	.87
Sex				
Male	22 (69)	34 (57)	20 (67)	.45
Female	10 (31)	26 (43)	10 (33)	
Diagnosis				
AML	14 (44)	19 (31)	16 (53)	.33
ALL	3 (9)	5 (8)	6 (20)	
MDS/MPN	5 (16)	16 (26)	6 (20)	
NHL/HL	6 (19)	16 (26)	2 (7)	
Other	4 (13)	4 (7)	0	
Disease risk index				
Low	4 (13)	4 (7)	0 (0)	.27
Intermediate	18 (56)	37 (62)	17 (57)	
High/very high	10 (31)	19 (32)	13 (43)	
Stem cell source				
PBSC	31 (97)	57 (95)	3 (10)	<.0001
BM	1 (3)	3 (5)	27 (90)	
Conditioning intensity				
MAC	4 (13)	14 (23)	28 (93)	<.0001
NMA/RIC	28 (87)	46 (77)	2 (7)	
TBI-based conditioning	25 (78)	48 (80)	3 (10)	<.0001
1-year OS	18 (44)	29 (48)	14 (47)	.71
1-year relapse	4 (13)	13 (22)	1 (3)	.06
Acute GVHD, all grades	7 (22)	23 (38)	6 (20)	.11
Acute GVHD, grade III/IV	2 (6)	10 (17)	1 (3)	.10
1-year chronic GVHD	4 (13)	11 (18)	2 (7)	.31
1-year CMV reactivation/ disease	5 (16)	19 (32)	6 (20)	.19

Abbreviations: ALL, acute lymphatic leukaemia; AML, acute myeloid leukaemia; BM, bone marrow; CMV, cytomegalovirus; HL, Hodgkin's lymphoma; MDS, myelodysplastic syndrome; MPN, myeloproliferative neoplasia; NHL, non-Hodgkin's lymphoma; NMA, non-myeloablative; OS, overall survival; PBSC, peripheral blood stem cells; RIC, reduced intensity conditioning; TBI, total body irradiation.

cost category was medication; in MRD and MUD HSCT, this was the third cost category. The costs of medication, blood products, laboratory tests and other costs were significantly different between donor types. The difference in other costs was almost fully explained by the difference in costs of radiation as part of the conditioning regimen.

Table 4 represents the resource utilisation of all donor types. The total length of stay of patients receiving a haploidentical donor HSCT was significantly longer (mean 36.67 days) compared to MRD (23.81 days) and MUD (24.77 days), $p < .0004$. There was no significant difference in the number of patients that needed to be admitted at the intensive care unit (ICU) and in the mean length of stay on ICU. However, there was a trend for an increased ICU admission in haploidentical HSCT compared to MRD that probably failed to have significance due to low numbers. In addition, the use of blood products in the haploidentical HSCT was more than double compared to MRD and MUD HSCT.

Since there was a large difference in medication costs and they were a significant cost driver in haploidentical HSCT, we divided the medication into seven categories: antibacterial agents, antifungal agents, antiviral medication, chemotherapy, immunoglobulins and all other medication. The percentages of costs in the different medication categories are presented in Figure 1.

Most striking is the difference in the use of chemotherapy between haploidentical HSCT versus MRD and MUD HSCT. The explanation for this is that in the haploidentical group, almost all

TABLE 2 Costs and resource utilisation in pre-transplantation phase

	MRD ($n = 32$)	MUD ($n = 60$)	Haplo ($n = 30$)	p
Pre-transplantation costs, mean (95%CI)	€15 356 (13 581–17,511)	€35 222 (32 993–37 656)	€16 097 (14 141–18 324)	
Family members HLA typed, mean (range)	2.94 (1–7)	1.53 (0–4)	3.93 (1–13)	<.0001
Unrelated donors HLA typed, mean (range)	0.25 (0–3)	2.57 (1–6)	0.57 (0–4)	<.0001
Total potential donors HLA typed, mean (range)	3.19 (1–8)	4.10 (1–8)	4.50 (1–14)	.06

TABLE 3 Costs during transplantation phase

	MRD ($n = 32$)	MUD ($n = 60$)	Haplo ($n = 30$)
Transplantation costs, mean (95%CI)	€35 874 (27 944–45 370)	€42 154 (33 237–52 270)	€59.568 (52 843–66 806)
Medication costs, mean (95% CI) % of total costs	€6514 (2942–12 629) 11.9	€5320 (3034–7970) 9.7	€14 870 (12 780–16 988) 25.0
Costs inpatient days, mean (95% CI) % of total costs	€16 122 (13 047–19 923) 49.0	€15 432 (13 502–17 527) 45.4	€23 274 (20 820–25 760) 41.6
Blood product costs, mean (95% CI) % of total costs	€2936 (1779–4407) 6.8	€3348 (2544–5079) 7.2	€8456 (6735–10 298) 13.6
ICU costs, mean (95% CI) % of total costs	€817 (0–2802) 0.6	€5231 (888–11 658) 4.1	€6175 (1482–11 648) 7.6
Laboratory costs, mean (95% CI) % of total costs	€2916 (2248–3680) 8.2	€3069 (2491–3715) 7.7	€5814 (5066–6619) 10.1
Other costs, mean (95% CI) % of total costs	€6569 (4627–9631) 23.5	€9354 (6282–13 271) 26.0	€980 (337–1751) 2.1

TABLE 4 Resource utilisation in the transplantation phase

	MRD ($n = 32$)	MUD ($n = 60$)	Haplo ($n = 30$)	p
Length of stay on transplantation ward, mean (days) (range)	23.44 (9–85)	22.37 (6–53)	33.83 (15–57)	<.0001
Number of patients with ICU admission (percentage)	3 (9.4)	6 (10.0)	8 (26.7)	.07
ICU admission, mean (days) (range)	0.38 (0–12)	2.4 (0–73)	2.83 (0–24)	.41
Number of transfusions, mean (range)	8.09 (0–43)	9.95 (0–50)	20.23 (4–50)	<.0001

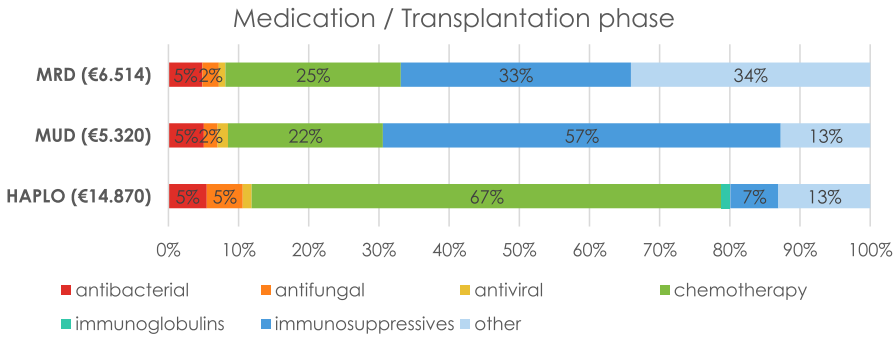

FIGURE 1 Mean percentage of medication costs per category for every donor type in the transplant phase

conditioning was chemotherapy based with thiotepa combined with fludarabine and busulphan. Thiotepa is expensive and mainly responsible for the difference medication costs in the transplant phase of the haploidentical group (€6233). Most patients in the MRD and MUD groups had a conditioning regimen with a combination of fludarabine, which is much cheaper than thiotepa, and total body irradiation (included in the other costs category, €6200). The difference in costs of immunosuppressive therapy between HLA-identical

and haploidentical HSCT is caused by the use of high dosage of anti-thymocyte globulin in myelofibrosis; in this disease category, there is a strong preference for a MRD or MUD according to local protocol.

3.1.3 | Post-transplantation phase

Table 5 presents the mean costs for the post-transplantation phase for all donor types. Like in the transplant phase, inpatient days were still the largest cost category in all groups, followed by medication and laboratory costs. All costs and the division of costs between subcategories were similar in the three groups.

Table 6 represents the resource utilisation in the post-transplant phase. There were no significant differences in resource utilisation (length of stay, ICU admission, number of re-hospitalisations and the use of blood products) for the different donor types.

In Figure 2, percentages of costs in the different medication categories are presented. The most striking difference here is the increased costs for immunoglobulins in the haploidentical HSCT. This high usage was caused by the standard use of immunoglobulins on several time points in our initial protocol for haploidentical HSCT. Another difference is the use of immunosuppressive medication between haploidentical HSCT versus MRD and MUD HSCT, which was caused by the use of ruxolitinib and anti-thymocyte globulin for GVHD in the last two groups.

3.2 | Total transplant costs

The total transplant costs for the patients that reached all transplant phases were similar for MUD ($n = 56$) and haploidentical donor ($n = 24$) HSCT (€115 724 (95%CI 103 858–128 836) for MUD and €113 312 (95% CI 95 910–131 583) for haploidentical donor HSCT). However, MRD ($n = 29$) HSCT seems the cheapest option (€92 331 (95% CI 76 384–111 447)). In the pre-transplantation phase, the total costs for the patients that reached all transplant phases were similar to the patients that died during the transplantation phase. In the transplantation phase, dying patients on average cost €5000 more than the surviving patients. There were no significant differences in the mean observation time after HSCT between groups (MRD: 275 (94–365) days, MUD: 236 days (46–365) and haplo: 245 days (17–365), $p = .37$).

TABLE 5 Costs in the post-transplantation phase

	MRD ($n = 29$)	MUD ($n = 56$)	Haplo ($n = 24$)
One-year post-transplantation costs, mean (95%CI)	€45 626 (28 794–65 007)	€41 927 (33 409–51 221)	€42 695 (27 825–58 280)
Medication costs, mean (95% CI) % of total costs	€10 530 (6660–15 204) 24.2	€11 720 (7287–15 420) 20.8	€6337 (4117–8828) 22.4
Costs inpatient days, mean (95% CI) % of total costs	€19 119 (10 983–29 273) 29.9	€17 111 (12 467–22 274) 34.4	€13 127 (6687–21 048) 24.2
Blood product costs, mean (95% CI) % of total costs	€4034 (1742–7027) 7.4	€3236 (2278–4276) 7.9	€5510 (2189–9567) 9.1
ICU costs, mean (95% CI) % of total costs	€2104 (363–4474) 2.4	€3386 (1055–6209) 4.7	€8172 (2076–15 801) 12.6
Laboratory costs, mean (95% CI) % of total costs	€7075 (5043–9495) 22.9	€7105 (5741–8626) 20.0	€7158 (4870–9740) 20.8
Outpatient visit costs, mean (95% CI) % of total costs	€1691 (1343–2052) 9.3	€1701 (1421–1988) 7.9	€1458 (960–2056) 7.8
Other costs, mean (95% CI) % of total costs	€1073 (675–1537) 3.9	€1580 (940–2523) 4.4	€932 (535–1429) 3.2

TABLE 6 Resource utilisation in the post-transplantation phase

	MRD ($n = 29$)	MUD ($n = 56$)	Haplo ($n = 24$)	p
Length of stay on transplantation ward, mean (days) (range)	28.21 (0–168)	24.89 (0–140)	19 (0–103)	.53
Intensive care unit admission (days) (range)	0.97 (0–10)	1.55 (0–23)	3.75 (0–27)	.13
Number of re-hospitalisations during first year, mean (range)	1.83 (0–7)	1.86 (0–6)	1.29 (0–4)	.27
Number of transfusions, mean (range)	11.55 (0–74)	10.14 (0–48)	15.08 (0–87)	.49

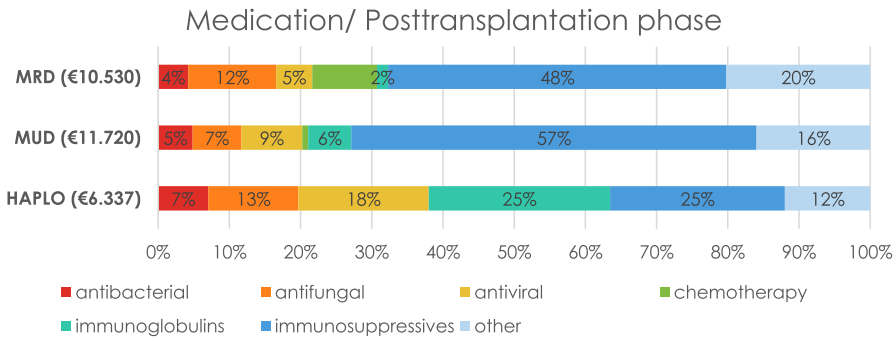

FIGURE 2 Mean percentage of medication costs per category for every donor type in the post-transplant phase

3.3 | Multivariate analysis

The model estimating the costs of complications included both baseline data and clinical events and was calculated with the total transplant costs over all phases. Among all the transplant recipients, significant increased costs were associated with CMV reactivation/disease (€31 366, $p = .001$) and death 100 days to 1 year after transplant (€42 407, $p < .0001$). Lower costs were seen with relapse (−€42 047, $p = .0002$) and early death (within 100 days after transplantation) (−€27 974, $p = .008$). We did not find an association between costs and the occurrence of all grades of acute GVHD, acute GVHD grade III/IV, chronic GVHD and ICU admittance. However, especially for severe acute GVHD and ICU admittance numbers might just have been too low to reach significance. We also did not find an association between any of the baseline characteristics of patients and transplant analysed (donor type, disease risk index, age, stem cell source, myeloablative conditioning). The r^2 of the model was 0.316. Analysis of only transplant and post-transplant phase together led to similar results.

4 | DISCUSSION

This single-centre study aimed to gain insight into the differences in costs among MRD, MUD and haploidentical donor HSCT from a hospital perspective (pre-, during and post-transplantation) and identify the main cost drivers.

In the pre-transplant phase, the mean costs for MUD were much higher than for MRD and haploidentical donors due to the costs of graft acquisition (mean €19 050). The number of potential donors that were HLA typed was similar in each group.

In the transplantation phase, using a haploidentical donor was most expensive since these patients were hospitalised longer, and with a haploidentical HSCT, more resources like medication and blood products were used. This difference in resource utilisation in the transplant phase is most likely caused by the increased use of myeloablative conditioning regimens in haploidentical HSCT, the use of bone marrow as graft source and the use of PTCY as GVHD prophylaxis, which all lead to longer and deeper cytopenia. During the time of the study, we did not use PTCY as GVHD prophylaxis in MRD and MUD allogeneic HSCT which might now been seen as standard treatment.[21] This might have an influence on the costs of MRD and MUD HSCT. In the last 10 months, we performed 14 HLA-identical HSCT (11 MRD and 3 MUD) using PTCY as GVHD prophylaxis. In those patients, the mean duration of hospitalisation in the transplant phase was 34.42 days, which is 10 days more than before and comparable with the hospitalisation in haploidentical HSCT. Those ten days of hospitalisation will cost only €6880, but the longer cytopenia will probably also lead to an increased use of blood products, medication and laboratory test as that has been seen by the haploidentical transplantations.

Noteworthy is also the effect of the conditioning regimen on costs. Haploidentical HSCT were mostly conditioned with thiotepa, busulphan and fludarabine, MRD and MUD mostly with fludarabine and total body irradiation (TBI). The use of thiotepa is the most important cost driver of the conditioning in haploidentical HSCT, but these costs are similar to the costs of TBI in MUD and MRD HSCT (€6200).

In the post-transplant phase, costs and resource use were equal among all three groups. In total, no significant difference in cost was seen between HSCT from MUD or haploidentical donors. None of the baseline characteristics of patient or transplant was predictive for higher costs. In addition, the use of bone marrow instead of peripheral blood in haploidentical HSCT did not have an effect on the costs. It is intuitive that occurrence of major complications would increase costs of transplantation. However, in this population, we only could see a significant raise in costs with CMV disease/reactivation and death between 100 and 365 days after transplantation. The costs of these complications are foremost related to long hospitalisation, ICU admittance and the use of expensive medication when having these complications. In these patients, we did not use the new antiviral drug letermovir as CMV prophylaxis in high-risk groups yet. It would be interesting to investigate the effect of letermovir on costs, since this treatment is very expensive (€32 700 for 100 days in the Netherlands) but could lead to a significant decrease of CMV disease/reactivation, which is also one of the major cost drivers in HSCT.[22]

No significant effect on costs was seen with acute GVHD. This is surprising in the light of findings of another investigator that did see increased costs with acute GVHD, but in this study almost double the number of patients were included and it was performed in the US where healthcare costs might be different than in the Netherlands.[23] Furthermore, we showed that in our situation, patients with early death within 100 days had lower costs, and so did patients with relapsed disease.

At the time of the study, there was a preference for a 10/10 MUD over a haploidentical family donor in our centre, and tests were done to find a potential MUD donor even though there was already a haploidentical family donor present. If there is no preference between MUD and haploidentical donors, it could reduce the number of potential donors to analyse, and thereby reducing costs. Recently, because of logistical problems with MUD due to COVID-19, we decided to change standard policy now choose a haploidentical family donor over a MUD if possible. Since that change, we had an increase in haploidentical donor HSCT at the cost of MUD HSCT (in the last months, 16 haploidentical donors versus 10 MUD, before 30 haploidentical donors versus 61 MUD, unpublished observation). In addition, by this strategy, it could be possible to save some costs for HLA typing a MUD donor if a haploidentical family donor is found.

There are several limitations to this study. One of them is the limited number of patients per group and the heterogeneity within and between groups. Furthermore, as in any single-centre study, some conclusions might be specific to our centre and reflect our specific patients and practice. Costs are also very sensitive to country rules and regulations and might only reflect our local Dutch situation. That is why we presented most of the data also with number of events, so that local cost can be calculated from these parameters as they might differ from ours. We obtained our real-world data from the hospital registration system, medical patient files and electronic information systems. Our results depend on the completeness of registration, and unregistered hospital activities were not included in our study. No costs for home-care services and other providers were included in the study, since they were thought to only make a very small contribution to the total costs of transplantation. However, all these factors might have caused an underestimation of actual costs. Even more, in the pre-transplantation phase, we decided only to gather data on search, selection and acquisition of the graft. This excludes various other activities that are done in preparation for the stem cell transplantation, such as consultations, laboratory tests and pulmonary and cardiac function tests. However, these activities are not very costly and it is difficult to differentiate between the use of the health resources in light of transplantation and other treatments, such as remission-induction therapy. Most other activities in this phase were more likely to be connected with disease characteristics and not transplantation and are thought to be not different between the donor groups as the availability of a certain type of donor is not connected to the type of treatment before transplantation and can be considered biological randomisation. However, this could explain that the total costs we calculated are lower than in the study by Blommestein et al. that also took place in the Netherlands.[3] Additionally, we only regarded costs from a hospital perspective, and not from a societal perspective. Furthermore, since we performed hardly any UCB HSCT, we were not able to compare the costs of this donor type. Noteworthy is a recent retrospective study on outcomes between MUD HSCT + PTCY versus haploidentical HSCT that showed an OS advantage of MUD in the RIC setting.[24] In that case, outcome is more important than costs. However, in the only prospective study on the effect of PTCY compared to traditional GVHD prophylaxis (with 69% MUD HSCT and 99% RIC), this survival advantage was not seen.[21]

Even though there are all these limitations, we believe that our results can be informative for centres that want to determine best donor choice also with respect to costs. These data can also be useful for other centres to determine opportunities to adapt protocols to decrease costs and health resource utilisation in HSCT, for instance, by replacing more expensive conditioning regimens or to use outpatient care in eligible HSCT candidates.

In summary, our study suggests that there is no substantial difference in total transplantation costs between allogeneic HSCT using a MUD and a haploidentical donor using the procedure described. Since clinical outcomes are similar as well in our procedure, the choice of donor type might be based on availability, speed and logistics. However, costs will only be comparable in the future, if the choice of donor and protocol has no influence on cost drivers, like post-transplant cyclophosphamide. A substantial cost driver in MUD HSCT, that will not change by changing the clinical procedure, is the graft acquisition (15% of the total costs). However, if the adaptation of protocols leads to a difference in GRFS between different donor types, the cost factor might be less relevant.

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CONFLICT OF INTEREST

The authors have no relevant conflicts of interest.

DATA AVAILABILITY STATEMENT

Data Available on reasonable request from the corresponding author.

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