Universiteit Leiden
The Netherlands

Perspectives on decision making in hematopoietic stem cell transplantation

Mekelenkamp, H.

Chapter 07

General discussion

Introduction

Hematopoietic stem cell transplantation (HSCT) is a curative treatment option for a broad spectrum of oncological and non-oncological diseases. Indications for HSCT can either have an urgent or a more elective character. Decision making is often more complex in these latter situations, and pros and cons depend on individual values.

With this thesis, we aimed to enrich the existing knowledge on decision making for pediatric patients with in-depth insights of patients, caregivers, and healthcare professionals (HCPs) considering an HSCT in circumstances in which there is no clear-cut answer on what the best option for the individual patient is.

Three main concepts were identified and developed within this thesis. Chapter 4 identified the theme 'frame of reference' from the HCPs' perspectives[1]. From the patients' and caregivers' perspectives, Chapter 6 described the 'hope for a normal life' as a guiding principle; and from the caregivers' perspectives, Chapter 2 and 6 identified 'being a good parent'[2,3]. We will discuss these three themes in the current chapter. Based on the described concepts, we recommend a specified framework that can be integrated into the clinical practice of decision making of patients with a hemoglobinopathy considering HSCT as a curative treatment option. Lastly, this chapter will outline future perspectives and reflect on the research methods.

Main concepts in HSCT decision making

Frame of reference

The results of our study reported in Chapter 5, showed that HSCT decision making in patients with a hemoglobinopathy significantly varied among HCPs[4]. When asked to judge hypothetical scenarios, HCPs made different choices based on varying explanations. We wondered whether these differences were related to respondent characteristics. Unfortunately, our sample size was not diverse and large enough to achieve acceptable statistical power for tests of interaction effects. However, our qualitative study in Chapter 4 showed that an important

influencing factor for HCPs in HSCT decision making for patients with a hemoglobinopathy appears to be their frame of reference[1]. HCPs' knowledge and past experiences directed their thoughts, considerations, and actions toward whether or not to offer and discuss the options of HSCT. HCPs also underlined the importance of a guided decision-making process. For HCPs with less experience with HSCT, translating this (limited) knowledge into balanced counseling of candidate patients was difficult. Previous experiences with individual patients impacted HCPs' views, especially when outcomes after HSCT in an individual case were unfavorable. Insights in the mostly positive outcomes of a larger cohort put the unfavorable outcome in individual cases in a different perspective for HSCT physicians. In line with shared decision making (SDM) principles, counseling patients for a possible HSCT includes providing information, exploring the patients 'values, hopes, and preferences, and integrating these with the available options[5]. Integrating patients' preferences with treatment options demands knowledge and experience of HCPs regarding the disease and treatment possibilities. In addition, patients and caregivers highly value being guided by the expertise of a knowledgeable HCP, as described in Chapters 2 and 6, because they will never have the same competence as HCPs[2,3]. A trustful physician-patient relationship is a vital condition to support patients in decision making, as also mentioned in Chapter 4 by HCPs[1].

Theoretically, four models of the physician-patient relationship can be distinguished: the paternalistic, informative, interpretative, and deliberative model, as described by Emanual and Emanuel[6], see Table 7.1. Depending on the clinical context, different models may be opportune, where, according to Emanuel and Emanual, the deliberative model is ideal[6]. A previous qualitative study found that physicians used a continuum of approaches in decision making for patients with sickle cell disease (SCD). Depending on different patient- and disease-related factors, physicians used a more collaborative approach at one end of the continuum or a proponent at the other, comparable with the deliberative versus paternalistic approach as described by Emanuel and Emanuel[6,7]. In Chapter 4, we found that HCPs acknowledged the importance of a guided decision-making process[1]. Within this guiding process, we found that HCPs used a more convincing or conservative (paternalistic versus deliberative) approach based on the disease, disease severity or -burden, their knowledge,

and past experiences[1]. Individualized information provision was found to be highly important within the decision-making process.

TABLE 7.1 - Comparing the four models of the physician-patient relationship according to Emanuel and Emanuel, Table from Emanuel and Emanual[6].

	INFORMATIVE	INTERPRETIVE	DELIBERATIVE	PATERNALISTIC
PATIENT VALUES	Defined, fixed, and known to the patient	Inchoate and conflicting, requiring elucidation	Open to development and revision through moral discussion	Objective and shared by physician and patient
PHYSICIAN'S OBLIGATION	Providing relevant factual information and implementing patient's selected intervention	Elucidating and interpreting relevant patient values as well as informing the patient and implementing the patient's selected intervention	Articulating and persuading of the most admirable values as well as informing the patient and implementing the patient's selected intervention	Promoting the patient's well-being independent of the patient's current preferences
CONCEPTION OF PATIENT'S AUTONOMY	Choice of, and control over, medical care	Self-understanding relevant to medical care	Moral self-development relevant to medical care	Assenting to objective values
CONCEPTION OF PHYSICIAN'S ROLE	Competent technical expert	Counselor or adviser	Friend or teacher	Guardian

An important reason for a deliberative approach is respect for autonomy[6]. Respecting the autonomy of patients and caregivers includes exploring and integrating their values, hopes, and preferences in the treatment options as part of SDM. Our study analyzing conversations between patients and physicians in Chapter 3 confirmed more objectively the results found in Chapter 4 that informing patients was the most prominent aspect of SDM but that exploring preferences could be given more attention[1,8].

Respect for autonomy is a main principle of biomedical ethics described by Beauchamp and Childress, together with the principles of *beneficence*, *nonmaleficence*, and *justice*[9]. *Respect for autonomy* refers to respecting the right of individuals to make their own decisions autonomously. It includes respect for their opinions, choices, and way of living. The patient must act autonomously, choose voluntarily, and be well-informed with all information about treatment

options. The principle of *beneficence* refers to the HCP's obligation to act for the best benefit of the patient and promote their welfare. The principle of *nonmaleficence* refers to the obligation first to do no harm to the patient. This means carefully weighing the harms and benefits to the individual patient. If the harms outweigh the benefits, the HCP will refrain from acting. Acting according to the principle of *justice* means that equal cases should be approached equally, and unequal cases should be treated unequally. This includes treating individuals fairly, equitably, and appropriately[10].

All four principles of biomedical ethics play a role in physicians' considerations regarding HSCT decision making based on their frame of reference, it may result in varying approaches or accents on one of the principles. As described in Chapter 4, the frame of reference influenced the HCPs' considerations, and this may also lead to counseling differently[1]. Chapter 5 showed a heterogeneity in considerations of HCPs regarding HSCT decision making for patients with a hemoglobinopathy[4]. Different ethical principles may be leading. Some HCPs may counsel more from the principle of beneficence or respect for autonomy, whereas others counsel more based on the principle of nonmaleficence or justice. HCPs in HSCT decision making may consider beneficence in offering a curative treatment option (HSCT) where they feel it could benefit the patient, improving their quality of life and life expectancy. This also includes the potential risks of the disease when no curative treatment is offered. With this frame of reference, counseling in successive cases could be more based on beneficence or respect for autonomy. HCPs may consider nonmaleficence while overthinking the potential risks of the HSCT and, therefore, consider supportive care as the best option or wait for better therapies, which could be of benefit with probably less harm. This could potentially lead to not discussing the possibility of HSCT because physicians feel discussing HSCT offers hope while they are not convinced it will meet those benefits. For instance, a referring HCP can have a negative experience with HSCT because a referred patient passed away during HSCT or ended with severe post-HSCT complications. These HCPs might be reluctant to offer or discuss HSCT because they want to protect patients from harm (non-maleficence) and a more protective (paternalistic) approach may be practiced. Justice may also play a role, as physicians feel they need at least counsel for curative treatment options equally to all patients of the same

category. Subsequently, the patient can opt for this possibility based on respect for autonomy. Justice may also play a role in low and middle-income countries where costs for HSCT and potential complications cannot be justified for specific patient categories, for example patients with SCD and less severe disease trajectories without an HLA-identical donor. How ethical principles are weighed depends on the frames of reference of HCPs, gained knowledge and experience and personal beliefs. These frames of reference are different for every HCP involved in the care of patients with hemoglobinopathies and are potentially subject to variation over time.

Hope for a normal life

As an underlying theme in our research on HSCT decision making for patients with a hemoglobinopathy, the hope for a normal life was guiding for both patients and caregivers. This hope guided the balancing of the risks and benefits of either HSCT or supportive care. A normal life is directed to the wish of having a future perspective with a good quality of life and a comparable life course as healthy peers. Previous research in HSCT decision making for patients with a hemoglobinopathy also identified the hope for a normal life as a decision-making factor[11,12]. Our study on end of life (EOL) decision making, showed that parental HSCT decision making relies on a strong survival-oriented hope. HSCT brought the possibility to sustain a future perspective for their ill child and parents focused on the hope for a good outcome. Almost all children in this latter study had an oncological or acute non-oncological disease and needed a short-term HSCT as a lifesaving, protocolized intervention. Therefore, decision making was different for this group of parents, where HSCT was a more intuitive step than for patients with a hemoglobinopathy. Parents followed the opportunity for survival according to care standards suggested by HCPs rather than that they experienced deciding themselves. This distinction in decision making for HSCT in an acute or elective care setting is also described in the literature, where comparable differences were found between patients with oncological and non-oncological diseases[13].

The role of hope is in the literature conceptualized as an expectation (referring to appraisal of a future outcome), resilience (referring to endurance of adversity), and a desire (referring to expression of meaning)[14]. All these three concepts of

hope were underlying in patients considering HSCT or supportive care as described in Chapter 6, labeled as hope for a normal life. Different aspects directed the hope, such as a more acute or plannable HSCT, the underlying disease, (experienced) disease impact, transplantation-related complications, and personal experiences[2]. The role of hope is mainly described as supportive in the literature. In adolescents with a chronic illness, hope promotes health, facilitates coping and adjustment, is essential in finding purpose in life and illness, improves self-esteem, is an important factor in resilience, affects maturation, and correlates positively with quality of life[15,16]. Interestingly, hope-inspiring relationships with especially peers were described as contributing factors[14]. We identified a strong wish for peer contact, mainly meant to broaden the patients' and caregivers' frame of reference. From a theoretical point of view, peer contact could also foster hope. At the same time, it could be wondered what effect less positive peer experiences could have because loss could negatively impact hope.

An ethical issue related to hope in healthcare in different circumstances was described previously concerning palliative care, focusing on the tension between hope and truth/realism[14]. Within HSCT decision making this tension also can be recognized, where the concepts of hope and realistically addressing all potential harms could be conflicting. From the patient's perspective, hope could probably function as looking away from or being blind to potential risks of either HSCT or supportive care. From the HCPs perspective, on the one hand, it is felt important to sustain hope because of its supportive character. Most HCPs know those patients who said, "No doctor, don't tell us (or my child) all the details that can go wrong; we want to be positive; all those complications make me anxious." On the other hand, realistic information needs to be given as part of the consent procedure and to prepare patients and families honestly.

Being a good parent

The hope for a normal life is described in the literature as a common verbal expression used by parents intended as a guiding principle while making decisions for their child with a life-threatening illness[17]. For proxy decision makers, the hope for a normal life is part of their parental guiding principles, covering more values, such as 'I want my child to be comfortable,' 'I want my child to have quality of life,' or 'I don't want my child to be in pain'[17]. In our study

on EOL decision making in Chapter 2 among bereaved parents of mainly children with malignant diseases, we observed that parents' perspectives on the meaning of good parenthood were underlying in decision making[3]. Decision making was survival- and cure-directed, where parents felt guided by HCPs rather than feeling to make their own decisions. Parental decision making reflected the following themes in this (survival-oriented) decision-making process: a) developing a frame of reference around the HSCT, b) having confidence in and hoping for a good outcome, c) preventing themselves from anticipated regret, d) advocating to get the most out of treatment, e) keeping going, and f) following their child's wishes. Parents convinced themselves that all possibilities for their children's survival were used. But in hindsight, they also doubted treatment decisions, which could have been turning points toward recovery and treatment decisions made with hope for cure but resulted in more suffering.

In our study on HSCT decision making for patients with a hemoglobinopathy in Chapter 6, we found that parents also used underlying parental values while considering HSCT or supportive care for their child[2]. These values included being well informed, feeling responsible for doing everything for the best possible future perspective for their child, and preventing anticipated decision regret. This regret anticipation could address both choosing HSCT and supportive care and include weighing its harms and benefits. The active role of the parent in decision making for HSCT in the case of a child with a hemoglobinopathy was difficult for most parents and felt like a huge responsibility. Their active decision, made with the best hope for a favorable future perspective, could potentially lead to curation but also to (new) complications or loss. Likewise, refraining from HSCT could also lead to a lower life expectancy and quality of life. The described underlying parental values were used to consider an HSCT and evaluate the decision made for HSCT or supportive care. This corresponds with our EOL decision-making study in Chapter 2, where parental decision making showed a reflected perspective on the meaning of parenthood in EOL decisions[3].

The concept of good-parent beliefs while making treatment decisions is thoroughly investigated and described for parents of seriously ill children[18-23]. The original definition covers: "the good parent makes informed, unselfish decisions in the child's best interest; provides the basics of food, shelter, and

clothing; remains at the child's side regardless of the circumstances; shows the child that he or she is cherished; tries to prevent suffering and protect health; teaches the child to make good choices, to respect and have sympathy for others, and to know a Greater Being; advocates for the child with the staff; and promotes the child's health"[20]. Good-parent beliefs served as an internal guiding (ethical) compass by parents when making decisions[17,18,24], which reflected what we found in Chapter 2 and 6 in our studies on parental decision making[2,3].

Shared decision making in clinical practice

As described in Chapter 1, in medical decision making, two types of decisions can be distinguished, effective- and preference-sensitive decisions. In the case of preference-sensitive decisions, SDM is a fitting approach because it enables HCPs to explore and integrate patients' preferences into the decision that has to be made. An often-used model for SDM is the model described by Stiggelbout[5], proceeding on the model of Elwyn[25]. This model consists of four steps: (1) explaining the choice, (2) informing about the options, (3) exploring patients' preferences, and (4) making the decision (Figure7.1, upper line). We suggest specifying this decision-making model with the main concepts from our research when considering an HSCT for patients with a hemoglobinopathy. The specified model could also be supportive for other non-oncological, chronic invalidating diseasing with an HSCT indication. In the following paragraphs, we describe how these concepts can be integrated into the decision-making process (Figure 1, bottom line). Additionally, we integrate two practical topics based on our findings in Chapter 6: the role of peer support and the involvement of children in decision making[2].

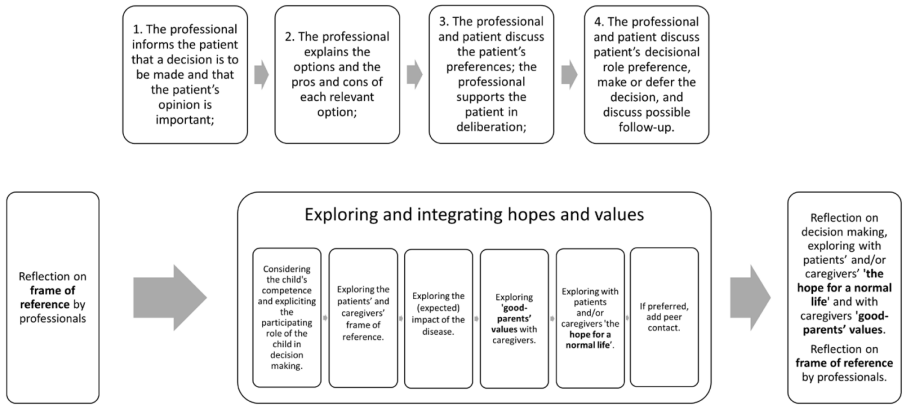

Figure 7.1 - The 4 steps of shared decision making according to Stiggelbout[5] specified with decision-making steps for patients with a hemoglobinopathy considering an HSCT.

Reflecting on frame of reference between healthcare professionals

Firstly, we identified the importance of the frame of reference among HCPs in Chapter 4, referring to their experiences and knowledge, influencing their viewpoint regarding HSCT decision making[1]. The HCPs' expertise and preferences are only sometimes part of SDM models[26]. Because HCPs are influenced by their frame of reference, we recommend reflecting on this frame of reference as part of the decision-making process. As a first step, being aware of one's frame of reference can lead to the most objective position possible and avoid unequal framing of the available options. This framing could be limited by exchanging knowledge and experiences within and between teams of referring and referred-to HCPs on general and case-specific levels. Disease-specific, treatment-specific, and case-specific knowledge and experiences should be included in the conversation between HCPs. Exchanging knowledge could lead to an equivalent enriching of each other's knowledge and insight into the disease impact of specific cases. Furthermore, with an open peer-review way of discussing patients between centers, HCPs will be acknowledged for their frame of reference as a base of their professionalism. In this way, patients will benefit from this enriched

knowledge because it will potentially increase an equal offer of treatments from the most knowledgeable HCPs. In case the decision is experienced as complex by one or more of the participants in the decision-making process, it can be beneficial for the patients to have a joint conversation with their referring and referred-to HCPs to establish a balanced information provision. Ideally, reflection is a continuous process that specifically demands attention before and after conversations where the decision is complex.

Exploring and integrating hopes and values

An important step during SDM is the discussion of the patient's preferences. This step scored relatively low in our study in Chapter 3, exploring the level of SDM as well as in the literature[8,27]. The concepts of hope for a normal life and being a good parent can support the conversation between patients and caregivers in the decision-making process.

Hope for a normal life

The hope for a normal life is grounded in the experienced or expected impact of the disease and expectations regarding curative therapy. We observed in Chapter 6 that patients and caregivers developed their own frame of reference based on their gained knowledge regarding the disease and HSCT[2]. To check whether this information is valid, the HCPs should pay attention to the patients' and caregivers' knowledge and expectations. During follow-up conversations, HCPs should check what information was remembered, for example, using the teach-back method. It is known that patients and caregivers remember only a selection from what has been explained and recalled information may be incorrect[28]. In addition, we suggest exploring the experienced and expected impact of the disease and what this means for patients and caregivers. The HCP should also reflect on the impact of the disease by explaining the medical facts. Patients with a hemoglobinopathy often learn to cope in a certain way with their disease and, therefore, are used to the disease's impact. Exploring patients' and caregivers' hopes and values regarding their disease and treatment should have a central role in the conversation. Hopes should be explored on whether they are realistic, specifying the known (possible) harms and benefits. Patient-reported outcomes for the specific patient category could support the information about

HSCT[29] because it provides objective insight into outcomes on a cohort level. Patients and caregivers value honest information from an involved HCP, and this can positively affect their involvement in SDM, see Chapters 2 and 6 [2,3,30]. Tools such as 'My positive health' can help children and adults around conversations about what is important for their health and well-being[31,32]. Patients can be asked to use this tool before the conversation as an opening to talk about their hopes and values. Another tool to support exploring the child's and caregiver's perspectives with a holistic approach is an advance care planning toolkit developed in Dutch. This toolkit provides conversation tools supporting SDM while talking with children and caregivers about the impact of the disease and hopes for the future[33,34]. Lastly, HCPs can train their SDM skills using simulation patient encounters. Recording conversations and evaluating to which extent a level of SDM was achieved, for example, using the OPTION scale or the 4SDM model[35-37] can support this training.

Peer support

Caregivers and patients almost unanimously expressed their need for the experiences of patients who had already undergone HSCT or of their caregivers as described in Chapter 6. Peer support from those who already underwent HSCT should be offered to patients who consider an HSCT and prefer this kind of support[2]. Peer support functions in broadening the patients' frame of reference but could also be supportive in fostering hope[14]. From previous research it is known that peer support can positively affect health outcomes[38,39]. Limited evidence is available on how peer support best could be applied in HSCT patients. Still, many patients would prefer to start peer support prior to HSCT[2,38]. HCPs should aim for well-balanced and, as much as possible, unbiased peer support for patients and caregivers. Different ways of peer support could be considered, like individual peer support, where HCPs connect patients or families. In this form of peer support, guiding and training of peer supporters should be considered. Patient organizations also could play an important role, and peer support at a group level can be used. An example of peer support at a group level is the use of patient experiences in informative webinars for patients considering HSCT.

Being a good parent

It is known that talking about their good-parent beliefs supports parents[18-21], suggesting that this could be a supportive intervention in reflecting on HSCT decision making. That is why we suggest asking about good-parent values while exploring patients' and caregivers' preferences during the decision-making process. How this could be applied in clinical practice has been described by Weaver using the phrase: "I have talked with many parents over the years, and I have learned they often have within themselves a sense of what they believe they need to do to be a good parent on their own terms. Do you have any feelings like that?"[18]. The previously mentioned advance care planning tool also supports talking about good-parent values[33,34].

Involvement of children

In current practice, pediatric patients from very young to early adulthood are transplanted for a hemoglobinopathy. Parents are increasingly advised to perform HSCT at a young age. Depending on national regulations, pediatric patients within specific age ranges are judicial owners of decision making (Chapter 1). The contribution to decision making depends on age, culture, individual maturity, and parental viewpoints. Age and active involvement in HSCT decision making were considered differently by caregivers and patients in Chapter 6 [2]. On the one hand, some parents consciously chose to have an HSCT for their child at a young age, with the idea that being transplanted at this young age is emotionally less difficult for their child and avoid progressive comorbidity, which would negatively impact the HSCT outcome[2]. On the other hand, adolescents and young adults stated that it was important to be able to make the decision themselves[2]. Previous research showed that adolescents and young adults are capable of meaningful deliberation regarding treatment decisions[40]. Even though it has been shown that parents and HCPs are the main decision makers in treatment decisions for children and adolescents, still, they and especially adolescents, want to be and must be involved in a certain way in the decision-making process[41-44]. For HCPS, involving children demands and individualized guiding process while considering children's competences and information needs while making an HSCT decision[45-47].

Reflection, not a one-off action

We described how the three main concepts a) frame of reference, b) hope for a normal life, and c) being a good parent, can be used for reflection while deciding on supportive care or HSCT. The decision for an HSCT is a one-time decision. However, the decision-making experience could be influenced by various variables, such as the age of the patient or the physical and psycho-social impact of the HSCT. As shown in Chapter 6, based on age, competence, and degree of involvement in decision making, children were less or more aware of their initial disease and the discussion for a curative option[2]. This awareness will most likely follow at a later stage while growing up. Therefore, patients and their caregivers can look back on HSCT differently because their perceptions of the disease or HSCT risks were different but also could change over time. As was shown in Chapter 6, the period post-HSCT was a period of mixed feelings[2,48]. Mixed feelings addressed the knowledge of a successful transplantation with new future perspectives. At the same time, patients and caregivers experienced tension regarding the impactful HSCT, recovery period, and possible late effects related to disease or treatment. These complications may include graft versus host disease, infertility, or impaired growth[49-51]. It is difficult to predict which patients will be confronted with specific complications and how this will impact their lives. Health-related quality of life (HRQoL) is frequently used to provide insight into the long-term mental health of transplanted patients. Several studies in the hemoglobinopathy population showed a stable or even improved HRQoL post-HSCT compared to baseline or norm groups[48,52-54]. Some studies reported an initial decline of HRQoL shortly post-HSCT compared to baseline, with an improvement over time, even exceeding the pre-HSCT situation. A study comparing child and proxy-reported HRQoL following HSCT showed that parents scored the HRQol of their child lower compared to the scores of the child[55]. Studies also showed a variety of outcomes between individual patients and that patients with worse HRQoL scores experienced more struggles related to encountered problems[48,56]. This was underlined by qualitative research showing that the struggles patients experienced post-HSCT, such as adapting to health limitations caused by late effects, impact their life course[57]. The HSCT also affects the caregiver's emotional functioning, where the HSCT is experienced by parents as a highly stressful period in the short and long term[58]. Clinical complications

and the acute phase may negatively impact parental stress; nevertheless, it is also described that parents showed growth after dealing with parental stress[59-64].

Since SDM aims to support patients in decision making, this support should continue post-HSCT. Therefore, we suggest adding a decision-making evaluation post-HSCT. This evaluation allows patients and caregivers to reflect on the past process to explore the current hopes and good-parent values in a comparable way as during HSCT decision making. This reflection can help acknowledge the intense process and identify possible difficulties. Subsequently, support can be offered. Also, for patients and/or caregivers who choose to continue with supportive care, a regular evaluation of hopes and values should be offered about discussing current available treatment possibilities.

The importance of time

Time is an important aspect of SDM, and we advocate for creating time for an SDM process with a family. Firstly, time during consultations to listen to questions, hopes, and values and explore these[65]. It is also essential to create time to live through the decision from the perspective of pediatric patients and their caregivers. It is even more important for different family members to know or be aware of each other's thoughts. This also applies to adult patients and their close relatives. We know from families that these conversations do not always occur spontaneously within families, so guidance should be offered. Parents can be encouraged to talk about their good-parent values; (pediatric) patients and parents should be invited to share their hopes for a normal life. These values should be explored considering the available treatment options. Lack of time for SDM could be experienced as a barrier, but the benefits of an SDM process could save time for patients later in the trajectory[66].

Future perspectives

Based on this thesis, new questions and opportunities arise, demanding further exploration in future research.

First, the specified decision-making framework, as described in this Chapter, should be translated into a decision-support tool in co-design with patients and caregivers. Since the studied population of patients with hemoglobinopathies is of a multicultural and multilingual origin, specific attention should be paid to the effect of culture, the language used, and the translation. Subsequently, the decision-making tool should be implemented and evaluated to determine its effects on decision making. Ideally, this should be studied quantitatively, where the outcomes of groups that used the tool are compared to those who received the standard of care. Different outcomes could be measured to evaluate the effect of the decision support tool, such as the level of shared decision making compared to what we did in Chapter 3[8]. Furthermore, participation, knowledge, decisional conflict, satisfaction, HRQoL, and treatment adherence could be evaluated, as is done more often to evaluate SDM interventions[67]. This method also contains restrictions. Firstly, evaluating the effect of an intervention between two groups demands comparable groups and circumstances to exclude bias and confounders. Comparability might be challenging to achieve for this intervention with different practices within centers and between HCPs. Secondly, it is questionable whether the standard of care has already evolved over time, based on previous experiences and lessons learned on SDM. This makes it difficult to measure an effect when comparing groups that receive the standard of care with those that will use the intervention. Lastly, sufficient numbers of participants are needed to measure an effect, which could be problematic for HSCT in pediatric patients. Therefore, a qualitative approach could be considered to evaluate the use and satisfaction of the decision tool.

Second, a more general SDM model could be developed for patients and families considering innovative therapies without clear-cut answers. This thesis identified concepts that could be further explored in the decision-making process of other non-oncological, chronic invalidating diseasing with an HSCT indication, which are known to have a closely related process. For example, patients with immunodeficiencies and bone marrow failures considering HSCT, or gene therapy. The impact of the disease, including its acceptance and the role of hope in different cultures, should be included in this future research because it is often thought that this might differ between populations of different cultural backgrounds. The provided insights can be supportive in the decision making

and consent processes. The insights might also be supportive in adjusting the decision tool for a wider group of patients. In this way, it may be possible to develop the previously mentioned decision tool further and examine its effect quantitatively.

Third, as described in the current Chapter and Chapter 6, peer support is an important desire of patients and families considering HSCT[2]. Different ways of peer support and practices exist, and different aspects need further exploration. First, which form is most beneficial to patients considering HSCT or future GT. In addition, how balanced and unbiased peer support can be achieved. Finally, what peer supporters might need to fulfill this role and how to select, train, and support them. The most beneficial form of peer support should be implemented, followed by evaluation to determine its effect on decision making. The effect of peer support on hope or fear can be included in this evaluation.

Finally, the role of nurses and nurse specialists in SDM should be further explored. We observed a modest supportive role in decision making by nurse specialists in Chapter 4; however, this was a very small sample[1]. Comparable findings were reported for the role of nurses in life-prolonging treatment[68]. Nurses' responsibility in final treatment decision making differs from those of the physicians, but their role seems supportive in decision making, and this could be further examined to support the decision making in a multidisciplinary team.

Conclusion

HSCT decision making in situations in which there is no clear-cut answer on what the best option is for the individual patient showed to be challenging and complex. From the HCPs side, HSCT decision making for patients with a hemoglobinopathy had a heterogeneous character influenced by disease complications in patients with sickle cell disease and the availability of an HLA-identical family donor. In conversations between patients and HCPs, SDM scored just under 50%. This thesis provided in-depth insights from patients, caregivers, and HCPs, which can be used to improve the decision-making process when considering an HSCT. Three main concepts were identified based on the

perspectives of patients, caregivers, and HCPs. These concepts can be used to reflect on HSCT decision making and to structure an exploration and integration of patients' preferences. Furthermore, identified concepts could be used to develop an SDM support tool. This tool needs further exploration, implementation, and evaluation, finally serving a larger group of patients deciding on HSCT when lacking clear-cut answers for their personal situation.

Reflexivity

In this thesis, we described the role of the frame of reference of HCPs and those of patients and caregivers. But the researchers of this study also had their own frame of reference. Therefore, this paragraph will reflect on the qualitative researcher's role in the conducted research. Qualitative researchers act as their own instruments, responsible for managing their biases alongside their team. This reflection aims to show that the researchers are not a 'tabula rasa' but active participants in the research, acknowledging and explaining their subjectivity. Also, how credibility and trustworthiness were enhanced in this thesis will be explained.

Dual role

As a specialized HSCT nurse and researcher in HSCT decision making, the author of this thesis had a dual role. She personally knew many of the HCPs involved in the studies. The author is a nurse at a pediatric HSCT ward but was not directly involved in the care of families in the EOL study. The researcher had no prior relationships with patients and families in the HSCT decision-making study for patients with hemoglobinopathies. Caring for these families as a nurse during their admissions for HSCT was unavoidable due to a limited size of the team. Navigating between these professional roles in both research and clinical settings undoubtedly was difficult at times.

The dual role had both advantages and challenges, particularly in situations with language barriers. The most significant challenge emerged when respondents questioned the interviewer as an HSCT professional, given her affiliation with the HSCT center. When acting as a researcher, the interviewer aimed to provide unbiased responses or directed respondents to consult with a physician, or she named that she shifted to a HCP's role. This shift in roles was often prompted by patients' or caregivers' informational needs. Despite its potential for confusion and non-neutrality, this role switch provided valuable insights into patients' informational needs, their desire for peer support, and their post-HSCT expectation management. These themes are important results of the study, and thereby, a pitfall also became a benefit. The dual role was also supporting for patients and caregivers because they could easily tell their story to someone who knew their disease and its impact in general. The ability to have multiples conversations with patients, creates a bond of openness and trust, and was even experienced as supportive for patients.

Memoing and reflection
Following each interview, an observational memo was written, reflecting on the setting, atmosphere, circumstances, and initial ideas of themes. These memos were used while analysing the interview data but also functioned to reflect on the personal role of the interviewer. The researcher reflected regularly on her role by writing additional memos or discussing situations with supervisors, especially in complicated situations or situations where the double role was explicitly felt. These reflections were also used to improve interview techniques and to adjust the topic list, a common practice in evolving qualitative research.

Building rapport
In qualitative research, creating an environment and trustful relationship in which respondents feel free to talk about their perspectives and experiences is crucial, referring to building rapport.
Throughout the study, the researcher established rapport by openly discussing her roles and the research team's goal of understanding respondents' perspectives on the topic. A topic list with open-ended questions facilitated an open dialogue, while active listening techniques were employed. Respondents were asked about their preferred interview locations. Given the multicultural and multilingual background of the hemoglobinopathy patient population, interpreters were frequently used, ensuring inclusivity in the studies. The depth of the interviews sometimes varied in translated conversations. Nevertheless, because the interviewer spoke more often with the respondents, she could rely on the built relationship and sometimes spoke partly without an interpreter. During interviews, the researcher paid attention to specific needs related to the topic of research by following up or arranging support.

Triangulation
To ensure the robustness of qualitative research, commonly used principles in qualitative research were followed. All conversations were recorded and transcribed verbatim, and a thorough analysis process was undertaken. Data were analysed by the author of this thesis, but also double coding was performed by other research team members not having a double role and/or not being involved in data collection. All steps of the research were discussed regularly with the supervisory team, where each specific role contributed to deepening and understanding the research topic. In addition to investigator triangulation, data triangulation was used, using different sources of information, such as the perspectives of different stakeholders, and using a questionnaire, recorded consultations, and interviews.

References

1. Mekelenkamp H, van Zanten H, de Vries M, Lankester A, Smiers F. How to Facilitate Decision-Making for Hematopoietic Stem Cell Transplantation in Patients With Hemoglobinopathies. The Perspectives of Healthcare Professionals. Front Pediatr. 2021;9:690309.
2. Mekelenkamp H, de Vries M, Saalmink I, Nur E, Kerkhoffs JL, Heijboer H, et al. Hoping for a normal life: Decision-making on hematopoietic stem cell transplantation by patients with a hemoglobinopathy and their caregivers. Pediatr Blood Cancer. 2023; 71(3):e30808.
3. Mekelenkamp H, Lankester AC, Bierings MB, Smiers FJW, de Vries MC, Kars MC. Parental experiences in end-of-life decision-making in allogeneic pediatric stem cell transplantation: "Have I been a good parent?". Pediatr Blood Cancer. 2020;67(5): e28229.
4. Mekelenkamp H, de Vries M, Markovitch B, Sirait T, Pieterse AH, Bense J, et al. Decision making on HSCT in patients with hemoglobinopathies; an EBMT Pediatric Diseases Working Party and Inborn Errors Working Party scenario-based survey on physicians' perspectives. Bone Marrow Transplant. 2023;58(5):584-6.
5. Stiggelbout AM, Pieterse AH, De Haes JC. Shared decision making: Concepts, evidence, and practice. Patient Educ Couns. 2015;98(10):1172-9.
6. Emanuel EJ, Emanuel LL. Four models of the physician-patient relationship. JAMA. 1992;267(16):2221-6.
7. Bakshi N, Sinha CB, Ross D, Khemani K, Loewenstein G, Krishnamurti L. Proponent or collaborative: Physician perspectives and approaches to disease modifying therapies in sickle cell disease. PLoS One. 2017;12(7):e0178413.
8. Mekelenkamp H, Smiers F, Camp N, Stubenrouch F, Lankester A, de Vries M. Decision making for hematopoietic stem cell transplantation in pediatric, adolescent, and young adult patients with a hemoglobinopathy-Shared or not? Pediatr Blood Cancer. 2021;68(9):e29099.
9. Beauchamp TL, Childress JF. Principles of Biomedical Ethics. 2009: Oxford University Press.
10. Varkey B. Principles of Clinical Ethics and Their Application to Practice. Med Princ Pract. 2021;30(1):17-28.
11. Schulz GL, Kelly KP, Holtmann M, Armer JM. Navigating decisional conflict as a family when facing the decision of stem cell transplant for a child or adolescent with sickle cell disease. Patient Educ Couns. 2021;104(5):1086-93.
12. Sinha CB, Bakshi N, Ross D, Loewenstein G, Krishnamurti L. Primary caregiver decision-making in hematopoietic cell transplantation and gene therapy for sickle cell disease. Pediatr Blood Cancer. 2021;68(1):e28749.
13. Schulz GL, Kelly KP, Holtmann M, Doering MM, Armer JM. Decision making in pediatric hematopoietic cell transplantation: Influential factors vary among diseases. Pediatr Blood Cancer. 2018;65(4).
14. Olsman E. Hope in Health Care: A Synthesis of Review Studies, in Historical and Multidisciplinary Perspectives on Hope, S.C. van den Heuvel, Editor. 2020, Springer International Publishing: Cham. 197-214.
15. Griggs S, Walker RK. The Role of Hope for Adolescents with a Chronic Illness: An Integrative Review. J Pediatr Nurs. 2016;31(4):404-21.
16. Mardhiyah A, Philip K, Mediani HS, Yosep I. The Association between Hope and Quality of Life among Adolescents with Chronic Diseases: A Systematic Review. Child Health Nurs Res. 2020;26(3):323-8.

17. Renjilian CB, Womer JW, Carroll KW, Kang TI, Feudtner C. Parental explicit heuristics in decision-making for children with life-threatening illnesses. Pediatrics. 2013;131(2): e566-72.
18. Weaver MS, October T, Feudtner C, Hinds PS. "Good-Parent Beliefs": Research, Concept, and Clinical Practice. Pediatrics. 2020;145(6):e20194018.
19. Feudtner C, Walter JK, Faerber JA, Hill DL, Carroll KW, Mollen CJ, et al. Good-parent beliefs of parents of seriously ill children. JAMA Pediatr. 2015;169(1):39-47.
20. Hinds PS, Oakes LL, Hicks J, Powell B, Srivastava DK, Spunt SL, et al. "Trying to be a good parent" as defined by interviews with parents who made phase I, terminal care, and resuscitation decisions for their children. J Clin Oncol. 2009;27(35):5979-85.
21. October TW, Fisher KR, Feudtner C, Hinds PS. The parent perspective: "being a good parent" when making critical decisions in the PICU. Pediatr Crit Care Med. 2014;15(4): 291-8.
22. Hill DL, Faerber JA, Li Y, Miller VA, Carroll KW, Morrison W, et al. Changes Over Time in Good-Parent Beliefs Among Parents of Children With Serious Illness: A Two-Year Cohort Study. J Pain Symptom Manage. 2019;58(2):190-7.
23. Robinson JE, Huskey D, Schwartz J, Weaver MS. The Many Roles of the Rock: A Qualitative Inquiry into the Roles and Responsibilities of Fathers of Children with Brain Tumors. Children (Basel). 2019;6(10):113.
24. Feudtner C, Schall T, Hill D. Parental Personal Sense of Duty as a Foundation of Pediatric Medical Decision-making. Pediatrics.2018;142(Supplement 3):S133-41.
25. Elwyn G, Frosch D, Thomson R, Joseph-Williams N, Lloyd A, Kinnersley P, et al. Shared decision making: a model for clinical practice. J Gen Intern Med. 2012;27(10):1361-7.
26. Bomhof-Roordink H, Gärtner FR, Stiggelbout AM, Pieterse AH. Key components of shared decision making models: a systematic review. BMJ Open. 2019;9(12):e031763.
27. Rake EA, Box ICH, Dreesens D, Meinders MJ, Kremer JAM, Aarts JWM, Elwyn G. Bringing personal perspective elicitation to the heart of shared decision-making: A scoping review. Patient Educ Couns. 2022;105(9):2860-70.
28. Shersher V, Haines TP, Sturgiss L, Weller C, Williams C. Definitions and use of the teach-back method in healthcare consultations with patients: A systematic review and thematic synthesis. Patient Educ Couns. 2021;104(1):118-29.
29. Bense JE, Haverman L, von Asmuth EGJ, Louwerens M, Luijten MAJ, Stiggelbout AM, et al. Late Effects in Pediatric Allogeneic Hematopoietic Stem Cell Transplantation for Nonmalignant Diseases: Proxy- and Patient-Reported Outcomes. Transplant Cell Ther. 2023;29(3):186.e1-186.e10.
30. Keij SM, Lie HC, Laidsaar-Powell R, Kunneman M, de Boer JE, Moaddine S, et al. Patient-related characteristics considered to affect patient involvement in shared decision making about treatment: A scoping review of the qualitative literature. Patient Educ Couns. 2023;111:107677.
31. de Jong-Witjes S, Kars MC, van Vliet M, Huber M, van der Laan SEI, Gelens EN, et al. Development of the My Positive Health dialogue tool for children: a qualitative study on children's views of health. BMJ Paediatr Open. 2022;6(1):e001373.
32. Van Vliet M, Doornenbal BM, Boerema S, van den Akker-van Marle EM. Development and psychometric evaluation of a Positive Health measurement scale: a factor analysis study based on a Dutch population. BMJ Open. 2021;11(2):e040816.
33. Implementing Pediatric Advance Care Planning Toolkit (IMPACT). [cited 2023 August 14th]; Available from: https://kinderpalliatief.nl/impact/.
34. Fahner J, Rietjens J, van der Heide A, Milota M, van Delden J, Kars M. Evaluation showed that stakeholders valued the support provided by the Implementing Pediatric Advance Care Planning Toolkit. Acta Paediatr. 2021;110(1):237-46.

35. Elwyn G, Tsulukidze M, Edwards A, Legare F, Newcombe R. Using a 'talk' model of shared decision making to propose an observation-based measure: Observer OPTION 5 Item. Patient Educ Couns. 2013;93(2):265-71.
36. Barr PJ, O'Malley AJ, Tsulukidze M, Gionfriddo MR, Montori V, Elwyn G. The psychometric properties of Observer OPTION(5), an observer measure of shared decision making. Patient Educ Couns. 2015;98(8):970-6.
37. Henselmans I, van Laarhoven HWM, de Haes HCJM, Tokat M, Engelhardt EG, van Maarschalkerweerd PEA, et al. Training for Medical Oncologists on Shared Decision-Making About Palliative Chemotherapy: A Randomized Controlled Trial. The Oncologist. 2018;24(2):259-65.
38. Amonoo HL, Harnedy LE, Deary EC, Traeger L, Brown LA, Daskalakis EP, et al. Peer support in patients with hematologic malignancies undergoing hematopoietic stem cell transplantation (HSCT): a qualitative study. Bone Marrow Transplant. 2022;57(8): 1277-86.
39. Amonoo HL, Harnedy LE, Staton SC, Longley RM, Daskalakis E, El-Jawahri A, Huffman JC. Peer support in patients with hematologic malignancies: a systematic review. Bone Marrow Transplant. 2022;57(8):1240-9.
40. Needle JS, Peden-McAlpine C, Liaschenko J, Koschmann K, Sanders N, Smith A, et al. "Can you tell me why you made that choice?": A qualitative study of the influences on treatment decisions in advance care planning among adolescents and young adults undergoing bone marrow transplant. Palliat Med. 2020;34(3):281-90.
41. Coyne I. Children's participation in consultations and decision-making at health service level: a review of the literature. Int J Nurs Stud. 2008;45(11):1682-9.
42. Coyne I, Amory A, Kiernan G, Gibson F. Children's participation in shared decision-making: children, adolescents, parents and healthcare professionals' perspectives and experiences. Eur J Oncol Nurs. 2014;18(3):273-80.
43. Jordan A, Joseph-Williams N, Edwards A, Holland-Hart D, Wood F. "I'd Like to Have More of a Say Because It's My Body": Adolescents' Perceptions Around Barriers and Facilitators to Shared Decision-Making. J Adolesc Health. 2019;65(5):633-42.
44. Jordan A, Wood F, Edwards A, Shepherd V, Joseph-Williams N. What adolescents living with long-term conditions say about being involved in decision-making about their healthcare: A systematic review and narrative synthesis of preferences and experiences. Patient Educ Couns. 2018;101(10):1725-35.
45. Coyne I, Harder M. Children's participation in decision-making: balancing protection with shared decision-making using a situational perspective. J Child Health Care. 2011; 15(4):312-9.
46. Quaye AA, Castor C, Coyne I, Söderbäck M, Hallström IK. How are children's best interests expressed during their hospital visit?-An observational study. J Clin Nurs. 2021;30(23-24):3644-56.
47. Quaye AA, Coyne I, Söderbäck M, Hallström IK. Children's active participation in decision-making processes during hospitalisation: An observational study. J Clin Nurs. 2019;28(23-24):4525-37.
48. Dovern E, Nijland S, van Muilekom MM, Suijk LMJ, Hoogendoorn GM, Mekelenkamp H, et al. Physical, Mental, and Social Health of Adult Patients with Sickle Cell Disease after Allogeneic Hematopoietic Stem Cell Transplantation: A Mixed-Methods Study. Transplant Cell Ther. 2023;29(4):283.e1-283.e9.
49. de Kloet LC, Bense JE, van der Stoep M, Louwerens M, von Asmuth EGJ, Lankester AC, et al. Late endocrine effects after hematopoietic stem cell transplantation in children with nonmalignant diseases. Bone Marrow Transplant. 2022;57(10):1564-72.

50. Cappelli B, Volt F, Tozatto-Maio K, Scigliuolo GM, Ferster A, Dupont S, et al. Risk factors and outcomes according to age at transplantation with an HLA-identical sibling for sickle cell disease. Haematologica. 2019;104(12):e543-6.
51. Lüftinger R, Zubarovskaya N, Galimard JE, Cseh A, Salzer E, Locatelli F, et al. Busulfan-fludarabine- or treosulfan-fludarabine-based myeloablative conditioning for children with thalassemia major. Ann Hematol. 2022;101(3):655-65.
52. Parsons SK, Rodday AM, Weidner RA, Morris E, Braniecki S, Shenoy S, et al. Significant improvement of child physical and emotional functioning after familial haploidentical stem cell transplant. Bone Marrow Transplant. 2022;57(4):586-92.
53. Badawy SM, Beg U, Liem RI, Chaudhury S, Thompson AA. A systematic review of quality of life in sickle cell disease and thalassemia after stem cell transplant or gene therapy. Blood Adv. 2021;5(2):570-83.
54. Liang H, Pan L, Xie Y, Fan J, Zhai L, Liang S, et al. Health-related quality of life in pediatric patients with β-thalassemia major after hematopoietic stem cell transplantation. Bone Marrow Transplant. 2022;57(7):1108-15.
55. Rodday AM, Terrin N, Leslie LK, Graham RJ, Parsons SK. Understanding the Relationship Between Child Health-Related Quality of Life and Parent Emotional Functioning in Pediatric Hematopoietic Stem Cell Transplant. J Pediatr Psychol. 2017; 42(7):804-14.
56. Hastings B, Patil C, Gallo AM. The Experience and Health-Related Quality of Life after Haploidentical Stem Cell Transplantation for Adults with Sickle Cell Disease. West J Nurs Res. 2019:193945919870828.
57. Bense JE, Ter Welle L, Mekelenkamp H, Schimmel M, Louwerens M, Lankester AC, et al. Exploring the long-term psychosocial impact of paediatric haematopoietic stem cell transplantation for nonmalignant diseases. Health Expect. 2022;25(5):2462-70.
58. Bense JE, Stiggelbout AM, Lankester AC, de Pagter APJ. Long-term parental distress after pediatric hematopoietic stem cell transplantation for nonmalignant diseases. Pediatr Blood Cancer. 2023:e30638.
59. Beckmann NB, Dietrich MS, Hooke MC, Gilmer MJ, Akard TF. Parental Posttraumatic Growth After Pediatric Hematopoietic Stem Cell Transplant. J Hosp Palliat Nurs. 2021; 23(4):331-8.
60. Beckmann NB, Dietrich MS, Hooke MC, Gilmer MJ, Akard TF. Parent Caregiving Experiences and Posttraumatic Growth Following Pediatric Hematopoietic Stem Cell Transplant. J Pediatr Oncol Nurs. 2021;38(4):242-53.
61. Vrijmoet-Wiersma CM, Egeler RM, Koopman HM, Bresters D, Norberg AL, Grootenhuis MA. Parental stress and perceived vulnerability at 5 and 10 years after pediatric SCT. Bone Marrow Transplant. 2010;45(6):1102-8.
62. Vrijmoet-Wiersma CM, Egeler RM, Koopman HM, Norberg AL, Grootenhuis MA. Parental stress before, during, and after pediatric stem cell transplantation: a review article. Support Care Cancer. 2009;17(12):1435-43.
63. Terrin N, Rodday AM, Tighiouart H, Chang G, Parsons SK. Parental emotional functioning declines with occurrence of clinical complications in pediatric hematopoietic stem cell transplant. Support Care Cancer. 2013;21(3):687-95.
64. Ward J, Fogg L, Rodgers C, Breitenstein S, Kapoor N, Swanson BA. Parent Psychological and Physical Health Outcomes in Pediatric Hematopoietic Stem Cell Transplantation. Cancer Nurs. 2019;42(6):448-57.
65. Pieterse AH, Stiggelbout AM, Montori VM. Shared Decision Making and the Importance of Time. JAMA. 2019;322(1):25-6.

66. van Veenendaal H, Voogdt-Pruis HR, Ubbink DT, van Weele E, Koco L, Schuurman M, et al. Evaluation of a multilevel implementation program for timeout and shared decision making in breast cancer care: a mixed methods study among 11 hospital teams. Patient Educ Couns. 2022;105(1):114-27.
67. Wijngaarde RO, Hein I, Daams J, Van Goudoever JB, Ubbink DT. Chronically ill children's participation and health outcomes in shared decision-making: a scoping review. Eur J Pediatr. 2021;180(8):2345-57.
68. Bos-van den Hoek DW, Thodé M, Jongerden IP, Van Laarhoven HWM, Smets EMA, Tange D, et al. The role of hospital nurses in shared decision-making about life-prolonging treatment: A qualitative interview study. J Adv Nurs. 2021;77(1):296-307.