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Balancing Research Interests and Patient Interests: A Qualitative Study Into the Intertwinement of Care and Research in Paediatric Oncology

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Background. Traditionally, in ethical guidelines and in research ethics literature, care and research are clearly separated based on their different objectives. In contrast, in paediatric oncology, research and care are closely combined. Currently, it is unknown how relevant actors in paediatric oncology perceive this combination of research and care. We conducted a qualitative study into the experiences of those involved in Dutch paediatric oncology with the intertwinement of research and care and the dual role of paediatric oncologists as researchers and treating physicians. ***Procedure.*** A qualitative study approach, using two focus groups and 19 semi-structured, in-depth interviews with paediatric oncologists, research coordinators, parents of children with cancer, and adolescents with cancer. ***Results.*** Four themes characterize how actors experience the intertwinement of research and care in paediatric oncology. First, research is considered of majorimportance, and paediatric oncology professionals convey this message to patients and their parents. Second, there is ambiguity about categorization of studies into cancer therapy as either research or treatment. Third, role conflicts appear within the work of the paediatric oncologists. Finally, the various benefits of combining treatment with research are emphasized. ***Conclusions.*** Research is regarded as a fundamental and indispensable characteristic of paediatric oncology practice. Paediatric oncology professionals, parents, and patients have a very positive outlook on combining research and care, but they may not be sufficiently critical with respect to potential conflicts. Increased reflection on how to optimally combine research and care could serve as an important protection of the interests of children with cancer and their parents. Pediatr Blood Cancer 2015;62:816–822.

Key words: combining research and care; dual roles; paediatric oncology; qualitative study; research ethics; role conflicts

INTRODUCTION

From the outset, paediatric oncology has been constructed as a practice that strongly combines research and care [1], which has helped to improve survival rates for children with cancer in the past few decades [2,3]. However, combining research and care also leads to normative issues such as the moral obligations of paediatric oncologists as physicians and researchers, and the question of whether paediatric oncologists should serve the interest of individuals or groups of patients [4].

De Vries and colleagues assert that paediatric oncologists 'continuously need to be aware of the potential conflict between research and treatment goals' [4] in order to be able to serve interests of current patients as well as those of future patients through research. It is currently unknown how relevant actors experience paediatric oncology practice, the intertwinement of research and care, and the double role of paediatric oncologists as researchers and treating physicians. Insight into these experiences is valuable for the evaluation of the close relationship between research and care in paediatric oncology [5].

Qualitative research on the ways in which actors in paediatric oncology experience the intertwinement of research and care is limited. Most previous qualitative studies focus on the ethical issues of paediatric oncology trials as such [6–16], rather than on issues related to the combination of research and care and the dual role of paediatric oncology physician-investigators. A study by Byrne-Davis and colleagues observed informed consent discussions between paediatric oncologists and families specifically for trials 'that are closely embedded into practice' [17]. They noticed that during these conversations the physicians switched between their clinical role and their investigator role, mainly by the language they used [17]. However, Byrne-Davis and colleagues did not investigate how the paediatric oncologists themselves perceived their double role. Furthermore, although they interviewed parents on their experiences with the informed consent process, they did not address how the parents experienced that their child's treatment was part of a clinical trial [17].

In this paper, we present our qualitative study into the experiences of those involved in paediatric oncology with the intertwinement of research and care and the dual role of paediatric oncologists as researchers and treating physicians.

METHODS

A qualitative study design allows for in-depth exploration of a topic and is therefore most suited to capture the experiences of paediatric oncology actors. As a first exploration of the topic, we conducted two focus groups; one with Dutch paediatric oncologists and one with parents of children with cancer. To validate and deepen our insights, a second stage of in-depth interviews was performed. We conducted 19 individual interviews with paediatric oncologists, research coordinators, parents of children with cancer, and adolescents with cancer (13–18 years old).

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Parents and adolescents provided written informed consent for their participation and, if applicable, parents provided written informed consent for the participation of their child. The study was approved by the research ethics committee of the University Medical Centre, Utrecht.

Sample

The inclusion criterion for all groups of respondents was to have experience with the combination of research and care. Parents and adolescents had to be able to speak the Dutch language. Also, the moment of inclusion in research should have been at most 2 years ago. In addition, we aimed for a large variety in types of cancer, age, gender, and experience with research participation. See Table I for the characteristics of the professionals (paediatric oncologists and research coordinators) and Table II for the parents and children. See Figure 1 for a flow chart of different respondents.

Focus Groups

Paediatric oncologists were recruited from the seven university paediatric oncology centres in the Netherlands, one from each centre. Six paediatric oncologists took part, one oncologist could not attend.

Parents of children with cancer for the focus group were recruited through one centre for pragmatic reasons. We considered that organizing a meeting for parents situated at different centres would entail too much burden (in terms of travel time) and was therefore unfeasible. A research nurse contacted twelve parents of eight children by telephone, who all accepted the invitation to participate in the focus group. In total, nine parents of six children attended; four mothers and five fathers. Three parents could not attend due to practical reasons.

Interviews

Paediatric oncologists from the seven Dutch paediatric oncology centres were contacted via two of our project advisors and the heads of the university paediatric oncology centres. Inclusion in the study

TABLE I. Characteristics of Professionals (Focus Group and Interviews)

Paediatric oncologists	(n = 16)[a]
Gender	
Male	8
Female	8
Experience (years)	
5–10	5
11–15	5
16–20	2
> 20	4
Areas of interest: clinical oncology[b]	
No specific	2
Solid tumours	9
Lymphomas	4
Leukaemia	8
Stem cell transplantation	4
Histiocytosis	2
Myelodysplastic syndrome	1
Areas of interest: research[b]	
Clinical drug trials	12
Laboratory research	6
Supportive care	6
Palliative care	3
Stem cell transplantation	4
Research coordinators	**(n = 3)**
Gender	
Male	1
Female	2
Experience (years)	
0–5	2
5–10	1

[a]Six from the focus group, nine from the interviews, and one additional from the expert meeting. [b]Paediatric oncologists could have various areas of interest.

TABLE II. Characteristics of Parents and Children (Focus Group and Interviews)

Parents	(n = 14)[a]
Gender	
Male	7
Female	7
Age (years)	
34–39	4
40–44	3
45–50	7
Education	
Primary, lower secondary general, or lower vocational	2
Higher secondary general or intermediate vocational	5
Higher vocational or university	7
Children	**(n = 12)[b]**
Gender	
Male	9
Female	3
Age (years)	
0–4	2
5–9	2
10–14	3
15–19	5
Diagnosis	
Acute lymphoblastic leukaemia	3
Chronic myeloid leukaemia	2
Rhabdomyosarcoma	1
Burkitt lymphoma	1
Hepatoblastoma	1
Osteosarcoma	1
Ewing sarcoma	1
Brain tumour (high grade glioma)	1
Hodgkin lymphoma	1

[a]Nine parents from the focus group and five from the interviews. [b]Six children from parents from the focus group and five children from the interviewed parents. One of these children, an adolescent female with a brain tumour, was also interviewed herself. The twelfth child was an adolescent male with Hodgkin lymphoma whom we interviewed. His parents were not interviewed.

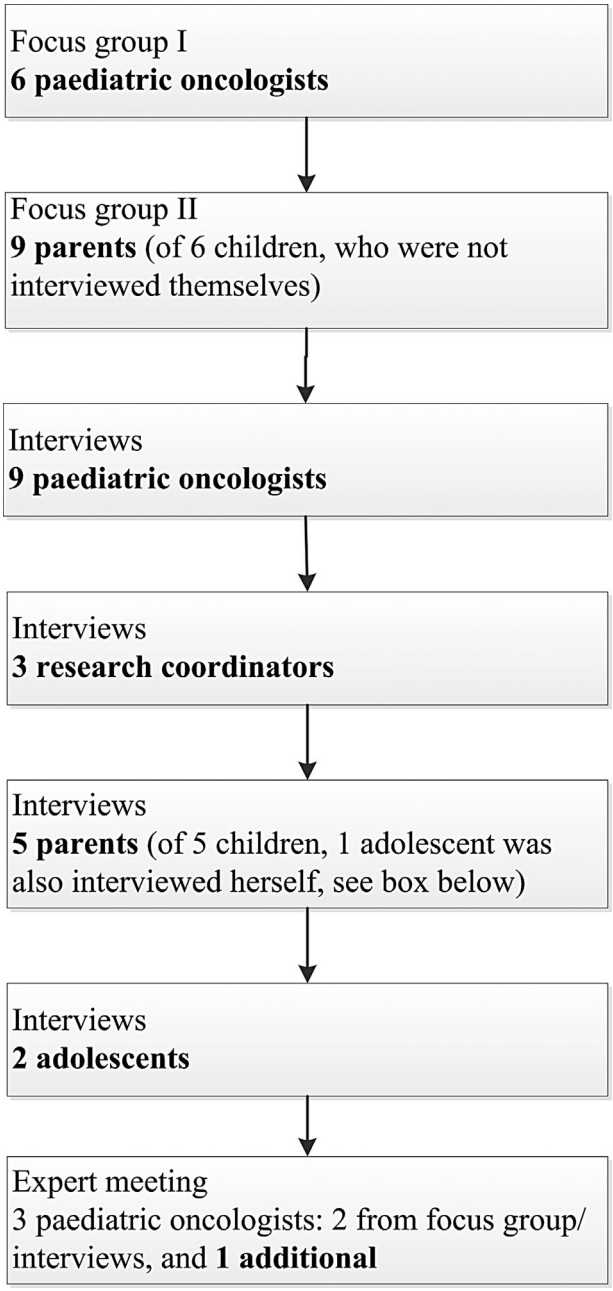

Fig. 1. Flow chart of respondents. *Numbers in bold added up = the total number of respondents* = 35.

was continuous via convenience sampling. Research coordinators were recruited from two different centres, since not all Dutch paediatric oncology centres employ research coordinators.

Parents and adolescents were approached via physicians and research nurses of three paediatric oncology centres and through a call on the website of the Dutch Association for Parents, Children and Cancer (VOKK).

We interviewed nine paediatric oncologists, three research coordinators, five parents of five different children, and two adolescents. One adolescent was the daughter of a mother we interviewed.

Data Collection

Focus groups lasted 2 hr each. Topics were formulated after examination of the relevant literature.

We conducted semi-structured, in depth interviews according to a predefined topic list (Table III). All but one interview took place at a paediatric oncology centre. One interview took place at home. Data collection took place from March 2013 to March 2014.

Analysis

The analysis was carried out according to thematic analysis, a method for identifying, analysing, and reporting themes within data [18]. The focus groups and interviews were transcribed verbatim and the data were imported in the software program NVivo 10, in order to facilitate the process of analysis. S.D. was the main analyst. She selected fragments of the data that were relevant in relation to the study purpose and coded these fragments with appropriate labels. M.K. and R.G. independently coded four interviews and all findings were compared and contrasted. The codes were grouped into conceptual categories or themes on the basis of their content, meaning, and interrelationships. These themes were regularly discussed during team meetings. Our themes were identified at the semantic level, meaning that we started with describing the experiences of the respondents followed by an interpretation in the light of the existing literature [18]. To enhance the validity of our findings, we held an expert meeting with paediatric oncologists in the last phase of data collection. We discussed our preliminary results with them, to assess whether these were an accurate representation of paediatric oncology practice and to obtain additional data.

RESULTS

All respondents reflected on their respective experiences with the situation in which research and care are intertwined and with the dual role of paediatric oncologists as researchers and treating physicians. Four themes characterize how actors experience the intertwinement of research and care in paediatric oncology. Representative quotations were chosen to illustrate the themes identified (Table IV).

Importance of Research

The paediatric oncologists emphasized the large role of research in their daily work and that every treatment includes a research component (Quote 1 in Table IV).

All paediatric oncologists and research coordinators expressed a strong desire to improve their field. To achieve this improvement, it

TABLE III. General Topic List

- Advantages of the dual role of physician and investigator;
- Disadvantages of the dual role of physician and investigator;
- Role conflicts due to the combination of research and care;
- Conflicts between conduct of research and provision of care;
- Suggestions to resolve these conflicts;
- Influence of the dual role on the child;
- Implications of taking part in a study;
- Categorization of paediatric oncology studies.

TABLE IV. Quotes from Focus Groups and Interviews

Number	Quotes
1	PO13 'Almost all treatments that we give have a research component. You always have to obtain informed consent, so you are always engaged with research in some way. That is part of your job. Almost every time you discuss treatment with people, a study is part of that discussion'.
2	PO14 'Sometimes I sense that parents do not want to say yes, but that they feel obliged in some way. To me as their doctor, to the hospital that is taking care of their child, to future patients. And also because they know that earlier research has made improvements in treatment from which their child benefits'.
3	PA7 'Every child that gets cancer is unique and is one too many. So you want to do everything you can to help with research that can accomplish that'.
4	AD2 'It is not a big effort to have some extra blood drawn and it was not a problem for me since they can help people with that'.
5	PO4 'We know that children with a certain deletion of genetic material in the leukaemia cells have a poorer prognosis. So a year of extra treatment has been added to the protocol, while we do not have evidence that that extra year will improve the prognosis. So we are testing a hypothesis, but it is presented as standard treatment'.
6	PA2 'I think that it also depends on the type of research, because if it can help others and does not have that much impact, I think that every parent will say they participate. But if the research is more invasive so to say, then you listen more to your oncologist. Who is also the one to introduce such a study so… there is some difference in types of research'.
7	PO1 'I think that we have not acted correctly with regard to this patient we had at our department, since I feel as though the study guided our decision rather than the patient himself'.
8	PO12 'You want patients to enrol in a study, because you want to learn from what you do. Therefore, you should make a real effort to include your patients, but you should not push people over the edge. You could push them towards the edge to take a look, but the final push…'
9	PO7 'I think people are overwhelmed by the diagnosis and do not have room for anything else. But that would mean that we could never do scientific research with this population, while research has brought us so much further. So, I definitely have the feeling that sometimes I ask too much, but I am convinced that this is the way to go to some extent, because it is the only way to learn from what we do'.
10	PO12 'And I cooperate with a lot of studies and I think… conducting research is fun. I mean, because you learn from it and it helps you to make progress and otherwise you will not be able to change the field. And you want to change the field, because you want to be able to cure more children. So I think that it is really important, for everybody. If someone did not think [research] important I doubt whether one could work here'.
11	PA14 'Those MRIs were a standard part of the study; these belonged to the study so to say. But I think that they would also have done these, if you just had the normal ... if you remove the word study, because that is the normal process for a patient with a brain tumour who needs a cure'.

PO, paediatric oncologist; PA, parent; AD, adolescent.

was regarded as natural to try to include all eligible patients in research. One oncologist said that she felt uncomfortable about approaching families about research in the beginning of her career. After a while, when she had realized what research is able to bring, she had lost this insecurity.

Paediatric oncologists and research coordinators stated they emphasize to families the importance of research and that research has helped to improve treatments and increase survival rates. They acknowledged that these statements could influence parents and older patients, who are generally not aware of medical research before their cancer diagnosis. According to both the health care professionals and parents themselves, parents are in a state of shock and disbelief and their only objective is to cure their child. Some paediatric oncologists thought that the existent emphasis on research might make parents feel obliged to consent to research participation of their child (Quote 2 in Table IV).

Parents themselves were motivated to contribute to the improvement of therapy for other patients, as long as a study would not require too much of their child or themselves in terms of time or physical burden, or if the research could also benefit their child (Quote 3 in Table IV).

Parents were told by the hospital staff that their child is treated in a university hospital, where research is an important part of daily practice. Therefore, parents realized that they can be invited to enroll their child, which they considered as reasonable. Several parents pointed at feelings of reciprocity: they should contribute what they can, since their child benefits from research in the past and from the participation of other children. Also adolescents were aware of the large role of research in paediatric oncology and were willing to contribute (Quote 4 in Table IV).

Ambiguity About Categorization of Studies

The paediatric oncologists distinguished different types of studies, based on whether a study investigated the effects of cancer therapy itself or something else (Table V). If studies did investigate cancer therapy, these were regarded as integral to the treatment options of patients, which in turn rendered it difficult to separate the roles of physician and researcher. For all other types of studies, such as laboratory research or supportive care studies, the oncologists considered it easier to separate conversation about these studies from conversation about treatment.

Furthermore, the paediatric oncologists considered it difficult to categorize the studies into cancer therapy as either research or treatment. This difficulty in particular concerned best available treatment protocols. According to the paediatric oncologists, these protocols form a grey area between research and treatment, since they call these protocols state-of-the-art treatment, while these are simultaneously designed to evaluate whether the protocol's modifications of previously used treatment regimens

TABLE V. Different Types of Studies in Paediatric Oncology and Their Relation to Cancer Therapy

	Cancer therapy studies	Description
Treatment ↑ ↓ Research	1. Best available treatment protocols	Single arm protocols that provide standard treatment, but also contain modifications to existing therapies that have not yet been fully studied. Therefore, these protocols are evaluated by clinical and epidemiological data collection and systematic analysis of disease characteristics, treatment results, side-effects and serious adverse events. Furthermore, treatment results are compared to historical results and to results obtained by international research groups. As such, these treatment protocols simultaneously serve treatment and research goals. Additional studies can be added to this protocol.
	2. Phase III randomized controlled drug trials	Protocols that provide standard treatment, but also involve one or more research questions for which randomizations are designed and added to the protocol. These trials are called phase III trials because in the intervention arm a drug that was previously tested in phase I/II trials is now tested in phase III for effectiveness. Phase III trials also test combinations of two or more familiar drugs, or a different dosage of a standard drug. Despite the research goal, these studies are seen as part of the (frontline) treatment options that patients have.
	3. Phase I/II studies*	These are studies into experimental cancer therapy that have a prominent scientific objective, but also serve a therapeutic function for children with refractory disease.
	Non-cancer therapy studies	Description
	4. Additional studies	All studies that do not investigate cancer therapy itself: Laboratory research on blood, bone marrow and other tissue; or supportive care studies, which can take the form of a phase III study involving a randomization. These studies are considered as clearly separated from the cancer therapy patients receive. These studies are usually added to best available treatment protocols or phase III randomized controlled drug trials.

*In the Netherlands the risks and burdens of paediatric research without a prospect of direct benefit for the child should be minimal. Phase I oncology trials are not considered as potentially beneficial and generally involve more than minimal risk and/or burden. Therefore, it is only possible to conduct combined phase I/II studies, for which it is more likely that the individual patient may benefit or a clinical effect is to be expected based on adult studies with comparable tumours or in preclinical studies with paediatric tumour models.

have improved survival rates. It was mentioned that with this type of treatment the paediatric oncology community primarily aims to prove that they were right to consider such a modified treatment protocol as best available treatment (Quote 5 in Table IV).

Parents also made a distinction between different types of studies based on the extent to which a study could benefit their own child. As such, studies into cancer therapy were perceived as providing treatment rather than research (Quote 6 in Table IV).

Role Conflicts

In general, paediatric oncologists stated that they functioned both as a clinician and as a researcher. Some had this dual role because they obtained informed consent, others because they also designed and conducted their own studies. With regard to which role had priority, they gave different answers. On the one hand, they indicated that being the treating doctor of their patients would always prevail over their researcher role. On the other hand, paediatric oncologists described situations in which research interests had played a large role. An example of such a situation concerned a patient with refractory disease, who did not fulfil the eligibility criteria for a certain phase I/II trial. Instead of giving him some other treatment, the oncologists decided to wait until the patient would become eligible and could be treated within the trial, while taking into account whether it was safe for the patient to have his treatment postponed (Quote 7 in Table IV).

Furthermore, paediatric oncologists reported the wish to include all patients in a study, leading to a conflict between their two roles in the context of informed consent. First, when informing families about research, they sometimes felt a tension between motivating and being too persuasive (Quote 8 in Table IV).

Second, both paediatric oncologists and research coordinators mentioned that they had included patients in a trial while they thought that parents had not really understood the study details, mainly right after hearing their child's cancer diagnosis (Quote 9 in Table IV).

Parents and adolescents felt that the treating oncologist of their child acted as a physician and not as a researcher. In their experiences, their child's wellbeing and interests prevailed over other interests of the paediatric oncologists. One father reported a moment where the researcher role of their paediatric oncologist took precedence over his care-giving role: as a family, they had decided to stop the experimental medication for their son because no sign of the disease could be detected in his blood. Since he was doing so well, they wanted to see if he could manage without medication. When they told their oncologist about this decision, he pointed at consequences for the study, making his researcher role very apparent to them.

Emphasis on Benefits

Both the paediatric oncologists and research coordinators expressed a strong belief in the benefits of combining treatment

with research. These benefits included therapeutic benefits for participating patients, due to close monitoring, following strict protocol guidelines, and the use of innovative interventions. In addition, the health care professionals had high expectations from research to improve the field of paediatric oncology, increase survival chances, and create benefits for future patients (Quote 10 in Table IV).

Simultaneously, paediatric oncologists were convinced that patients are not harmed by research. Also, they thought that risks and burdens of additional studies are low, while for studies into cancer therapy these would generally be outweighed by the benefits. Approval of the study protocol by a Research Ethics Committee was considered a further safeguard.

Parents and adolescents said that participating in research increased their feeling of safety, due to the extra tests and check-ups. Also, they expressed a belief in the potential benefit of the intervention arm of an RCT. A father did not think research would be conducted if it was risky. For a mother, it was unclear whether the procedures her daughter underwent were part of the standard treatment or were extra because she participated in an RCT (Quote 11 in Table IV).

DISCUSSION

Our study shows that in the Netherlands, research is considered a fundamental and indispensable characteristic of paediatric oncology practice. First, paediatric oncology professionals display and convey a strong motivation to perform research and are generally involved in the conduct of studies in a variety of ways, such as obtaining informed consent or designing studies themselves. Parents and children are also motivated to participate in studies within paediatric oncology and are even more willing to contribute themselves when they learn about the successes that research has brought so far. As such, it appears that paediatric oncologists and research coordinators influence the way patients and parents perceive research, which in turn increases their preparedness to take part in oncology studies.

Second, according to our respondents, research is often combined with the provision of treatment. On the one hand, this finding confirms the standard view of paediatric oncology. On the other hand, our study adds a specification to the general statement that in paediatric oncology research and care are intertwined. Commonly, it is meant to indicate that the majority of children with cancer participate in clinical trials (i.e., phase III RCTs) and sometimes can only receive treatment through research participation (phase I/II studies) [3]. Our study adds that research and care are also intertwined in paediatric oncology because standard treatments have research elements. Examples are best available treatment protocols, which provide best current treatment, but also contain modifications to existing treatment regimens, of which the merits are systematically investigated. Although the study protocols used in clinical trials clearly qualify as research, best available treatment protocols can best be categorized as 'hybrid' protocols. So, all studies into cancer therapy combine research and treatment, but this is most apparent in best available treatment protocols, since the standard treatment is also research. As such, best available treatment protocols invoke the question of what type of ethical oversight is appropriate. This has implications for the protection of children with cancer who participate in paediatric oncology studies, since protocols with relatively high risks should not be introduced as standard treatment without ethics review.

Third, whereas paediatric oncologists considered their care-giving role as primary, research considerations sometimes appeared overriding. This happened both in the informed consent context and in decisions about whether to treat a patient within a clinical study. So, although the paediatric oncologists indicated that their role as physician would always have priority over their researcher role, this was not always reflected in the choices they made.

Finally, our respondents displayed a strong belief in the beneficial potential of research, both for individual children and for other children and the field of paediatric oncology in general. In contrast, risks and burdens of research were referred to as low or were considered being outweighed by the importance of the research question. Arguably, because both paediatric oncologists and parents and patients hope that participation in a trial will provide therapeutic benefit [4,9], the various benefits of research receive relatively more attention than its risks and burdens for individual patients. As in research with adults, in paediatric research both the potential benefits to individual patients and the societal benefits are important to assess the acceptability of research with children, in addition to the risks and burdens [19]. However, due to the intertwinement of research and care and its accompanying emphasis on the various benefits of research, it could become unclear for parents which additional risks and burdens children are exposed to in comparison with care as usual [4].

We see the advantages of combining the provision of treatment with research. Survival rates for most childhood cancers have rapidly improved in the past decades [2,3,20,21], which has frequently been linked to the high rates of participation in medical research [4,13,15,17,22–24]. Especially in the field of paediatric medicine, where much is unknown or uncertain about which drugs are effective and how they work [25–30] this certainly is desirable. However, it seems that due to the self-evidence of combining treatments with research, the paediatric oncologists and research coordinators as well as parents and adolescents may not reflect critically enough on the possible conflicts that arise when research and care are intertwined. Since managing the conflicts between treatment and research is only possible if they are recognized by relevant actors [4,31], it is essential that paediatric oncology stakeholders recognize potential tensions and discuss how to properly manage these in order to optimally combine research and care. This discussion could function as an important protection of the interests of children with cancer and their parents [31], if within the inherent tensions that exist, explicit choices are made on how to safeguard patient and parent interests.

A strong feature of our study is that we invited different groups of respondents, to obtain an overall picture of the field from a variety of perspectives. A second strength is the combination of two different qualitative methods: focus groups and individual interviews. This enabled us to receive answers to our questions both in a setting in which respondents could discuss different topics and in a more personal setting, allowing respondents to elaborate on their experiences.

A first limitation is the small number of interviewed adolescents. This is due to the complexity of approaching adolescents with cancer, who are already burdened by a severe disease and everything it entails. Yet, we do not consider this small number problematic, since qualitative research does not aim to provide generalizable results, but seeks to present relevant experiences of

those involved in a certain practice. A second limitation is that we only discuss the Dutch paediatric oncology context. Ethical issues and their implications could vary, due to differences between the paediatric oncology contexts in different countries. Finally, there may be a bias in included patients and parents, since only those parents and adolescents could be contacted that were well enough to participate rather than those who had difficulty with coping with the disease.

CONCLUSIONS

Our study shows that in paediatric oncology, the conduct of research is considered a fundamental and indispensable characteristic of practice. This follows from the strong motivation of respondents to contribute to research, the research elements of standard treatments, choices made in favour of research interests, and the emphasis on benefits of research. Paediatric oncology professionals, parents, and patients have a very positive outlook on combining research and care, but may not reflect critically enough on potential conflicts that arise when research and care are intertwined. Yet, potential conflicts of combining research and care should also receive appropriate attention, since managing the conflicts between treatment and research is only possible if they are recognized as such by relevant actors. Increased discussion could function as an important protection of the interests of children with cancer and their parents if, within the inherent tensions that exist, explicit choices are made on how to safeguard patient and parent interests.

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REFERENCES

1. Krueger G. Hope suffering children, cancer and the paradox of experimental medicine. Baltimore: Johns Hopkins University Press 2008; 216 p.
2. Jemal A,Thomas A, Murray T, Thun M. Cancer statistics, 2002. CA Cancer J Clin 2002;52:23–47.
3. Ablett S, Pinkerton CR. Recruiting children into cancer trials–Role of the United Kingdom Children's Cancer Study Group (UKCCSG). Br J Cancer 2003;88:1661–1665.
4. de Vries MC, Houtlosser M, Wit JM, Engberts DP, Bresters D, Kaspers GJ, van Leeuwen E. Ethical issues at the interface of clinical care and research practice in pediatric oncology: A narrative review of parents' and physicians' experiences. BMC Med Ethics 2011;12:18.
5. Van Thiel GJMW, Van Delden JJM. Reflective equilibrium as a normative empirical model. Ethical Perspectives 2010;17:183–202.
6. Baker JN, Leek AC, Salas HS, Drotar D, Noll R, Rheingold SR, Kodish ED. Suggestions from adolescents, young adults, and parents for improving informed consent in phase 1 pediatric oncology trials. Cancer 2013;119:4154–4161.
7. Yap TY, Yamokoski AD, Hizlan S, Zyzanski SJ, Angiolillo AL, Rheingold SR, Baker JN, Kodish ED. Informed consent for pediatric phase 1 cancer trials: Physicians' perspectives. Cancer 2010;116:3244–3250.
8. Miller VA, Baker JN, Leek AC, Hizlan S, Rheingold SR, Yamokoski AD, Drotar D, Kodish E. Adolescent perspectives on phase I cancer research. Pediatr Blood Cancer 2013;60:873–878.
9. Kupst MJ, Patenaude AF, Walco GA, Sterling C. Clinical trials in pediatric cancer: Parental perspectives on informed consent. J Pediatr Hematol Oncol 2003;25:787–790.
10. Oppenheim D, Geoerger B, Hartmann O. Ethical issues in pediatric oncology phase I-II trials based on a mother's point of view. Bull Cancer 2005;92:E57–E60.
11. de Vries MC, Wit JM, Engberts DP, Kaspers GJ, van Leeuwen E. Pediatric oncologists' attitudes towards involving adolescents in decision-making concerning research participation. Pediatr Blood Cancer 2010;55:123–128.
12. Deatrick JA, Angst DB, Moore C. Parents' views of their children's participation in phase I oncology clinical trials. J Pediatr Oncol Nurs 2002;19:114–121.
13. Eder ML, Yamokoski AD, Wittmann PW, Kodish ED. Improving informed consent: Suggestions from parents of children with leukemia. Pediatrics 2007;119:e849–e859.
14. Chappuy H, Doz F, Blanche S, Gentet JC, Pons G, Treluyer JM. Parental consent in paediatric clinical research. Arch Dis Child 2006;91:112–116.
15. Eiser C, Davies H, Jenney M, Glaser A. Mothers' attitudes to the randomized controlled trial (RCT): The case of acute lymphoblastic leukaemia (ALL) in children. Child Care Health Dev 2005;31:517–523.
16. Stevens PE, Pletsch PK. Ethical issues of informed consent: Mothers' experiences enrolling their children in bone marrow transplantation research. Cancer Nurs 2002;25:81–87.
17. Byrne-Davis LM, Salmon P, Gravenhorst K, Eden TO, Young B. Balancing high accrual and ethical recruitment in paediatric oncology: A qualitative study of the 'look and feel' of clinical trial discussions. BMC Med Res Methodol 2010;10:101.
18. Braun V, Clarke V. Using thematic analysis in psychology. Qualitative Research in Psychology 2006; 77–101.
19. Shaddy RE, Denne SC. Clinical report–guidelines for the ethical conduct of studies to evaluate drugs in pediatric populations. Pediatrics 2010;125:850–860.
20. SEER Cancer Statistics Review, 1975–2011, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2011, based on November 2013 SEER data submission, posted to the SEER website, April 2014. 2014.
21. Gatta G, Zigon G, Capocaccia R, Coebergh JW, Desandes E, Kaatsch P, Pastore G, Peris-Bonet R, Stiller CA. Survival of European children and young adults with cancer diagnosed 1995–2002. Eur J Cancer 2009;45:992–1005.
22. Berg SL. Ethical challenges in cancer research in children. Oncologist 2007;12:1336–1343.
23. Bond MC, Pritchard S. Understanding clinical trials in childhood cancer. Paediatr Child Health 2006;11:148–150.
24. Pritchard-Jones K, Dixon-Woods M, Naafs-Wilstra M, Valsecchi MG. Improving recruitment to clinical trials for cancer in childhood. Lancet Oncol 2008;9:392–399.
25. 't Jong GW, Vulto AG, de Hoog M, Schimmel KJ, Tibboel D, van den Anker JN. Unapproved and off-label use of drugs in a children's hospital. N Engl J Med 2000;343:1125.
26. Conroy S, Newman C, Gudka S. Unlicensed and off label drug use in acute lymphoblastic leukaemia and other malignancies in children. Ann Oncol 2003;14:42–47.
27. Kimland E, Nydert P, Odlind V, Bottiger Y, Lindemalm S. Paediatric drug use with focus on off-label prescriptions at Swedish hospitals–A nationwide study. Acta Paediatr 2012;101:772–778.
28. Lindell-Osuagwu L, Korhonen MJ, Saano S, Helin-Tanninen M, Naaranlahti T, Kokki H. Off-label and unlicensed drug prescribing in three paediatric wards in Finland and review of the international literature. J Clin Pharm Ther 2009;34:277–287.
29. Pandolfini C, Bonati M. A literature review on off-label drug use in children. Eur J Pediatr 2005;164: 552–558.
30. van den Berg H, Tak N. Licensing and labelling of drugs in a paediatric oncology ward. Br J Clin Pharmacol 2011;72:474–481.
31. Miller FG, Rosenstein DL, DeRenzo EG. Professional integrity in clinical research. JAMA 1998;280:1449–1454.