Targeted Informed consent : empowering young participants in medical-scientific research

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CHAPTER 2

Research Information for Minors: Suitable Formats and Readability.

A Systematic Review

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Abstract

As children age, their capacity to consent or dissent to research participation increases. Numerous regulations and guidelines require that children should receive information 'according to their capacity of understanding'. In order to gain more insight in the quality of patient information forms for minors, a systematic literature search was performed. Two aspects of quality will be analyzed in this chapter: the effect of format on understanding and the readability of text in the documents. A systematic search was executed in PubMed, Embase and PsycINFO. Seventeen papers on format were included. Interventions testing information formats indicate that improvement is possible, but outcome measurement varied per study and no apparently successful intervention was repeated. Only three readability papers were found, all indicating a readability gap between patient information forms and children's actual reading level. The results indicate an urgent need for further research on how to adequately inform minors about clinical trials.

Background and Objective

Informed consent and assent are a major issue in the ethics of pediatric care, especially when it concerns parents' and children's consent for research (Bos, Tromp, Tibboel, & Pinxten, 2013; Committee on Bioethics, 1995). As approximately 45-60% of medication is currently prescribed off-label to minors, clinical trials among children are necessary to improve medication outcomes (WHO, 2013). This implies that patients under the age of 18 can be confronted with the choice to participate in clinical research. Depending on age, children do not always possess the legal right to consent to research participation, but can however have the mental capacity to understand the implications of participation. Since this capacity increases as children age, the ethical ideal of respect for the developing autonomy of children in making decisions comes into play (Committee on Bioethics, 1995). Numerous regulations require that assent or consent be obtained from children capable of providing it (Office for Human Research Protections, 2009). Article 12 of the UN Convention on the Rights of the Child states that "children shall be provided with the opportunity to be heard in any judicial or administrative proceeding affecting the child directly" (Unicef, 1989). Although this statement is not specifically aimed at medical situations, it follows that children should also be heard in the decision process for clinical research. The Second Directive 2001/20/EC by the European Parliament and the Council of the European Union, indicates that "A clinical trial on minors may be undertaken only if […] the minor has received information according to its capacity of understanding" (EU, 2001). These international regulations are translated to various national regulations in different countries. For example, in the Netherlands children from the age of 12 have the right to legally co-consent, together with their parents. In other countries, including the UK and the US, laws and regulations require that research participants who are not competent to provide consent, are informed, not with the primary aim to give true informed consent but from the moral principle of respect for persons and the more pragmatic aim to create commitment of the pediatric research participant (Alderson, 2007).

Although the variation between national laws and regulations, there is a rule of thumb for information provision and age. Children under the age of 9 are not fully capable of understanding concepts such as aim, benefits and risks of research (Gill, 2004; Ondrusek, et al. 1998). Children from the age of 14 appear to have an abstract understanding similar to that of adults (Kurz, Gill, & Mjones, 2006; Ondrusek et al., 1998), thus following that children between 9 and 14 have a developing understanding of research participation.

Therefore, these minors should be addressed in such a way that they can comprehend what is involved in research participation.

Research information is offered by means of the patient information form, often accompanied by verbal explanations from a researcher, doctor, or nurse. Contrary to verbal explanations, the patient information form itself can be taken home and read again, allowing a child to take the time to process the information. Pediatric forms therefore play a pivotal role in informing children and supporting their decision to provide assent, consent or dissent. In order to offer more insight in the quality of written information provided to children in pediatric research, two aspects of quality will be analyzed in this chapter: the effect of format on understanding and the readability of the text in the documents.

Format

Numerous studies indicate that consenting adult research participants do not understand essential research aspects, such as risks involved in participation (Falagas, Korbila, Giannopoulou, Kondilis, & Peppas, 2009). Therefore, the effect of different formats, such as simplified text and multimedia use, on understanding has been studied in adults (Dunn & Jeste, 2001; Flory & Emanuel, 2004; Palmer, Lanouette, & Jeste, 2012). However, information needs and preferred communication formats differ between children and adults (Broome, 1999). In order to gain more insight in the specific modes of communication suitable for children, a literature search was performed.

Readability

Readability analyses of adult consent documents indicate without exception a large gap between the required reading level to understand the information and the actual reading ability of research participants (Berto, Peroni, Miller, & Spagnolo, 2000; Franck & Winter, 2004; Gribble, 1999; Kass, Chaisson, Taylor, & Lohse, 2011; Ogloff & Otto, 1991; Melman, Kaplan, Caloustian, Weinberger, Smith, & Anbar, 1994; Paasche-Orlow, Taylor, & Brancati, 2003; Raich, Plomer, & Coyne, 2001; Sanders, Federico, Klass, Abrams, & Dreyer, 2009; Sudore, Landefeld, Williams, Barnes, Lindquist, & Schillinger, 2006; Terranova, Ferro, Carpeggiani, Recchia, Braga, et al. 2012). In addition to the use of complex terminology, the length of patient information forms is an obstacle for understanding (Kass et al., 2011). Even surveillance by Institutional Review Boards does not guarantee adequate document readability (Hammerschmidt & Keane, 1992; Paasche-Orlow et al., 2003). We

expect a similar readability gap in pediatric information material. In order to examine this hypothesis, a systematic literature search was performed.

Methods

A. Format

Research Question

Which way of presenting research information ensures understanding, satisfaction or fear reduction for children who are asked to participate in medical scientific research?

Search string

The search was originally executed in combination with a publication restriction for high quality evidence (reviews, meta-analyses, RCTs). As only four papers were included, the search was performed without publication restriction, in order to collect all available evidence. The search strings were executed in three databases: PubMed, EMBASE and PsycINFO, on May 2, 2013. These databases were chosen as they cover most of the publications in health care and information.

In- and exclusion

Inclusion was performed independently by the main researcher (PGW) and a second reader. Papers were excluded if the study was not performed with children or was irrelevant for the research question. Subsequently, all papers were read full-text, and eventually 20 papers were included. Three papers could not be accessed in the Netherlands; two conference proceedings and one conference abstract. In total, 17 papers were included, including 4 papers from the first search. A flow chart of the inclusion process is displayed in figure 1.

B. Readability

Research Question

What readability level of research information leads to understanding, satisfaction or fear reduction for children who are asked to participate in medical scientific research?

Search string

The search was executed in combination with a publication restriction: only high quality evidence (reviews, meta-analyses, RCTs) was included. As there were no papers included, the original search string was adapted to find all papers on the readability of pediatric research information (i.e. instead of evidence on target-group based *preferred* readability level). The search strings were executed in three databases: PubMed, EMBASE and PsycINFO, on May 2, 2013.

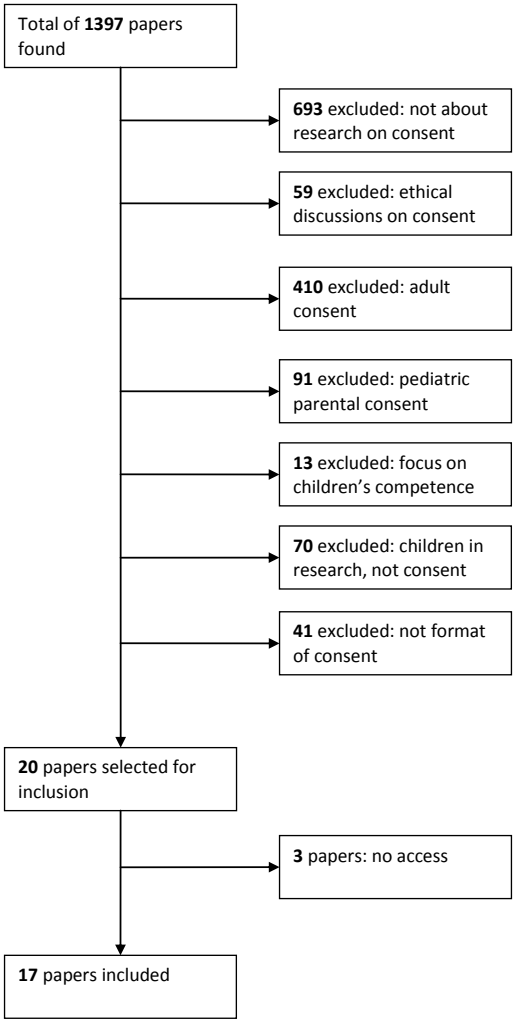

Figure 1. Detailed flow chart consent formats: no publication limit.

In- and exclusion

Paper in- and exclusion was performed independently by the main researcher (PGW) and a second researcher. Papers from the first search were excluded in case the research was not performed with children and when the research topic was not readability of research or hospital information. After exclusion, no paper remained. A number of papers on readability were found, but these only tested readability with readability instruments, and did not triangulate outcomes with the target group.

Only one paper investigated the actual readability for the intended target group, which consisted of adults (Sudore et al., 2006). An adapted search was executed for readability analyses of pediatric information forms. Papers were excluded when there was no actual measurement (e.g. qualitative interviews without readability analysis), when the topic was parental consent or ethical discussions, and when the study was irrelevant for the research question.

Selection

A total of 811 unique papers were found. Of these, 5 papers were selected for inclusion. A large amount of papers were excluded, because no actual measurements were reported, or the analyzed documents were intended for adults or parents (see figure 2). Two papers were excluded full-text as they did not measure pediatric documents for children as target group. As a result, 3 papers were selected in which a readability analysis of research information was performed. The included papers were used as a starting point for snowballing for more literature. However, no other papers were found that could be included in our review.

Results

A. Format

A total of seventeen papers were found, of which eight focused mainly on understanding of research information (Burke, Abramovitch, & Zlotkin, 2005; Chappuy et al. 2008; Dorn, Susman, & Fletcher, 1995; Fogas, Oesterheld, & Shader, 2001; Hurley & Underwood, 2002; Ondrusek et al., 1998; Tait et al., 2003; Swartling, Hansson, Ludvigsson, & Nordgren, 2011) and nine investigated the effect of adaptations of the patient information form or process (Adcock, Hogan, Elci, & Mills, 2012; Barnett et al., 2005; Carr et al., 2012;

O'Lonergan & Forster-Harwood, 2011; Shani, Ayalon, Hammad, & Sikron, 2003; Tait, Voepel-Lewis, & Malviya, 2007; Tait, Voepel-Lewis, McGonegal, & Levine, 2012; Ulph, Townsend, & Glazebrook, 2009; Wright, Fleming, Sharma, & Battagel, 2010). Papers were graded for level of evidence as indicated in table 1; a description of the evidence per paper can be found in table 2 (both at the end of this paper).

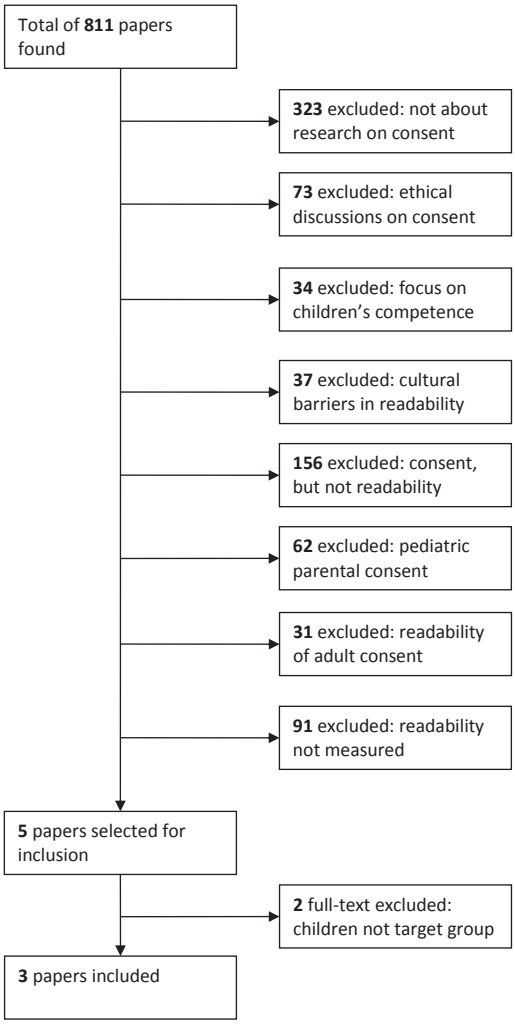

Figure 2. Detailed flow chart readability; second round.

Understanding of pediatric research information

Seven studies found that understanding of pediatric research information is related to age, where children older than 9 or 11 appeared to have better understanding than younger children (Adcock et al., 2012; Barnett et al., 2005; Burke, et al., 2005; Carr et al., 2012; Hurley & Underwood, 2002; Ondrusek et al., 1998; Shani et al., 2003; Tait et al., 2003, 2007; Tait et al., 2012; Ulph et al., 2009; Wright et al., 2010). However, others have criticized these findings as the documents were aimed at children age 14, influencing understanding in younger children (Ford, Sankey, & Crisp, 2007).

Timing of the information might also play a role in understanding, as in one study participants showed significantly higher understanding when information was offered more than 7 days after diagnosis (Chappuy et al., 2008). Five studies indicated variations between understanding of different research components. Specifically, understanding was low for research aim, right to withdraw, and possible risks and benefits (Burke et al., 2005; Ondrusek et al., 1998; Swartling, et al., 2011; Tait et al., 2003, 2007). In one study, children did not understand the word 'confidentiality', but did grasp the meaning of the concept (Hurley & Underwood, 2002). This indicates that children might be able to understand the meaning even though they do not understand the jargon. Another study found that emotional, rather than cognitive factors are predictors for understanding (Dorn et al., 1995). One study showed that pediatric participants were satisfied with their participation and with the supplied information, when interviewed 8 months after participation (Fogas, et al., 2001).

Interventions to improve information material

Studies on interventions to improve patient information showed inconsistent results. Four studies investigated the effect of a multimedia procedure (Carr et al., 2012; O'Lonergan & Forster-Harwood, 2011; Shani et al., 2003; Tait et al., 2012). Multimedia use improved understanding in three studies (Carr et al., 2012; O'Lonergan & Forster-Harwood, 2011; Tait et al., 2012), particularly when information was customized (Carr et al., 2012), and appeared ineffective in one study (Shani et al., 2003). Supplemental information next to the document did not improve understanding in two studies (Adcock et al. 2012; Wright et al. 2010), but in one study participants did have a higher feeling of understanding (Adcock et al., 2012). Another study investigated the effect of different presentations of probability information, and found that children best understood pie charts and percentages (Ulph et al., 2009). In two studies, enhanced patient information forms were

investigated (Barnett et al., 2005; Tait, Voepel-Lewis, & Malviya, 2007). In one study (Barnett et al., 2005) children preferred a story format to a standard or Q&A format; understanding was significantly improved, and in addition, a significantly lower number of children chose to participate in the proposed research after reading this format. In another study (Tait et al., 2007) children preferred an enhanced form with bullet points, bolding, larger font size and illustrations, over a standard form. The enhanced form also lead to increased understanding.

Conclusion

Based on the reviewed papers, there is no clear conclusion as to which intervention or information format is the most successful in empowering children in decision making. Understanding was investigated with different methods (RCTs, but also qualitative interviews). The other outcomes, satisfaction and fear reduction, were only recorded in a few studies. Interventions effective in enhancing understanding in one study, appear ineffective in another study. Also, no apparently successful intervention was repeated in a follow-up study.

B. Readability

Detailed description of the evidence in this round can be found in table 3 (at the end of this chapter).

Conclusion

The evidence on readability of pediatric information forms is scarce; only three papers could be included for review. These papers indicate that a readability gap is present in pediatric information forms. In one study, analyzed forms had a Flesch Reading Ease comparable to academic journals (Tarnowski, Allen, Mayhall, & Kelly, 1990). A comparison between research information and non-medical texts illustrates this gap: a large difference was found for the Flesch Reading Ease (Menoni et al., 2011). The third study described the development of research information material together with children, resulting in a Flesch Reading Ease of 86.3 and Flesch-Kincaid Grade of 3.9 for children age 6-12 years old (Ford et al., 2007).

Discussion

Information format and empowerment

There is a lack of studies on the quality of pediatric research information material; only 17 papers on format and 3 papers on readability were included. Positive effects of interventions were found for the use of a story format, multimedia use and presenting probabilities as pie charts or percentages (Barnett et al., 2005; Carr et al., 2012; O'Lonergan & Forster-Harwood, 2011; Tait et al., 2012; Ulph et al., 2009). No effects were found for the use of a supplemental folder or a Q&A format (Barnett et al., 2005). The understanding of children seems to be related to age and timing of the information provision. There is an association between research aspects and understanding: papers reported that children often are unaware of their right to withdraw and possible benefits and risks of participation (Burke et al., 2005; Ondrusek et al., 1998; Swartling et al., 2011; Tait et al., 2003, 2007).

As different studies have used different methods, it is difficult to compare results. Furthermore, the nature of the research for which consent is being asked might influence anxiety and thereby understanding, but this factor is not analyzed in the studies. Therefore, we conclude that based on the current evidence, it is difficult to draw a conclusion or provide recommendations on which formats lead to better understanding, satisfaction or lower anxiety.

This is not to say that nothing is known about appropriate ways to engage children in the consent process. Our study indicates that the literature on consent in clinical trials is very scarce. There is however a growing body of knowledge from the social sciences, which could be drawn on even though it does not meet our selection criteria for a systematic review. A key point in approaching children is the use of plain language (Alderson & Morrow, 2011; Farrell, 2005; J.B. Green, Duncan, Barnes, & Oberklaid, 2003) and text written in an active voice (Ford et al., 2007). In addition to written information, it is important to offer verbal explanations and time to ask questions and check understanding (Alderson & Morrow, 2011). A guideline for consent writers is developed in collaboration with children (NIHR, 2014). This guideline underscores the importance of plain language, and stimulates researchers to use colors and images to relate to children. Also, a separate sheet could be provided next to the study-specific information, to explain what research is (NIHR, 2014). In addition, it can be very helpful to test the information in a pilot with

children (Alderson & Morrow, 2011). The authors are currently developing research information together with children, which has provided us with interesting and valuable insights that we would otherwise not have had.

Limitations

The two systematic searches were performed in three databases (PubMed, PsycINFO, Embase) and it is possible that evidence exists which is not included in these databases. However, we believe that the most influential studies were found with our approach.
Only a small number of papers on information format were included, therefore more applied research is required before a conclusion for pediatric consent practice can be drawn.

Conclusion and recommendations

As aging children have a growing influence in the assent/consent process, they need to be provided with information 'according to their capacity of understanding' (EU, 2001). Our systematic review shows that a readability gap exists between the reading level of information material and reading ability of children. In addition, very little research has been performed on adequate formats of informing minors. Our systematic literature search did not yield many results, which in itself is a result worth reporting. The lack of studies on research information for children is remarkable, as hospitals often have targeted websites, brochures and booklets for children about specific diseases or treatments in the hospital. It appears that efforts to target information material to children remains restricted to ´regular´ hospital matters, and does not extend to research information. This apparent lack of research and thus attention for improving information in the consent/assent process is concerning. The ethical and sometimes legal necessity to involve children in the decision to participate in clinical research should create an urge to find the most optimal way to do so. Therefore, we conclude that there is a need for better readable information for children, and for more research and practice guidelines on informing minors about research participation.

Table 1 Level of evidence

Level of evidence	Intervention
A1	Systematic review of at least two independently executed studies of A2-level
A2	Randomized double-blind research of good quality and sample size
B	Comparative research, but not with all the characteristics of A2 (patient-control research, cohort studies)
C	Non-comparative research
D	Expert opinion

Table 2 Evidence for format and understanding, with evidence levels

Author, year	Study Design	Study Objective	Outcomes	Limitations
Adcock, 2012	Randomized crossover study Setting: local elementary school Inclusion: Children of local elementary school enrolled in general education curriculum Enrolled: 217 (195 intervention; 190 control) Participant characteristics: children age 7-11	Intervention: assent booklet with pictures and written information. Control: standard assent form Measurements: comprehension measured by 6-item quiz. Assessment in two days: first day one type of assent, 3 days later the other (two forms for different studies, to prevent information crossover)	Outcomes: significant difference in perfect scores; control 34.7%, intervention 22.1% More females had a perfect score than males, perfect score increased with age Other outcomes: majority reported to understand booklet better than standard text, style may not be only factor in comprehension	Critical Appraisal: simulation study, no standardized questionnaire Level of evidence: B
Barnett, 2005	Piloted comparative intervention study Setting: school Enrolled: 342 (Q&A format 115; story format 110; standard text 117) Participant characteristics: school children age 9-11 from seven different schools.	Intervention: Q&A format and story format Control: standard text format Measurements: understanding of 4 concepts (randomization, safety and effectiveness, voluntariness and avenues of redress) tested by 12-item questionnaire	Outcomes: significant difference in understanding; story format most correct answers, Q&A format least understandable. Other outcomes: inclusion: Q&A 72%, story 58%, text 71%	Critical Appraisal: simulation, no standardized questionnaire, some questions reported difficult to read. Sampled school had higher than average educational achievement Level of evidence: B
Burke, 2005	Interviews Setting: waiting room in Hospital for Sick Children in Toronto Inclusion: children and adolescents Enrolled: 251 children, 237 adults Participant characteristics: children: age 6-15; adults	Intervention: 6 information forms on 2 procedures for fractured thigh, cast or pins. Treatment options manipulated for risks and benefits, creating 'correct' or ambiguous choice for procedure. Control: two treatment options presented Measurements: interviews on understanding of 1. term 'research' 2. purpose of research in general 3. general procedure 4. cast procedure 5. pins procedure 6. benefits research 7. disadvantages research	Outcomes: 1. sign less young children understood definition (24% ages 6-10 vs. 45% 10-12 and 65% 13+, 72% adults) 2. understanding sign higher with age (73% vs. 87% vs. 93% vs. 90%) 3. no difference between ages, average around 70% understanding 4. sign age effect (80% vs. 92% vs. 95% vs. 96%) 5. sign age effect (78% vs. 90%, 96% and 92%) 6. sign age effect (56% vs. 75%, 82% and 76%) 7. sign age effect (64% vs. 80%, 76%, 86%) Other outcomes: younger children significantly preferred cast over pins, older children significantly preferred pins over cast. Even young children can (partly) understand research information.	Critical Appraisal: hypothetical study, forms might have been too difficult, as understanding among adults was not 100% Level of evidence: B

Author, year	Study Design	Study Objective	Outcomes	Limitations
Carr, 2012	Structured interview and questionnaire Setting: orthodontist Inclusion: patients scheduled for orthodontic treatment Enrolled: 80 patient-parents pairs Participant characteristics: children age 12-18	Intervention: A. customized slide show + presentation + consent form, B. customized slide show + consent form Slides shows customized for risks associated with treatment Consent form simplified Control: C. standard slide show and customized consent form Measurements: recall and comprehension by interview, consent domains treatment, risk and responsibility, literacy	Outcomes: group A significant higher risk recall than B and C Group B higher overall comprehension, treatment recall and risk recall than group C Other outcomes: better recall for information on consent presented early in slide show compared to later in slide show	Critical Appraisal: understanding of risks and limitations still inadequate, internal reliability of subjects in interviews ranged from slight to substantial Level of evidence:B
Chappuy, 2008	Qualitative interviews Setting: children in trials for cancer or HIV Inclusion: children of parents who participated in a previous study, exclusion when <5yrs old Enrolled: 29 children Participant characteristics: children age 8-15.	Intervention: semi-directive interview Measurements: understanding of 9 items of consent (goal, protocol, risks, direct/indirect benefits, right to withdraw, duration, alternatives, voluntariness)	Outcomes: lower understanding of procedures (17%), duration (21%), voluntariness (21%), right to withdraw (21%) and alternative treatments (31%) Higher understanding of goal (62%), risks (58%), self-benefits (62%), benefits to others (58%). Understanding better when the information was offered >7 days after diagnosis. Understanding related to time and age.	Critical Appraisal: it is difficult to disentangle the understanding of a child and the interaction with the parents. Level of evidence: C
Dorn, 1995	Interviews Setting: patients of an academic hospital Inclusion: children at pediatric dept. of hospital Enrolled: 20 for research, 24 for obesity treatment Participant characteristics: age 7-20 (research average age 14.6; treatment average age 13.9); 23 patients had prior experience in hospital	Intervention: interview on 12 aspects of research, global control and trait anxiety Measurements: 1. knowledge 2. weighted knowledge (based on importance) 3. global control 4. trait anxiety and Piagetian task for cognitive development	Outcomes: 1. sign correlation knowledge and global control (r=.40) 2. sign correlation weighted knowledge and global control (r=.38) 3. and 4. global control only or combined with anxiety best predictor for knowledge Other outcomes: knowledge of research aspects in children linked to psychological factors, rather than to cognitive factors.	Critical Appraisal: small sample size, anxiety in children with life-threatening illness not generalizable, control in obese children possibly not generalizable. Level of evidence: C

Author, year	Study Design	Study Objective	Outcomes	Limitations
Fogas, 2001	Structured telephone interviews Setting: minimal risk study Inclusion: participants of study on medication for ADHD Enrolled: 115 of 189 asked Participant characteristics: children age 6-19 (average 11.34; 66.1% <12) in 27.8% other psych diagnosis next to ADHD	Intervention: structured phone interview with 14 questions on participation Measurements: experience of participation 1. voluntariness 2. accuracy consent information 3. reason for participation 4. satisfaction with experience	Outcomes: 1. 89% thought participation was voluntary 2. 80% though information was accurate 3. 47% participated for him/herself 4. 97% was satisfied with participation Other outcomes: subtest in 25 children, test-retest higher than 72%	Critical Appraisal: interviews 8 months after experience, time could influence opinions. Results hard to generalize because of specific sample characteristics. Level of evidence: C
Hurley, 2002	Survey Setting: study of peer provocation (not medical research) Inclusion: random subsample of 382 original participants of research Enrolled: 178 Participant characteristics: age 8-12 (74 in 2nd grade, 52 in 4th , 52 in 6th	Intervention: post-assent questionnaire for understanding before and after debriefing Measurements: understanding of 1. voluntary assent 2. procedure 3. confidentiality	Outcomes: 1. children understood almost everything, but not the aim of the study. After debriefing still almost 50% did not understand aim 2. understanding of procedures before debriefing better for 4th- and 6th graders than 2nd, after debriefing correct for most children 3. poor understanding of the concept of confidentiality Other outcomes: debriefing: 2nd graders did not understand how they were misled in the research, 4th and 6th graders did. Although the concept of 'confidentiality' was not understood well, most children could explain who would know what they did in the research	Critical Appraisal: research was fairly complex to understand for children Level of evidence: B
O'Lonergan, 2011	I: Prestudy; II: RCT Setting: children's hospital or outpatient facility Inclusion: Parent-child dyads, exclusion for mental/visual/ hearing deficits or with previous experience of DXA or ultrasound Enrolled: I. 24 parent-child dyads II. 170 parent-child dyads Participant characteristics: children age 11-14, parents	Intervention: Multimedia-information (video or animated presentation) Control: standard text Measurements: Understanding for 8 aspects (purpose, procedures, risks, direct benefit, indirect benefit, alternatives, right to withdraw, voluntariness)	Outcomes: prestudy: feedback on methods used for adaptations RCT: better understanding with the use of multimedia vs. text, but still over 70% did not understand risks. All parents and children overestimated their own understanding. Other outcomes: all children understood the right to withdraw	Critical Appraisal: hypothetical study Level of evidence: A2

Author, year	Study Design	Study Objective	Outcomes	Limitations
Ondrusek, 1998	Cross-sectional survey Setting: nutrition study in Canadian hospital Inclusion: participants of nutrition study <18 Enrolled: 18 Participant characteristics: Healthy children 5-18	Intervention: survey and interview Measurements: understanding based on questionnaire and semi-structured interview	Outcomes: Understanding of aim, risks, right to withdraw and benefits was age-related, these concept were not well understood when age <9. Other outcomes: participants indicated a total of 5 different reasons for 18 participants	Critical Appraisal: different disclosures: children over 12 read the form by themselves, children under 12 were read to. This might indicate that the readability of the form was low for children under 12. Level of evidence: C
Shani, 2003	RCT Setting: 2 schools in the Negev (Bedouins, economic and social deprivation increases risk of burn wounds) Inclusion: Schools involved in burn wound prevention program Enrolled: 179 (2 schools, originally 3, but eliminated because of technical problems) Participant characteristics: Children age 12-13	Intervention: Information on Slides (S), video (V) or first slides then video (S+V) Measurements: survey on health beliefs before intervention and 2 months later: 1. threat 2. internal/external control 3. self-efficacy 4. sense of coherence 5. post-intervention fear reaction, knowledge improvement, safety behavior	Outcomes: no significant difference post-intervention for 1,2,3,4. 5. In S-group highest level of fear and lower perceived luck control in case of wounds, S+V group lowest within-change Other outcomes: improvement predicted by self-efficacy, fear, higher SES and woman. Health belief and demographics better predictor for effect than medium of intervention	Critical Appraisal: very specific type of information and specific sample No comparison with standard text information Level of evidence: B
Swartling, 2011	Qualitative interviews Setting: children in a large-scale longitudinal screening Inclusion: children involved in longitudinal study now or in the past Enrolled: 39 Participant characteristics: children age 10-12	Intervention: 6 focus group interviews Measurements: questions on six topics (research, children&research, information&consent, data collection, research consequences, risk to get a disease)	Outcomes: All groups, regardless of experience, considered research to be important Children thought that age of 10 years would be the age when children can understand research information, and age 5-7 would be when to start informing children Children could not identify any risk related to research participation Other outcomes: All children indicated that research participation can help other people	Critical Appraisal: small sample size Level of evidence: C

Author, year	Study Design	Study Objective	Outcomes	Limitations
Tait, 2003	Semi-structured interviews Setting: hospital/clinic Inclusion: Children who assented for participation in anesthesiology study Enrolled: 102 Participant characteristics: children age 7-18	Measurements: interview within 24h after surgery for 8 aspects of research (purpose, protocol, risks, direct benefits, indirect benefits, freedom to withdraw, alternatives, voluntariness)	Outcomes: understanding ranged between 30.4-89.4% children older than 11 had a significant better understanding than under 11, specifically for procedures, benefits and right to withdraw Other outcomes: subjective understanding higher than objective understanding, children under 11 had a better understanding when reading the form instead of verbal explanation	Critical Appraisal: interview after surgery, might have affected anxiety and thereby recall Level of evidence: C
Tait, 2007	RCT Setting: hospital Inclusion: inpatients for treatment or surgery, exclusion when unable to read, mental impairment of serious illness Enrolled: 392 asked, 190 included Participant characteristics: children age 7-17 (average age 11)	Intervention: Information on hypothetical study, with improved readability and clarity Control: standard information Measurements: survey for 8 research aspects (aim, procedure, risks, benefits direct/indirect, alternative, voluntariness, right to withdraw)	Outcomes: better understanding for adapted information in general, for procedure and indirect benefits. Association age-understanding stronger for standard info than for adapted info, all groups overestimate own understanding Other outcomes: understanding of research information among children is very poor	Critical Appraisal: hypothetical study, bias in motivation to participate, difference in reading grades could influence understanding and is not similar to age differences Level of evidence: B
Tait, 2012	Design: pilot study with qualitative interviews Setting: waiting room in American hospital Inclusion: children and parents in waiting room Enrolled: 4 children, 5 unrelated parents Participant characteristics: children 8-14, parents	Intervention: prototype interactive consent program Measurements: pre-interview for baseline understanding, semi-structured interviews for understanding (clinical trials, randomization, placebo, blinding); responses to questions embedded in the program real-time ability to respond on first attempt	Outcomes: Understanding pre-post per concept Clinical trials; adult 60%-80% child 25%-50% Randomization; adult 20%-60% child0%-0% Placebo adult 80%-100% child 0%-50% Blinding adult 80%-80% child 25%-50% Results not significant Correct responses to embedded questions on first attempt 90.2% for parents, 61.1% for children Other outcomes: children thought program was 'fun to use', liked the interactive nature and would like to receive study information in this format the next time	Critical Appraisal: pilot study, so small sample size Understanding not sufficient for all concepts Level of evidence: C

Author, year	Study Design	Study Objective	Outcomes	Limitations
Ulph, 2009	Cross-sectional study Setting: school children in the UK, sampled for academic achievements, free school meals and percentage of ethnic minorities Inclusion: Children from representative schools in the UK Enrolled: 106 Participant characteristics: children age 7-11	Intervention: verbal labels, percentages, proportion-word, proportion-notation, top view-pie charts, mixed format condition Measurements: picture of three cups presented, with different probability depicted, child has to select cup most likely to contain the ball	Outcomes: sign better performance by pie chart vs. percentages, proportion-notation/word and mixed format. In pie chart most children correct response (84%) and sign more certain of response, in percentages second-best response (70%) Other outcomes: older age associated with better comprehension for all formats except percentages, when using verbal labels almost half of participants asked for explanation	Critical Appraisal: simulation study, cup game not same as in medical setting Level of evidence: B
Wright, 2010	RCT Setting: orthodontist Inclusion: children who started fixed appliance therapy Enrolled: 60 Participant characteristics: children age 12-16	Intervention: verbal + written info Control: verbal info Measurements: Survey before consult (T1), after consent (T2) and 12 weeks after treatment (T3). Measurements of: 1. anxiety, motivation, understanding 2. compliance	Outcomes: 1. no difference in anxiety between T1 and T2 for intervention and control group. Sign higher motivation in intervention At T3 no differences for anxiety, understanding, motivation 2. compliance improved in intervention group, but not sign	Critical Appraisal: Very specific sample and procedure, small sample size Level of evidence: B

Table 3 Evidence for readability

Author, year	Study Design	Study Objective	Outcomes	Limitations
Ford, 2007	Improvement of consent form by users, readability analysis Setting: primary school children 6-12 Enrolled: 12 children involved in development	Measurement: Readability scores of user-developed consent form, measured by FRE and F-K Grade Level	Outcomes: FRE 86.3, F-K Grade Level 3.9 Other outcomes: children preferred use of active voice	Critical Appraisal: small group of children involved in development
Menoni, 2011	Readability analysis Setting: 3 French pediatric clinical research units Enrolled: 104 forms	Measurement: Readability by length, FRE, presence of illustrations, material compared to texts specifically written for children	Outcomes: average length 608 words, FRE of 40, for non-medical FRE 67. Medical texts 14% illustrated, many illustrations in non-medical texts Other outcomes: information of industrial sponsors significantly longer, more readable and more likely to be illustrated compared to institutional sponsors.	Critical Appraisal: analysis without test group
Tarnowski, 1990	Readability analysis Setting: large children's hospital in the U.S.A. Enrolled: 238 forms from between 1978 and 1987, inclusion when full committee review	Measurement: three 100-word samples randomly selected from each form. Readability by FRE Formula and Fry Readability Scale.	Outcomes: mean FRE of 26.91 +- 8.77, Fry 16.24 +- 1.24 (graduate school reading level) Other outcomes: significant increase in length over time, readability findings highly consistent with those of adult forms	Critical Appraisal: analysis without test group, readability of forms might have developed over time.