Parental and Clinical Perception of Informed Consent in Neonatal Research

Niamh O Shea
Royal College of Surgeons in Ireland, n.oshea@ucc.ie
Creative Commons Licence:

This work is licensed under a Creative Commons Attribution-Noncommercial-Share Alike 4.0 License.

This dissertation is available at e-publications@RCSI: http://epubs.rcsi.ie/mscttheses/83
Parental and Clinical Perception of Informed Consent in Neonatal Research

Niamh O Shea

Department of General Practice

A dissertation submitted in partial fulfilment of the requirement for the
Masters in Healthcare Ethics and Law

Supervisor: Professor Eugene Dempsey
Co Supervisor: Dr Kieran Doran

July 2015
Declaration

I declare that this thesis, which I submit to RCSI for examination in consideration of the award of a higher degree, MSc in Healthcare Ethics and Law, is my own personal effort. Where any of the content presented is the result of input or data from a related collaborative research programme this is duly acknowledged in the text such that it is possible to ascertain how much of the work is my own. I have not already obtained a degree in RCSI or elsewhere on the basis of this work. Furthermore, I took reasonable care to ensure that the work is original, and, to the best of my knowledge, does not breach copyright law, and has not been taken from other sources except where such work has been cited and acknowledged within the text.

Signed __________________________________________________________

Student Number __________________________________________________

Date ____________________________________________________________
# Table of Contents

A. List of Abbreviations .......................................................................................................................... 5

B. Table of Figures ................................................................................................................................. 6

C. List of Tables ....................................................................................................................................... 7

D. Abstract .............................................................................................................................................. 8

E. Acknowledgements ............................................................................................................................. 9

Chapter 1: Background and Literature Review ..................................................................................... 10

1.1 What is consent .................................................................................................................................. 10

1.2 Informed consent in clinical research .............................................................................................. 10

1.3 Elements of valid informed consent .............................................................................................. 11

1.4 When informed consent should be sought in clinical research ...................................................... 11

1.5 Clinical research and informed consent in minors .......................................................................... 11

1.6 Informed consent and neonatal research ....................................................................................... 12

1.7 Aim/objectives of literature review .............................................................................................. 14

1.8 Methods .......................................................................................................................................... 14

1.9 Critical appraisal of studies reviewed .............................................................................................. 17

1.10 Data collection ............................................................................................................................... 33

1.11 Results .......................................................................................................................................... 33

1.12 Parent perceptions of informed consent in neonatal research ...................................................... 33

1.13 Informed Consent Form ................................................................................................................ 36

1.14 Clinicians perceptions of informed consent in neonatal research .............................................. 36

1.15 Conclusion ..................................................................................................................................... 39

Chapter 2: Ethical and Legal Issues of Informed Consent in Research .................................................. 42

2.1 Background to clinical research involving human participants ...................................................... 42

2.2 The Tuskegee Syphilis Experiment ................................................................................................. 42

2.3 The Willowbrook State School Hepatitis Experiments .................................................................. 43

2.4 Second World War and the Nuremberg Trials .............................................................................. 45

2.5 European Directive 2001/20/EC .................................................................................................... 46

2.6 Informed Consent ............................................................................................................................ 46

2.7 Informed Consent Form .................................................................................................................. 47

2.8 Informed Consent in Ireland – A General Overview ....................................................................... 48

2.9 European Legislation for informed consent in neonatal research .............................................. 49

2.10 Research Ethics Committees ......................................................................................................... 50

2.11 Conclusion ..................................................................................................................................... 50

Chapter 3: Original Research .................................................................................................................. 52
<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.1 Background information</td>
<td>52</td>
</tr>
<tr>
<td>3.2 Aim and objectives of the study</td>
<td>53</td>
</tr>
<tr>
<td>3.3 Inclusion Criteria</td>
<td>53</td>
</tr>
<tr>
<td>3.4 Methods</td>
<td>54</td>
</tr>
<tr>
<td>3.5 Parent questionnaire</td>
<td>55</td>
</tr>
<tr>
<td>3.6 Clinicians questionnaire</td>
<td>57</td>
</tr>
<tr>
<td>3.7 Research setting</td>
<td>58</td>
</tr>
<tr>
<td>3.8 Ethics approval</td>
<td>58</td>
</tr>
<tr>
<td>3.9 Recruitment</td>
<td>59</td>
</tr>
<tr>
<td>3.9.1 Recruitment of parent group</td>
<td>59</td>
</tr>
<tr>
<td>3.9.2 Recruitment of clinician group</td>
<td>60</td>
</tr>
<tr>
<td>3.10 Recruitment challenges</td>
<td>60</td>
</tr>
<tr>
<td>3.11 Data collection</td>
<td>61</td>
</tr>
<tr>
<td>3.12 Statistical plan</td>
<td>61</td>
</tr>
<tr>
<td>Chapter 4: Results</td>
<td>62</td>
</tr>
<tr>
<td>4.1 Parent questionnaire</td>
<td>62</td>
</tr>
<tr>
<td>4.2 Clinicians questionnaire</td>
<td>71</td>
</tr>
<tr>
<td>4.3 Discussion of study results</td>
<td>79</td>
</tr>
<tr>
<td>Chapter 5: Conclusion and Future Direction</td>
<td>90</td>
</tr>
<tr>
<td>5.1: Future Direction</td>
<td>92</td>
</tr>
<tr>
<td>Appendix 1</td>
<td>94</td>
</tr>
<tr>
<td>A. CREC cover letter</td>
<td>94</td>
</tr>
<tr>
<td>B. Parent questionnaire</td>
<td>96</td>
</tr>
<tr>
<td>C. Parent information leaflet</td>
<td>101</td>
</tr>
<tr>
<td>D. Clinicians questionnaire</td>
<td>102</td>
</tr>
<tr>
<td>E. Clinicians information leaflet</td>
<td>106</td>
</tr>
<tr>
<td>F. CREC application form</td>
<td>107</td>
</tr>
<tr>
<td>References</td>
<td>118</td>
</tr>
</tbody>
</table>
### A. List of Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CASP</td>
<td>Critical Appraisal Skills Programme</td>
</tr>
<tr>
<td>CREC</td>
<td>Clinical Research Ethics Committee</td>
</tr>
<tr>
<td>CUMH</td>
<td>Cork University Maternity Hospital</td>
</tr>
<tr>
<td>GCP</td>
<td>Good Clinical Practice</td>
</tr>
<tr>
<td>NICU</td>
<td>Neonatal Intensive Care Unit</td>
</tr>
<tr>
<td>RCT</td>
<td>Randomised Controlled Trial</td>
</tr>
<tr>
<td>UCC</td>
<td>University College Cork</td>
</tr>
</tbody>
</table>
B. Table of Figures

Figure 1: Gestational age in weeks at birth .................................................................63
Figure 2: Overview of parents approached with information about a study either antenatally or postnatally. ..................................................................................65
Figure 3: Five point scale measuring parents preferences to antenatal consent. ..........66
Figure 4: Five point likert scale measuring parent preferences to postnatal consent. ......67
Figure 5: Overview of clinical position of doctors completing the questionnaire............72
Figure 6: Rate of importance of informed consent training. ........................................73
Figure 7: Time clinicians spend with parents during the consent process. ...................75
Figure 8: Do clinicians believe parents understand the randomisation process? ...........76
Figure 9: Likert scale measuring if clinician’s agree to a waiver of consent in neonatal research..................................................................................................................77
C. List of Tables

Table 1: Inclusion Criteria...........................................................................................................15
Table 2: Online database search................................................................................................17
Table 3: Summary of critically appraised studies, including key findings...............................19
Table 4: Inclusion criteria - parents............................................................................................54
Table 5: Inclusion criteria - clinicians .......................................................................................54
Table 6: Waiver of consent in neonatal research. ......................................................................78
Table 7: Parent description of clinical staff who approached them for consent to a neonatal study........................................................................................................................................81
D. Abstract

**Objectives:** To systematically explore the perceptions parents and clinicians have of the informed consent process in neonatal research.

**Methods:** A comprehensive literature review of peer reviewed studies, all of which are related to the topic of this dissertation. Additionally, an original questionnaire based study was conducted. The study recruited parents of newborn infants who had been an inpatient of the Neonatal Intensive Care Unit of the Cork University Maternity Hospital and clinicians currently employed in either a paediatric or neonatal setting.

**Results:** Parent perception of informed consent in neonatal research is a relatively well studied area. Parents have a lack of understating of certain study procedures including the element of randomisation. 72% of clinicians believe approaching parents antenatally with information about a neonatal study leads to a greater uptake in consent and 57% of parents stated a preference to being approached with information prior to the birth of their baby. Parents expressed confusion to some content in the consent forms and junior clinicians expressed a lack of understanding of good clinical practice. Parental vulnerability during the informed consent process was highlighted.

**Discussion/conclusion:** Parents are generally supportive of neonatal research. They are aware of their vulnerability during the neonatal period. They take part in neonatal studies for altruistic reasons such as helping babies of the future and stressed the importance of protecting parents in a similar situation. There is a need for increased consultant support during the informed consent process for parents and junior clinicians. It is essential junior clinicians receive training in the acquisition of informed consent from senior colleagues. The establishment of consenting guidelines for junior doctors to assist them during in the informed consent process is recommended. There is a need for further research to be completed in this complex legal and ethical area to ensure valid, informed consent is obtained and to enhance the consenting experience for this vulnerable cohort.
E. Acknowledgements

First and foremost I would like to express my sincere gratitude to my dissertation supervisor Professor Gene Dempsey. Professor Dempsey provided me with constant support throughout the last year. He continually pointed me in the right direction when lost and always made time for our many meetings during this past year. As the clinical trial coordinator for his project “The HiP Trial” I would like to extend a special thank you to him for allowing me dedicate many working hours to this dissertation and would like to acknowledge the funding provided to me by the HiP trial consortium to support this Masters degree. I am truly grateful.

In the same vein, it is with immense gratitude that I acknowledge the unwavering support of Dr Kieran Doran, solicitor and senior law lecturer, UCC who acted as a co supervisor for this dissertation. He attended all supervisory meetings, provided me with feedback on my various drafts and always made feel that I could pick up the phone when in need of advice. Professor Dempsey and Dr Doran are supervisors for which student’s dream of having the opportunity to work with.

To the many parents and clinicians who took the time to complete my questionnaire, I thank you profusely. Without this my dissertation would not have been possible. I would like to acknowledge the guidance and assistance provided by Dr David Smith and Ms Laura Hayes in the last two years. I am also indebted to my friends and colleagues for their kind words of encouragement through this process. Without all of their support, I could not have succeeded in what I have done.

Finally, to my parents Tim and Siobhan, siblings Ciaran, Noelle, Neil my extended family John and Ber, all who expressed unwavering faith and belief that I could complete this dissertation (even when I did not quite believe so myself), to my nephew Darragh for his constant love and hugs and to my family Shane, Ella and Freya, who showed resolute faith in me throughout this entire process. I dedicate this dissertation to them all.

Niamh O’Shea
Chapter 1: Background and Literature Review

1.1 What is consent

Consent, except in unusual circumstances is an indispensible requirement of ethical and lawful medical treatment or research and is considered a key element of clinical practice (1). If a clinician chooses to examine, treat or operate on a person without firstly obtaining a valid consent (in a situation where consent should have been sought) then that clinician has committed an unlawful act (1). To treat patients without their consent is a breach of their constitutional rights and transgresses a primary principle of medical law (2).

1.2 Informed consent in clinical research

The process of informed consent, as described in national and international guidelines state that certain measures must be followed to ensure a research participant has made an informed decision about their participation in a research study (3-6). In order for consent to be considered valid research participants should receive necessary information about a research study, must display an obvious competency for understanding the information and also have adequately understood the information and finally, must be allowed to make their decision free from coercion, undue influence, inducement or intimidation (4).

Certain situations will render it impossible for valid informed consent to be obtained. Examples include the age of the potential research participant (a newborn baby is unable to give their consent to a research study) and those lacking mental capacity (7).

Obtaining valid informed consent from research participants is key to conducting ethical research and is also a legal requirement of clinical research (8). It is the legal and ethical duty of investigators to ensure valid informed consent is acquired from parent(s) or guardian(s).
1.3 Elements of valid informed consent

There are three (3) fundamental components of informed consent which must be present for consent to be considered valid. These are voluntariness of consent, an individual’s capacity to consent and disclosure of relevant information to that individual (1);

1. The concept of voluntariness is one which highlights the absence of outside pressure and manipulation by others during a research participants decision making process to clinical research (9). When a decision regarding participation to a research study is not deemed voluntary it cannot be considered that valid informed consent was obtained (1).

2. A person is considered to have the capacity to consent to a research study provided sufficient capacity is proven in terms of their age and mental capacity (1). It has been noted that there is a general assumption that a person can be considered competent unless there is a reason to question that presumption (such as age or mental capacity) (9).

3. Disclosure of relevant information relating to a research study ensures the potential research participant has sufficient knowledge of the research study to allow them make an informed decision about consenting or refusing consent to that study (1).

*It is essential that investigators discuss all study procedures, including risk benefit ratio with research participants/proxy consenters during the consent process.*

1.4 When informed consent should be sought in clinical research

Informed consent in clinical research adheres to the same medical and ethical principles of informed consent in medical treatment. Informed consent should always be sought from a research participant prior to any procedure being performed (10).

1.5 Clinical research and informed consent in minors
In accordance with the Non-Fatal Offences against the Person Act (1997) the age in which a minor can give consent to a medical treatment is 16 (11). In clinical research the definition of a minor is a person under the age of 16 years (12). It is a requirement of all clinical research studies involving minors that proxy consent is obtained from the parent(s) or guardian(s) of the minor.

There are certain requirements of the consenting process which must be adhered to by clinicians and investigators engaging in the proxy consenting process. If a minor is of a certain age which allows them to engage in discussions about their participation in a research study the minor must make an expressed wish to take part in that particular study. Investigators must ensure the minor has received adequate information about the study according to their mental capacity or level of understanding. This information must be given to the minor from research staff with experience in dealing with minor patients. 

Like adult participants minors must be informed of the potential risks and benefits of the research study during the consenting discussion (12).

It is essential that parent(s) or guardian(s) acting as proxy consenters have the capacity understand information received about the study. This will ensure they make an informed decision regarding participation or refusal of consent on behalf of the minor (13).

1.6 Informed consent and neonatal research

Informed consent in neonatal research remains a sensitive and controversial subject. There are several documented reasons for this. The Euricon study, assessed the validity of consent obtained in the neonatal setting. Results showed that of 200 parents who took part only 30% were found to have given valid consent or refusal of consent (14). This study highlighted that an alarming number of parents had issues with one or more of the components which constitute a valid consent. Results of this nature add to the theory that it is virtually impossible for parents to have full comprehension of information received during the consenting process whilst in a situation where they are experiencing severe emotional distress (15).
The element of randomisation in a clinical trial can cause confusion amongst parents (16, 17). Where clinical equipoise is present, a randomised control trial presents the opportunity to answer important clinical questions in a non biased fashion. Clinical equipoise can only exist when investigators have a genuine uncertainty regarding the comparative therapeutic benefit of each arm in a clinical trial (18). Randomisation occurs when research participants are randomly assigned to receive one of two different treatment arms (one of which may be a placebo). It is generally accepted that random allocation of a study treatment/drug is methodologically appropriate however it’s application has caused much debate amongst healthcare professionals and ethicists (16). It has been suggested that parents are so apprehensive about the wellbeing of their newborn that they are not competent to give valid informed consent and that consent given may not be truly voluntary (19).

It is the responsibility of investigators who conduct clinical research to ensure compliance of the core ethical principles which govern research involving human study subjects. These core principles are outlined in the Belmont Report (20). This includes ensuring that a valid informed consent is obtained from all research participants. In the case of neonatal research, it can prove difficult for investigators to allocate sufficient time to parents during the consenting process, particularly if antenatal consent is required. Protocols completed for neonatal studies usually include strict timelines for obtaining consent, screening and ultimately enrolling newborn babies. Investigators responsible for acquiring informed consent are also frequently part of the clinical team caring who care for newborn infants. This would mean that the time for which they can allocate to the consenting process with the parents may be limited depending on severity of illness of the newborn.

It is clear that if improvements are to be made in the quality of the clinical care given to sick newborn infants there is a need for clinical research studies (21). Drazen et al. (2013) suggests that without clinical research studies neonatologists would be guessing what the best treatment is for extremely premature infants rather than actually knowing (22). While research exploring into the perceptions of the informed consenting process in neonatal research is gaining momentum, it is clear that further research is needed into this sensitive and complex area.
1.7 Aim/objectives of literature review

The aim of this literature review is to provide the reader with an outline of the perceptions and experiences parents and clinicians have regarding the informed consent process in neonatal research.

The objectives of this literature review are:

- To extensively review published studies whose main objective was to explore into the perceptions/experiences parents and clinicians had of the informed consent process in neonatal research;

- To identify and assess key problem areas of informed consent in neonatal research described by parents and clinicians who have been involved in the consenting process and;

- To suggest ways to improve the informed consent experience for parents and clinicians after identification of the potential pitfalls in the process as described in the literature.

1.8 Methods

Study Selection

Selected studies specifically related to parents and clinicians perceptions of the informed consent process in neonatal research were chosen. I began my literature search from the year 1985. I chose 1985 as this was the year the House of Lords issued their landmark ruling on the Gillick Case (23). As a result of the Gillick case, minors (under 16 years) were afforded the right to consent or refuse a medical treatment depending on their capacity, without the requirement of parental permission (23).

A set of inclusion criteria was developed in order to assist with locating studies directly linked to this literature review topic.
The inclusion criteria is described in table one below;

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>English language text only</td>
</tr>
<tr>
<td>Published literature only</td>
</tr>
<tr>
<td>Population: Parents and investigators involved in neonatal research studies</td>
</tr>
<tr>
<td>Year: 1985 to 2015</td>
</tr>
<tr>
<td>Primary research directly related to the topic (parents and clinicians perceptions of the informed consent process in neonatal research)</td>
</tr>
</tbody>
</table>

**Search strategy**

Initially I completed a Google search to establish the general information available regarding parents and clinicians perceptions of informed consent in neonatal research. This yielded several articles relating to the topic and provided further information regarding the most appropriate online databases to search. With these results I conducted searches of the following databases:

**Pubmed**

To begin I completed a general search entering the following sentence to pubmed; “perceptions of informed consent in neonatal research”. This produced 30 results. Of these, 9 studies were applicable to my literature review and were free full texts. The studies ranged in years from 1997 to 2011. Finally I entered a combination of the following words; “clinician’s views, informed consent, neonatal”. This yielded no results.
I then entered a combination of the words “neonatal research, informed consent, perceptions”. This search produced 30 results with 9 studies relevant to my literature review. However I had previously located all 9 studies in my initial search of pubmed. My penultimate search used the following combination of words “neonatal consent, randomised controlled trials”. This yielded 129 results and produced 6 new studies to review. The studies ranged in years from 1999 to 2011.

For my final search of pubmed I included a combination of the words “informed consent, neonatal research”. This yielded 372 results and produced five new studies to review. These studies ranged in years from 2005 to 2012.

**The Cochrane Library**

For my first search I entered a combination of the words “informed consent, neonatal research, randomised trial”. This produced two studies relevant to my literature review. However both studies had been previously located in my pubmed search. I then carried out a second search using a combination of the words “neonatal research, randomised trial, informed consent”. This produced two studies, however both had had been located in my first Cochrane search.

**Google Scholar**

I searched Google Scholar from 1985 to 2015 in attempt to locate any studies that may have been omitted from the 6 previous searches. I used the following combination of words “neonatal research, informed consent, parents views, randomised control trials”. This search presented thousands of studies. After reviewing 300 articles it became obvious that no further suitable studies would be found. This search yielded three new studies relevant to my literature review.

Finally, I conducted a thorough examination of the reference list of each of the 23 key studies previously located. This did not produce any new studies relevant to my literature review.
1.9 Critical appraisal of studies reviewed

I conducted a critical appraisal of the studies produced from my literature searches. To assist with this I utilised the ‘Critical Appraisal Skills Programme’ (CASP) which was developed by the Oxford Regional Health Authority in 1993 (24). The core CASP checklists (randomised controlled trials & systematic reviews) are based on JAMA 'Users guides to the medical literature’ published in 1994 (25). I specifically used the CASP Qualitative checklist. A copy of this checklist can be found in appendix two.

A summary of the main findings from the critical appraisal and quality assessment of the 23 studies included in the literature review is below:

- The aims and objectives of the studies reviewed were clear and comprehensively explained;
- The 23 studies included in the literature review were designed to be either interview based, questionnaire based or a combination of both;
- Each study adequately addressed the aim of the research question (perceptions of

Table 2: Online database search

<table>
<thead>
<tr>
<th>Electronic database searched</th>
<th>Search term(s) used</th>
<th>Total number of searches</th>
<th>No. of potential studies located</th>
<th>No. of applicable studies</th>
</tr>
</thead>
</table>
| Pubmed                       | *Mesh of the words:* clinician’s views, informed consent, neonatal consent, randomised controlled trials.  
*Combined words:* perceptions of informed consent in neonatal research | 5                        | 561                              | 20                       |
| Cochrane Library             | *Mesh of the words:* neonatal research, randomised trial, informed consent  
*Combined words:* informed consent, neonatal research, randomised trial | 2                        | 30                               | 2 (both already located in pubmed search) |
| Google Scholar               | *Combined words:* neonatal research, informed consent, parents views, randomised control trials | 1                        | 300+                             | 3                        |
informed consent in neonatal research);

- Two of the studies reviewed had a randomised design. For one study the parents of newborn babies were randomly allocated to receive one of two consenting processes (a standard or enhanced consent) and in the other parents were randomly allocated to receive one of two information leaflets either with or without a standardized verbal explanation;

- Of the 23 studies reviewed, two studies recruited a parent and clinician cohort. The remainder of studies involved a parent cohort only. Each study recruited an appropriate cohort to address its research question;

- All 23 studies included adequate details of the study setting, background information and study population (parents, clinicians or both);

- Demographic data collected ranged from basic (gender, maternal/paternal age, gestational age, marital status, race and education) to more detailed data collection such as previous birth history, mode of infant delivery, maternal medication and condition of mother after birth. The variance in data collected in each study was relevant to address the specific research question of each study;

- Ethical approval was obtained for the majority of studies reviewed. It was unclear in one study if ethical approval was necessary or sought however the study did discuss ethical considerations when being conducted;

- Written informed consent was obtained for the majority of studies. One study required oral consent only and one questionnaire based study did not seek consent from parents as they could refuse to complete the questionnaire;

- 21 of the studies explored into the perceptions parents had of the informed consent process in neonatal research and two explored into the perceptions that parents and clinicians had of the consenting process;

- Data analysis was presented and discussed in all studies reviewed. Computer analyzing software was used in most studies. All reported data results were deemed adequate;

- Study results and subsequent discussion from the 23 studies reviewed included a summary of explicit findings and clear discussion of these findings including positive and negative discoveries;

- The validity of the findings to the research questions asked in each of the studies was clear and discussed in the discussion/conclusion section of each study;
Table 3: Summary of critically appraised studies, including key findings.

A brief summary of the 23 studies critically appraised, including key findings can be found in table three below:

<table>
<thead>
<tr>
<th>Author and study title</th>
<th>Study aim</th>
<th>Research design and sample details</th>
<th>Data collection</th>
<th>Perception: Parent/ Clinicians or both</th>
<th>Key findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wen-Jun Tu et al. (2011)</td>
<td>Chinese parents on research participation and informed consent.</td>
<td>To understand parents perception of the consenting process and how they felt the research had affected their experience as a parent of a sick infant.</td>
<td>Pilot questionnaire based study. Sample details: Parents of newborn infants admitted to the NICU who had consented to a neonatal clinical trial.</td>
<td>Parent</td>
<td>Parents did not disapprove of the consenting process. Parents believe a detailed consent form is necessary. Parents want to take part in the decision process about enrolling their baby to a clinical trial and believe it should not be the sole decision of clinicians.</td>
</tr>
<tr>
<td>Marc-Aurele K et al. (2012)</td>
<td>Evaluation of the Content and Process of Informed Consent Discussions for Neonatal Research.</td>
<td>An investigation of parental perceptions and investigator disclosure during the neonatal consent process.</td>
<td>A pilot, exploratory, interview based study. Sample details: Parents and trial investigators.</td>
<td>Both</td>
<td>Gaps in investigator disclosure and parent understanding were found. Parents reported comprehension of a greater number of research elements than were actually disclosed by investigators.</td>
</tr>
<tr>
<td>Cartwright et al. (2011)</td>
<td>Parent perceptions of their infant’s participation in randomized controlled trials (RCT).</td>
<td>To explore parents perceptions of their infant’s participation in randomized control trials (RCTs) and the implications of the RCT for their infant and themselves.</td>
<td>A qualitative, interview based study. Sample details: 16 parents of newborn infants who participated in clinical trials whilst an inpatient in the NICU.</td>
<td>Parent</td>
<td>Parents reported mostly positive experiences related to their involvement in the RCTs. Clinicians should be encouraged to approach parents about enrolment to clinical trials. It was noted that appropriate measures should be taken to ensure that the individual needs of parents are being met throughout the entire research process from enrolment to follow-up.</td>
</tr>
<tr>
<td>Author and study title</td>
<td>Study aim</td>
<td>Research design and sample details</td>
<td>Data collection</td>
<td>Perception: Parent/Clinicians or both</td>
<td>Key findings</td>
</tr>
<tr>
<td>------------------------</td>
<td>-----------</td>
<td>-----------------------------------</td>
<td>----------------</td>
<td>-------------------------------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Ballard et al. (2011)</td>
<td>Parents understanding and recall of informed consent information for neonatal research.</td>
<td>To measure parent understanding and recall of key information they received about a phase II neonatal clinical trial.</td>
<td>A randomised study. An enhanced consent process was developed to determine whether parents in the enhanced consent group had better recall of a phase II neonatal clinical trial over parents randomised to a standard consent process. Group 1: received the standard consenting process. Group 2: received an enhanced consenting process.</td>
<td>60 parents in total (30 in control group/30 in enhanced consent group). The enhanced consent group received extra information about the study during consent process and completed a questionnaire immediately after consenting to see how much information they understood. Both groups then received a follow-up validated questionnaire upon their infants discharge.</td>
<td>Parent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Key findings from validated follow up questionnaire: For most questions there was no significant difference in the responses of parents in either consent group. Enhanced Group: Better recall of study information relating to the trial, its risks and the right to withdraw. However none of the follow-up questionnaire responses from parents in the enhanced consent group reflected optimized recall of informed consent information. This study highlighted the presence of the therapeutic misconception. Parents believed the primary purpose of the clinical trial was to help their newborn’s lungs, rather than to obtain generalized medical knowledge that might benefit the health of other newborns in the future. They incorrectly believed taking part in the phase 2 trial would directly benefit their baby.</td>
</tr>
<tr>
<td>Ward (2010)</td>
<td>Parents' views of involvement in concurrent research with their neonates</td>
<td>To discover whether parents previously asked to enrol their newborn to clinical trials would have found concurrent research about their decision-making overly burdensome.</td>
<td>A qualitative, descriptive, interview based study. Sample details: Parents of critically ill newborns who were approached about enrolling their infant to a clinical trial were asked to take part. Parents were asked what they believed about the potential burden or value of being interviewed to explore/discuss the reasons consenting their newborn to a clinical trial. This was called ‘concurrent research’.</td>
<td>Interviews were audio-recorded, transcribed, and analyzed using content analysis techniques. 27 parents in total consented to the interview.</td>
<td>Parent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Participants considered concurrent research acceptable for them but potentially problematic for others. Some parents felt discussing concurrent research may lead to unintentional coercion</td>
</tr>
<tr>
<td>Author and study title</td>
<td>Study aim</td>
<td>Research design and sample details</td>
<td>Data collection</td>
<td>Perception: Parent/ Clinicians or both</td>
<td>Key findings</td>
</tr>
<tr>
<td>------------------------</td>
<td>-----------</td>
<td>------------------------------------</td>
<td>-----------------</td>
<td>----------------------------------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Korotchikova et al. (2010)</td>
<td>Presence of both parents during consent process in non-therapeutic neonatal research increases positive response.</td>
<td>To investigate factors that influenced parental consent/non-consent in a non-therapeutic electroencephalogram (EEG) study in healthy newborns.</td>
<td>Sample details: Parents of healthy newborn infants were asked to enrol their baby in a neonatal EEG study. In the case of refusing/withdrawing consent, an informal interview was conducted to investigate reasons for refusal.</td>
<td>Parent</td>
<td>Parent consent to the study was obtained in 82 cases. 10 parents subsequently withdrew consent. Total number of participating parents was 72. Approximately 33% refused to consent their newborn baby to the study. Consent was more likely to be given if both parents were present. When mothers were approached alone, obtaining consent was significantly more difficult within the first 6 hours of delivery compared to a later approach (37% vs. 67% respectively). Refusals were classified into issues of voluntariness (7%), informed choice (10%), understanding (54%) and competence (29%).</td>
</tr>
<tr>
<td>Jollye (2009)</td>
<td>An exploratory study to determine how parents decide whether to enrol their infants into neonatal clinical trials.</td>
<td>To determine how parents decide to enrol their baby into neonatal clinical trials.</td>
<td>Semi structured, interview based, qualitative study. Sample details: Families who had decided to enrol or not enrol their baby into non urgent clinical trials took part. Parents took part in the semi structured</td>
<td>The semi structured interviews took place two months after their baby was discharged home. A total of 7 families took part. Interviews with parents were recorded, transcribed and analysed using an open coded mechanism.</td>
<td>Parents</td>
</tr>
<tr>
<td>Author and study title</td>
<td>Study aim</td>
<td>Research design and sample details</td>
<td>Data collection</td>
<td>Perception: Parent/ Clinicians or both</td>
<td>Key findings</td>
</tr>
<tr>
<td>------------------------</td>
<td>-----------</td>
<td>----------------------------------</td>
<td>-----------------</td>
<td>----------------------------------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Ward (2009)</td>
<td>This study examined parents beliefs about participating in clinical trials which involve a greater than minimal risk to their neonate and explored into their views of the experience.</td>
<td>A qualitative, descriptive, interview based study. Sample details: Parents of newborn babies in the NICU who had been approached to consent their newborn to research were asked to describe their decisions about consenting or not consenting their infant to the study.</td>
<td>A total of 27 parents from three different hospitals took part. The majority of interviews took place via phone and were audio taped. An interview guide was used by the interviewer to ensure the same line of inquiry was assumed with each participant. Data collection stopped when interviews yielded minimal new information to expand the findings.</td>
<td>Parent</td>
<td>Analysis of interviews yielded 3 key themes: chaos, vulnerability and control. Parents expressed fear and confusion for their infant. Parents voiced perceptions of their own vulnerability, acknowledged other parents’ susceptibility and showed vulnerability through their misunderstandings of the infants research protocol. Factors influencing a sense of control included the time parents believed they had to make a decision, gathering information and participation in the trial.</td>
</tr>
<tr>
<td>Hoehn et al. (2009)</td>
<td>To assess the impact of time on parental decision-making for research participation of their newborn infants with congenital heart disease.</td>
<td>Interview based study. Sample details: Parents of newborn infants with congenital heart disease.</td>
<td>Interview based study. 18 father and 19 mothers were interviewed separately within 10 days of their neonate’s cardiac surgery. All parents were asked the same questions: (1) “Did you have adequate time to make a decision about research?” and (2) “Why?” Interviews were audio taped and transcribed for further review and analysis.</td>
<td>Parent</td>
<td>Of the 37 parents, 14 said they had insufficient time to make a decision regarding their baby’s participation in at least one of the studies however some of these parents still permitted their baby to be enrolled. A total of 23 parents reported that they did have enough time to make a decision regarding their baby’s participation in the studies presented to them.</td>
</tr>
<tr>
<td><strong>Author and study title</strong></td>
<td><strong>Study aim</strong></td>
<td><strong>Research design and sample details</strong></td>
<td><strong>Data collection</strong></td>
<td><strong>Perception:</strong> <strong>Parent/Clinicians or both</strong></td>
<td><strong>Key findings</strong></td>
</tr>
<tr>
<td>----------------------------</td>
<td>---------------</td>
<td>---------------------------------------</td>
<td>--------------------</td>
<td>---------------------------------------------</td>
<td>------------------</td>
</tr>
<tr>
<td>Freer et al. (2009)</td>
<td>To explore the impact of various information-sharing approaches on parents' understanding of a research study and the validity of their consent.</td>
<td>Randomized, controlled study. Sample details: Parents of parents of immature but well infants admitted to the NICU were randomly assigned within 72 hours of the infant's admission to receive 1 of 2 information leaflets either with or without a standardized verbal explanation, for a hypothetical intensive care research study. Leaflets differed in length and in the amount of detail in which the study process, risks, benefits and patient rights were described. A questionnaire was used to elicit parents understanding of the purpose, design and procedures involved in the study and the consent process.</td>
<td>Parents were randomly assigned to receive 1 of 4 different styles of information leaflets: group 1 - US leaflet; group 2 - US leaflet and explanation; group 3 - UK leaflet; group 4 - UK leaflet and explanation. Demographic data and previous experience with neonatal research were collected. A total of 41 parents took part.</td>
<td>Parent</td>
<td>Parents who received the longer leaflet without verbal explanation gained only limited understanding of the purpose of the research study. Study procedures were understood better by those who received the shorter leaflet. Issues relating to consent and study design were readily understood in all groups. Irrespective of documentation style, verbal explanation significantly improved understanding. Differences in understanding had little effect on whether a parent would enrol his or her infant into the study.</td>
</tr>
<tr>
<td>Author and study title</td>
<td>Study aim</td>
<td>Research design and sample details</td>
<td>Data collection</td>
<td>Perception: Parent/ Clinicians or both</td>
<td>Key findings</td>
</tr>
<tr>
<td>------------------------</td>
<td>-----------</td>
<td>-----------------------------------</td>
<td>-----------------</td>
<td>---------------------------------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Snowdon et al. (2006)</td>
<td>&quot;It was a snap decision&quot;: Parental and professional perspectives on the speed of decisions about participation in perinatal randomised controlled trials.</td>
<td>This study explored the pace of decision-making for parents who were asked to enrol their newborn infant to perinatal or neonatal trials.</td>
<td>An interview based qualitative study. Sample details: Parents of infants associated with perinatal or neonatal clinical research. Involving 78</td>
<td>The study was conducted in 8 UK centres and focused on two antenatal and two neonatal trials. The study involved 51 parent interviews describing 56 trial-related decisions. 78 parents in total took part. When taking part 62 parents had surviving infants and 16 parents had infants who had died. Most interviews were conducted in parents’ homes. Two were conducted by telephone. Interviews were tape-recorded with parental permission. The transcripts were read and coded using the textual analysis computer package Atlas - ti.</td>
<td>Parent</td>
</tr>
<tr>
<td>Author and study title</td>
<td>Study aim</td>
<td>Research design and sample details</td>
<td>Data collection</td>
<td>Perception: Parent/ Clinicians or both</td>
<td>Key findings</td>
</tr>
<tr>
<td>------------------------</td>
<td>-----------</td>
<td>-----------------------------------</td>
<td>----------------</td>
<td>--------------------------------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Morley et al. (2005)</td>
<td>To investigate parents' opinions about enrolling their premature baby into several research studies in the few days after birth.</td>
<td>Questionnaire based research study. Sample details: Mothers and fathers of preterm newborn infants admitted to the NICU.</td>
<td>In total 50 mothers and 42 (of 48) fathers completed the questionnaire independently. The newborn infants had been asked to join two or more studies. Parents were invited to complete a questionnaire about each study which involved their baby. The questionnaire was piloted on 10 sets of parents before final modification. There were two styles of question. Parents were either asked to circle the most appropriate answer to each question or to answer on a seven point likert scale. They were to fill in the questionnaire during their baby’s third week of life. They were asked to complete it independently of their partner and return it anonymously in a sealed envelope.</td>
<td>Parent</td>
<td>71% of the parents thought it was good for their baby to be in a hospital which carried out research. 93% thought their baby would get the same or better care in a study. 15% thought their baby was too small for research studies. 98% wanted to be involved in the decision about their baby joining a study. 22% were worried about the number of studies. 10% would not enrol their baby in any studies. 74% were willing for their baby to join two or more studies. 10% would enrol in all the studies. 94% believed that their baby’s participation would improve care of future babies. From this study, it appears that parents are supportive of neonatal research and participation in multiple studies.</td>
</tr>
<tr>
<td>Author and study title</td>
<td>Study aim</td>
<td>Research design and sample details</td>
<td>Data collection</td>
<td>Perception: Parent/ Clinicians or both</td>
<td>Key findings</td>
</tr>
<tr>
<td>------------------------</td>
<td>-----------</td>
<td>-----------------------------------</td>
<td>----------------</td>
<td>--------------------------------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Cultbert et al. (2005)</td>
<td>This study aimed to evaluate parental preferences for hypothetical consent procedures in neonatal resuscitation research.</td>
<td>Pilot questionnaire based study. Sample details: Randomly selected parents who had received obstetrical or neonatal care at a tertiary perinatal centre.</td>
<td>Questionnaires were posted to parents. The response rate was 34%. The respondents were a group of highly educated women with a higher family income than would be expected in the general population.</td>
<td>Parents</td>
<td>This study showed parent preferences to receive prenatal information and consent for studies of neonatal resuscitation. A low response rate and potentially skewed demographics of the respondents prevent generalisability of this result. Parents valued the impact the research would have on their baby and the importance of a positive interaction with the physicians conducting the research study. Parents felt most comfortable with prospective consent in the setting of prenatal classes or prenatal visits with a physician, but they were somewhat uncomfortable with prospective consent upon admission to hospital after labour had begun. Parents were uncomfortable with waived consent, deferred consent, and opting out.</td>
</tr>
<tr>
<td>Hoehn et al. (2005)</td>
<td>To determine the reasons for parents' decisions about participation in research studies.</td>
<td>Semi structured qualitative interviews. Sample details: Parents of newborn infants.</td>
<td>Qualitative analysis of the unsolicited comments of 34 parents regarding their reasons for agreeing or declining to participate in neonatal research studies. The study represents a qualitative analysis of these unsolicited and originally unanticipated, parental comments about research participation. All the interviews were audio-taped, transcribed, and analysed using N-Vivo qualitative software. The transcripts were reviewed independently to identify parental reasons during the interviews.</td>
<td>Parent</td>
<td>Parents cited five types of reason for or against permitting their newborn to participate in research studies: societal benefit (n = 18), individual benefit for their infant (n = 16), risk of study participation (n = 10), perception that participation posed no harm (n = 9), and anti-experimentation views (n = 4).</td>
</tr>
<tr>
<td>Author and study title</td>
<td>Study aim</td>
<td>Research design and sample details</td>
<td>Data collection</td>
<td>Perception: Parent/ Clinicians or both</td>
<td>Key findings</td>
</tr>
<tr>
<td>------------------------</td>
<td>-----------</td>
<td>------------------------------------</td>
<td>-----------------</td>
<td>----------------------------------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Stenson et al. (2004)</td>
<td>To investigate the recollections of parents consenting for their infants to be research subjects and determine their views about the need for consent.</td>
<td>Questionnaire based research project. Sample details: Parents of sick infants who had been enrolled to a RCT.</td>
<td>Questionnaire and letter was posted to 154 parents, 18 months after the RCT finished. All parents gave written consent and received an information leaflet about the RCT. Questionnaire based on likert scale and had open and closed ended questions all regarding their experiences of the consent process. The questionnaires were to be returned by post.</td>
<td>Parent</td>
<td>Response rate was 64% (99/154). Some respondents (12%) did not remember being asked to consent to their baby joining a study and a further 6% were unsure. Most of the respondents (79%) were happy, 13% neutral, and 8% unhappy with their decision to give consent. None felt heavy pressure to agree. Entering the trial caused 24% of respondents to feel more anxious, 56% neutral, and 20% less anxious about their baby. Most of the respondents (83%) would be unhappy to forgo the consent process for trials passed by the institutional ethics committee.</td>
</tr>
<tr>
<td>Author and study title</td>
<td>Study aim</td>
<td>Research design and sample details</td>
<td>Data collection</td>
<td>Perception: Parent/Clinicians or both</td>
<td>Key findings</td>
</tr>
<tr>
<td>------------------------</td>
<td>-----------</td>
<td>-----------------------------------</td>
<td>----------------</td>
<td>--------------------------------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Ballard et al. (2004)</td>
<td>Neonatal research and the validity of informed consent obtained in the perinatal period</td>
<td>To determine the validity of informed consent obtained from parents of infants enrolled in a multicenter randomized research study, neurologic outcomes and pre-emptive analgesia in the neonate (NEOPAIN).</td>
<td>Interview based study. Sample details: Subjects: Parents of infants enrolled to an RCT.</td>
<td>In total 64 parents were interviewed by investigators either in the NICU or by phone. The questionnaire was developed by investigators and had open ended questions based on a likert scale. Parents were asked 20 open ended questions to determine their level of understanding (including memory of consenting) of the RCT. Results were analysed using SAS.</td>
<td>Parent</td>
</tr>
<tr>
<td>Author and study title</td>
<td>Study aim</td>
<td>Research design and sample details</td>
<td>Data collection</td>
<td>Perception: Parent/ Clinicians or both</td>
<td>Key findings</td>
</tr>
<tr>
<td>------------------------</td>
<td>-----------</td>
<td>-----------------------------------</td>
<td>----------------</td>
<td>--------------------------------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Burgess et al. (2003)</td>
<td>To understand parental perceptions of the process of recruitment and enrolment for research in the neonatal intensive care unit.</td>
<td>Questionnaire based study. Sample details: Parents of newborn infants who were enrolled in trials in a neonatal intensive care unit. The questionnaire was used in both a retrospective and a prospective study.</td>
<td>The questionnaire had 35 questions based on a likert scale. Closed ended and open ended questions were included as well as demographic questions. It was either posted or given to parents who 1; had a baby enrolled in a study in the NICU in the past or 2; parents who at present had a baby enrolled in a study in the NICU. 29 parents completed the retrospective study and 44 parents completed the prospective study.</td>
<td>Parent</td>
<td>The retrospective survey had a 79% response rate. 90% of parents felt that they had made informed decisions. 93% were opposed to allowing doctors decide if newborns should be enrolled into a study, rather than the parent. 38% found that recruitment did add “stress to an already stressful situation”. 90% felt that they had made informed decisions. Parents thought that they would be comfortable with enrolment into two studies. Parents suggested that information about a study be made available to them before delivery. The responses of parents in the prospective study were mostly consistent with those from the retrospective survey.</td>
</tr>
<tr>
<td>Author and study title</td>
<td>Study aim</td>
<td>Research design and sample details</td>
<td>Data collection</td>
<td>Perception: Parent/ Clinicians or both</td>
<td>Key findings</td>
</tr>
<tr>
<td>------------------------</td>
<td>-----------</td>
<td>----------------------------------</td>
<td>----------------</td>
<td>---------------------------------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Singhal et al. (2002)</td>
<td>To examine beliefs and attitudes of parents about research with babies.</td>
<td>Questionnaire based study. Sample details: 72 parents of newborn babies admitted to the in the NICU and 159 parents of normal newborns.</td>
<td>The questionnaire was developed to assess the general attitudes of parents about research with newborns. In the NICU 72 families participated in the study and 52 returned completed questionnaires giving a response rate of 72%. A total of 207 families with normal newborns were asked to take part; 166 agreed and 107 returned completed questionnaires for a response rate of 64%.</td>
<td>Parent</td>
<td>Parents showed favourable attitudes toward research with babies. There were few differences between the two groups of parents, but there was a trend toward increased trust in doctors by &quot;NICU parents.&quot; Couples with newborns in the NICU were significantly more likely to enrol their newborn in a study involving moderate risk and possible major direct benefit. Almost a third of the sample in both groups was willing to enrol their newborn in a study with moderate risk and no direct benefit.</td>
</tr>
<tr>
<td>Mason et al. (2000)</td>
<td>Questions have been asked about whether the process of obtaining informed consent from parents to clinical trials on neonates leads to valid consent. The aim of this study was to assess this issue and to seek any practical improvements.</td>
<td>Semi-structured interview based study. Sample details: Parents of 200 babies who had been asked for consent to neonatal trials and 107 neonatologists seeking consent to neonatal trials.</td>
<td>Parents and investigators were interviewed by research assistants. Most questions were open-ended. Interviews were taped where consent was given and telephone interviews were also permitted. For telephone interviews, the answers to questions were written onto the schedules during the interview whereas in taped, face-to-face interviews answers were transcribed later onto the schedules by the interviewer.</td>
<td>Both</td>
<td>59 of the 200 parents had given valid consent or refusal. Impaired consent was greatest for research in an emergency situation and for that associated with risk or discomfort greater than standard treatment. Information sheets were little used by parents in deciding whether to consent. Parents highly valued their involvement in the informed consent process, and clinicians generally agreed on the value of the consenting process.</td>
</tr>
<tr>
<td>Author and study title</td>
<td>Study aim</td>
<td>Research design and sample details</td>
<td>Data collection</td>
<td>Perception: Parent/ Clinicians or both</td>
<td>Key findings</td>
</tr>
<tr>
<td>------------------------</td>
<td>-----------</td>
<td>----------------------------------</td>
<td>----------------</td>
<td>----------------------------------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Oberle et al. (2000)</td>
<td>The purpose of this study was to begin an exploration of parents' perceptions about research with newborn babies through the development and validation of a survey instrument.</td>
<td>Questionnaire based study. Sample details: 72 parents with infants in a NICU/SCN and 159 parents of normal newborn babies. It was explained to the parents that in order to complete part of the questionnaire they would be required to imagine that their baby was ill and that if they experienced severe distress there would be counselling immediately available.</td>
<td>231 parents completed the questionnaire. Descriptive statistics were calculated on all variables. The questionnaire looked for demographic information. The questionnaire consisted of likert scale questions. The final section was developed to determine the circumstances under parents would enrol their newborn into a trial.</td>
<td>Parent</td>
<td>Factor analysis revealed seven factors corresponding to issues identified in the literature, providing evidence of construct validity. Parents had no difficulty completing the instrument and all questions were answered by the majority of participants. It was concluded that the questionnaire had adequate psychometric properties and that a mixed method approach can be fruitful in exploring sensitive issues.</td>
</tr>
<tr>
<td>Snowdon et al. (1999)</td>
<td>This study describes how 44 parents recruited to a difficult neonatal trial that used conventional randomization reacted to the idea of Zelen randomization.</td>
<td>Qualitative interview based study. Sample details: A total of 44 parents were interviewed (including two parents present at the interview as well as lone parents). Pilot study completed initially with 8 parents, then main study with 36 parents.</td>
<td>Interviews were carried out in parents home or over the phone in UK and Ireland. All interviews were tape recorded with the permission of the parents.</td>
<td>Parents</td>
<td>All but 3 parents expressed an opinion on Zelen randomisation. 21 in favour of Zelen randomisation, 20 opposed, 1 unable to decide and 2 parents did not give clear enough answer regarding their feeling toward Zelen to be able to distinguish if they were for or against it.</td>
</tr>
<tr>
<td>Author and study title</td>
<td>Study aim</td>
<td>Research design and sample details</td>
<td>Data collection</td>
<td>Perception: Parent/ Clinicians or both</td>
<td>Key findings</td>
</tr>
<tr>
<td>------------------------</td>
<td>-----------</td>
<td>------------------------------------</td>
<td>----------------</td>
<td>---------------------------------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Zupancic et al. (1997)</td>
<td>Determinants of parental authorization for involvement of newborn infants in clinical trials.</td>
<td>This study was completed to determine the degree to which a parental decision to enrol their newborn infant to a clinical trial is influenced by risk and benefit considerations compared with other factors.</td>
<td>Cross sectional survey. Sample details: Parents who had recently given or declined consent to one of 3 clinical trials in a NICU.</td>
<td>124 parents were asked to complete the questionnaire which consisted of 15 sociodemographic items and 13 scaled responses to statements assessing the probability and magnitude of risk and benefit as well as perceived illness severity, attitudes toward research, and the consent process. Responses were subjected to factor analysis to identify underlying constructs. The sample was then randomly split, and multiple regression was performed on each half. Response rate was 83% (103 of 124) for those who had consented and 86% (37 of 43) for those who had declined.</td>
<td>Parent In making consent decisions on behalf of their newborn infants, parents are influenced by risk and benefit considerations, attitudes toward research, and the integrity of the consent process. A significant minority of parents (32%) would prefer to have clinicians advise them whether to volunteer their infants for a clinical trial.</td>
</tr>
<tr>
<td>Snowdon et al. (1997)</td>
<td>“Making sense of randomization”; responses of parents of critically ill babies to random allocation of treatment in a clinical trial.</td>
<td>To explore in detail parental reactions to randomisation allocation of treatment in a neonatal randomised controlled trial involving ECMO.</td>
<td>Two part study involving completion of a questionnaire and face to face interviews. Sample details: Parents of critically ill newborns</td>
<td>Parents of critically ill newborns were initially asked to complete a questionnaire which focused on their satisfaction relating to the information they received at the time of consent. 71 parents returned a completed questionnaire. The questionnaire enquired if parents would like personal contact with a researcher. 42 said yes and 21 couples were invited to take part in interview part of study. (21 = 16 couples and 5 mothers).</td>
<td>Parent There was some clear confusion over randomisation and ECMO for most if the parents interviewed. A subtle distortion of the aims of randomisation was evident in a number of interviews.</td>
</tr>
</tbody>
</table>
1.10 Data collection

From each study the aim, design, data collection methods and key findings/conclusions were extracted and assessed. I separated the studies to review data that explored the perceptions parents had of the informed consent process, then studies which explored the perceptions clinicians had of the informed consent process and finally, studies which explored the perceptions both groups had of the informed consent process in neonatal research.

1.11 Results

My Pubmed search yielded a total of 561 articles. Of these, 20 were applicable to my literature review. My Cochrane Library search did not produce any further articles. Finally, my Google Scholar search produced a total of three new articles relevant to my literature review. In total I had 23 articles to review and analyse. 21 were studies exploring the perceptions parents had of the informed consent process and two explored the perceptions parents and clinicians had of the informed consent process in neonatal research.

1.12 Parent perceptions of informed consent in neonatal research

For this portion of my literature review I read and analysed 23 studies which examined parent perceptions of informed consent in neonatal research. Studies included both randomised controlled clinical trials and non therapeutic neonatal research.

From my review it appears that in general, parents are supportive of neonatal research (26) (27). They expressed altruistic motives for allowing their newborn infant to participate in a research study. They believed that their newborn infant’s participation will help future generations of sick, newborn infants. Other reasons for allowing their newborn infant participate in neonatal research include a belief that participation would be of a personal benefit to their newborn infant and the belief that participation in a research study posed no harm to their child (28-30).
Parents reflected positively toward their experience of the consenting process; in one study reviewed, approximately one year after consenting their newborn infant to a neonatal clinical trial, parents did not express disapproval of the consenting process they had taken part in (31).

A study conducted by Cartwright et al. (2011) enrolled sick premature newborn infants to randomised controlled trials. The study had two aims; to investigate the perception parents had of their newborn infant’s participation in randomized control trials (RCTs); and the implications of the RCT for both their infant and themselves (29).

This study concluded that clinicians should be encouraged to approach parents about enrolment to neonatal clinical trials. In turn, parents stated that the ability to make decisions on behalf of their newborn infant regarding participation in clinical trials gave them some control of medical decision making in an otherwise uncontrolled situation. However, the vulnerability of parents was noted and it was highlighted by parents that appropriate care should be provided to parents both during a clinical trial and after the clinical trial has ended (29).

The vulnerability of parents has been noted by other researchers. In a study completed by Ward (2009) parents specifically acknowledged their own vulnerable status and that of other parents in the neonatal period. This study also found that parents demonstrated confusion relating to their infants research protocol (32). It is clear that parents are aware of their own vulnerability and also have a heightened awareness of the vulnerability of parents in a similar position them. It could be possible that parents approached with information about a neonatal research study, who are fearful for their newborn infants health, fearful for themselves as they attempt to make the ‘correct decision’ about consenting to a neonatal research study, also experience additional stress relating to feelings of concern for other parents in a similar position to themselves. The vulnerability of parents and elements which can add additional stress to them is an area within neonatal consenting which will probably warrant further research and discussion.

A variety of studies have shown that in general parents want to be involved in the decision making process regarding their infant’s participation in neonatal research (14).
However in a study carried out in 1997 a significant minority of parents (37%) would rather the clinician advise them about whether they should volunteer their newborn infant into a clinical trial, rather than making the decision independently (33). It should be noted that in this study parents specifically asked for clinician’s advice regarding consent. Parents did not want clinicians to make the decision about consenting on their behalf.

Parents are not supportive of the concept of a waiver of consent (34). In a study completed Stenson et al. (2004) 83% of participants would be unhappy to forgo the consent process for trials which were granted approval by a research ethics committee (35). It is clear that while parents value the communication they have with clinicians regarding their infant’s participation in neonatal research, they feel it necessary to be ultimate decision holders.

Ballard et al (2004) suggests it is virtually impossible to obtain a valid informed consent during the antenatal/perinatal period (36). In 2009 the University of Kentucky conducted the NEOPAIN study. NEOPAIN evaluated the effect of continuous infusion morphine vs placebo on the neurologic outcome of premature. Infants enrolled to this clinical trial were between 23 to 33 weeks gestational age.

Parents whose newborn infants were enrolled in NEOPAIN and survived to discharge were asked to complete a questionnaire to determine their level of understanding about NEOPAIN study procedures. Of the 64 parents interviewed, five (7.8%) did not recall the study nor signing consent. For those who did remember the study only 68% had comprehension of the purpose of the study. Alarmingly, only 5% could name even one risk of the study. Using a stringent set of criteria, only 3% of parents were deemed to have given valid informed consent (36, 37). This study involved very sick preterm infants and parents under severe emotional stress.

The distressing results of the NEOPAIN trial indicate both an urgent need for further exploration specifically into the validity of consent currently being obtained from the parents of sick preterm newborn infants during the antenatal/perinatal period and the need for guidance for clinicians in relation to obtaining a valid consent from this
vulnerable population. On a positive note, parents stated in the questionnaire that they did not feel pressure or coerced to enrol their newborn infant to the trial and would consider taking part in additional studies if requested. This finding also noted in a previous study by Morley et al (26).

1.13 Informed Consent Form

According to Wen-Jun Te et al. (2012) parents involved in the consenting process in neonatal research should be provided with a detailed informed consent form (31). These results directly conflict the results of a study completed in 2009 entitled “More information, less understanding: a randomised study on consent issues in neonatal research”. For this study the parents of premature infants were randomly assigned to receive 1 of 2 information leaflets. The leaflets differed in content and length and one leaflet provided greater detail of study procedures.

Results showed that parents who received the longer information leaflet without a verbal explanation of study procedures had limited understanding of the purpose of the study. Those who received the shorter, more concise leaflet appeared to have a greater understanding of study procedures (38). It was also suggested that verbal explanation of study procedures significantly increases understanding of the research process for parents regardless of the style of information leaflet written documentation (38).

When one compares the results of both studies it becomes clear that further research needs to carried out, in particular, to determine the appropriate amount of information which should be provided on consent forms.

It has been suggest that oral and written information should be provided to parents concurrently at the time of consent (14). It has also been noted that the presence of both parents during the consenting process can lead to a higher uptake of consent to neonatal research (39).

1.14 Clinicians perceptions of informed consent in neonatal research
It is the responsibility of researchers/clinicians to provide detailed information to parents about a neonatal research study and, to establish if the information received has been processed and understood (21). However, despite the critical role clinicians have in the informed consenting process in neonatal research, there is a lack of studies available which explore their views. I located two studies applicable to this section of my literature review.

The first study, by Marc-Aurele et al. (2012) explored into the information disclosed by investigators to parents and parental perceptions of information received during the consenting process in neonatal research (40). A total of 9 Investigators and 30 parents took part. Both consented to having the informed consenting discussion audio taped. Tapes were analysed for the content disclosed and discussed by both parties during the consenting process.

The following results were noted; a total of 10% of Investigators assessed parent recall of the information received at the end of the consenting discussion, 71% of Investigators asked parents if they had any concerns about the research study, 48% of Investigators asked parents if they understood the information received about the study and 38% of Investigators provided a summary of the discussion for parents.

These figures highlight an alarmingly low percentage of Investigators who request feedback from parents and also provide feedback to parents about the information received and discussed during the consenting process. The parents of newborn infants eligible to take part neonatal research are both emotional and vulnerable at the time of consent. It is essential that Investigators take the time to ensure parents understand the information received during the consenting process. It is their duty to ensure adequate discussion including a summary of the dialogue is provided to parents where necessary is provided.

Parents subsequently completed a questionnaire relating to their research participation and level of comfort with the contact between themselves and the Investigator. Results were both positive and negative. 100% of parents understood the voluntary nature of the research participation, 95% understood the societal benefit of the research, 90%
understood that they were free to withdraw from the study at any time and 85% understood the possible risks associated with the study. However 58% agreed or strongly agreed that discussing their newborn infants participation in a research study was stressful. It is also important to note that only 50% of parents expressed understanding of the randomisation process (where randomisation was part of the research study).

Parental confusion surrounding the element of randomisation was highlighted in another study completed by Snowdon et al (1997). In this study clear confusion relating to the process of randomization was noted by researchers (16).

It is clear there is a need for further research in this area to be completed to try to understand why some parents can find discussing neonatal research with investigators stressful. It is essential the neonatal community attempt to minimise if not eliminate any extra burden clinical research may have on parents.

The second study applicable to this literature review was completed by the Euricon Study Group (41). The Euricon Study was funded by the European Union. The objective of the study was to examine informed consent in neonatal research throughout European clinical sites (42). Briefly, the parents of 200 infants and 107 neonatologists involved in the consenting process to a neonatal clinical trial were interviewed by research assistants. Interviews were analysed to explore the validity of the consenting process focusing on four areas; parental competency, information given by Investigators, parental understanding of the information received and the voluntariness of the consent.

Results showed only three Investigators were satisfied with the consenting process in general and had obtained a satisfactory consent. A total of 79 Investigators indicated concerns about the competency of parents. Investigators expressed conflicting views in relation to the amount of information that should be made available to parents. In total 66 Investigators thought parents should receive all information relating to the clinical trial whereas 47 Investigators believed certain information should be withheld from parents.

Results generated from this study were quite alarming. Although 79 Investigators expressed concern relating to the competency of parents, they proceeded to allow
parents consent their newborn infant into a clinical trial. The causes of concern for Investigators included the vulnerability parents, who, according to Investigators, at that time did not have the ability to make an informed decision about enrolling their newborn to a clinical trial. This was due to the lack of knowledge, intellect or emotional state of the parents at that particular time of their lives. All of which could lead one to argue that Investigators should never approach parents in a neonatal intensive care setting to seek their consent if questions can be raised about their capacity to understand information received about a neonatal research study. In total 59 parents out of 200 were deemed to have provided a valid consent or refusal to a clinical trial. It is suggested that further research is warranted in the highly sensitive area of consenting in neonatal research to maximise the ability to obtain valid consent from parents.

1.15 Conclusion

It is clear from this literature review that parental perception of informed consent in neonatal research is a relatively well investigated and documented area. The views and experiences parents have of various types of neonatal research, including randomised controlled clinical trials and non interventional neonatal research has been studied (32) (43). Certain results were found to be consistent with each other. It is stated in many studies that in general parents are supportive of neonatal research (29) (39) (28) (26). Parents want to help babies born in the future, by allowing their newborn infant participate neonatal research studies and, in most cases parents want to be the sole decision makers regarding consent or refusal of consent.

There has also been novel information produced in relation to randomisation in the neonatal research setting including Zelen randomisation in a neonatal clinical trial (44). Zelen randomisation is a process whereby randomization occurs automatically prior to consent being sought from parents. Consent is sought from parents if the infant is randomized to an experimental arm of a neonatal randomized controlled trial. Thus parents of infants in the control group will remain unaware that randomization has taken place.
It has been noted that for therapeutic clinical trials, this method of randomisation is probably unethical (45). However a study which explored into parents views of zelen randomisation results showed that half of the parents who took part were in favour of the process (44). Due to the novel nature of zelen randomisation further research into the views parents have of the process is warranted. It is also suggested that research into the views ethics committees and clinicians have of zelen randomisation should be undertaken.

It is clear that ample information is available which relates to the perceptions parents have of the informed consent process in neonatal research. However there is an urgent need for further exploration of other aspects of informed consent in neonatal research including parents understanding of the randomisation process and, as shown by Ballard et al. (2011) the appropriate content and amount of content which should be included in the informed consent form (46).

The complex ethical issue of the vulnerability of parents during the neonatal period is another area in need of further research. A study completed by Snowdon et al. (2006) investigated into the speed of decision-making of parents who were asked to enrol their newborn infant to either perinatal or neonatal trials. A total of 51 parental interviews took place. The 51 interviews described 56 trial related decisions. Evidence of parental vulnerability was noted in this study (47).

There is a scarce amount of information available which deal with investigator perceptions of the informed consent process in neonatal research. The two studies described in this literature review outline important results in relation to investigator perceptions; however there are many gaps in this area in need of further exploration.

In the EURICON study Investigators allowed parents to consent their newborn infant to a clinical trial despite the fact that Investigators expressed concerns relating to their competence. Could it be noted that the Investigators were acting in an unethical manner by allowing consent to be given? It was also noted that some Investigators gave limited disclosure of information relating to the risks of the trial. The reasons for this was to not
cause any further concern to parents at such a vulnerable time but to also to obtain consent.

It is clear that Investigators act in a manner which they believe to be in the best interest of parents, study subjects and indeed society by carrying out neonatal research. Results from this literature review would suggest that increased training in acquiring informed consent is necessary for Investigators when consent is being sought from such a vulnerable population. There is an obvious lack of such requisite training in published studies which obtain perceptions of informed consent from a clinician’s point of view.

This is an area in urgent need of further research. It could also be suggested that a tool to assist Investigators assess the validity of consent be produced, for example a checklist that the Investigator must complete after the consenting process to check for the areas of competence, understanding of information given and the voluntariness of consent.
Chapter 2: Ethical and Legal Issues of Informed Consent in Research

2.1 Background to clinical research involving human participants

Clinical research is governed by strict guidelines and regulations whose main objective is to protect human study subjects from harm. Before exploring into the regulations overseeing clinical and non-therapeutic research, it is important to investigate into the historical background of clinical research to fully appreciate why such stringent guidelines and regulations are in place. Clinical trials involving human study subjects are now strictly monitored for compliance by regulatory bodies in the various member states.

There has been a horrifying legacy of unethical exploitation of human research subjects by the scientific and medical communities in the past. Victims of unethical research studies include some of the most vulnerable citizens of society such as children with mental disabilities, prisoners of war and the economically disadvantaged. At no time were any of these participants afforded the opportunity of giving informed consent.

The goal of this chapter is to discuss two of the most controversial, unethical clinical trials which took place during the twentieth century, the Tuskegee Syphilis Study and the Willowbrook State School Experiments. I will also outline the guidelines enacted after the atrocities of experiments conducted on prisoners of war in various Nazi Concentration Camps during World War 2 came to light during the Nuremberg Trials.

2.2 The Tuskegee Syphilis Experiment

It is a cruel testament to human nature that we possess the ability to take advantage of those more vulnerable than ourselves. The Tuskegee syphilis experiment is an unfortunate demonstration of such unethical conduct where the fascination of science took precedence over the value of human life (48). This federally funded research experiment began in 1932 and continued until 1972, was carried out by the United States Public Health Service. The study chartered the natural progression of untreated syphilis in African/American men living in rural Alabama. Researchers recruited a total of 600 impoverished males to the study.
The research participants were offered incentives to encourage them to take part in the study including free physical examinations, free meals, and burial insurance. They were not told of their diagnosis of syphilis nor did they receive adequate treatment for the disease. This was despite the discovery of penicillin as the “gold standard” treatment for syphilis in 1947 (49) (50).

The Tuskegee Syphilis experiment is an abhorrent example of an abuse of power from one human to another. Researchers conducted themselves in both an unethical and unprofessional manner. They chose to withhold the treatment for syphilis from this vulnerable population, whilst all the time having an effective cure to the disease at their disposal. The study finally came to a halt in 1972 after a newspaper report was published linking the study to unethical practices which led to a review of the study.

The report highlighted gross misconduct by researchers who withheld crucial information about the risks of the research study from participants, and in effect, did not acquire informed consent. The unethical treatment of research participants in the Tuskegee Syphilis experiment resulted in the publication of the infamous Belmont Report in 1978 (51). The report describes three core principles which govern the ethics of research involving humans which should be adhered to (51);

1. Respect for Persons: Research participants should be treated as autonomous agents and their autonomy must be respected. However a person classes as having diminished autonomy must be protected;

2. Beneficence: In the context of medical research, to act in a beneficent manner researchers must do not harm to research participants and maximize possible benefits and minimize possible harm to them; and

3. Justice: The report states that the principle of justice allows fair distribution of the benefits of research and that people should be treated as equals (51).

2.3 The Willowbrook State School Hepatitis Experiments
Unethical conduct of clinical research involving humans was not limited to vulnerable adults. During the mid 1950s researchers working in the state funded Willowbrook School, New York purposely infected mentally disabled children, aged three to 11 with strains of the hepatitis virus in an effort to study the development of the infection (52, 53). Researchers also wanted to determine the effectiveness of gamma globulin injections as protection against hepatitis.

To facilitate the research, the lead investigator Dr Saul Krugman established a specialist unit in the school for the children participating in the study. The unit offered improved living conditions than the main school including higher hygiene standards and improved nutrition. Researchers tried to encourage parents to enrol their child to the study by offering expedited entry to the school. At the time Willowbrook School was overcrowded and with extensive waiting lists.

While ‘consent’ was obtained from parents on behalf of their children, a clear abuse of power by researchers is evident. This included the vulnerability of the children and their parents, the fact that the children were exposed to procedures which offered no therapeutic benefit, the coercion used by researchers to encourage parents to permit enrolment of their infant and finally the lack of acquiring an informed consent.

Attempts were made by the researchers to defend the study. Dr Krugman highlighted the fact that 90% of the children involved in the study would eventually contract hepatitis and studies performed produced important information on the different strains of hepatitis, which did eventually advance research for a vaccine (52, 53). While the development of a vaccine against the hepatitis virus was assisted by the research, the unethical actions of Dr Krugman and his research team were both damning and are undeniable.

Informed consent, as defined by the Nuremberg code states that consent must be given free from coercion (54). This crucial element of consent, along with many others, was not adhered to during the consenting process therefore it must be assumed that informed consent was not obtained from parents of these mentally ill children.
2.4 Second World War and the Nuremberg Trials

After the conclusion of the Second World War, the world watched as 23 scientists and physicians stood trial in Nuremberg, Germany. They were accused of committing a wide range of depraved experiments and procedures on prisoners in concentration camps in between 1933 and 1945 (55). All experiments were conducted against the will of prison inmates and at no point informed consent was sought for any procedure.

Prison inmates were at the mercy of physicians and scientists, whose actions often resulted in the disability, disfigurement and/or death of prisoners. At that time no clear regulations existed which governed research on humans in Germany, thus allowing the accused to try to justify their actions. Of the 23 scientists and physicians, 15 were found guilty of these heinous crimes and the rest acquitted (56), but most importantly the Nuremberg Code was drafted.

The Nuremberg Code is a set of 10 guiding principles for researchers taking part in human experimentation. The aim of the code is protection of human subjects. It is the duty of researchers to adhere to principles set out in the code when performing research on human subjects (54). The Nuremberg Code states it is essential that consent to medical research be given by a subject on a voluntary basis, free from coercion (57). It is also noted in the code that a person must have the capacity to make an informed choice (54). Other important principles outlined in the code include the obligation to avoid unnecessary harm to subjects and potential benefits to society as a result of research undertaken (54).

To further streamline conduct for research involving humans, the Declaration of Helsinki was compiled by the World Medical Association in 1964, most recently updated in October 2013. The Declaration of Helsinki is a set of ethical principles which aim to provide guidance to physicians and staff involved in medical research with human subjects (3). This declaration expanded on the principles outlined in the Nuremberg Code and linked them to those of the Declaration of Geneva, which requires physicians to put the health and wellbeing of their patients first, and to respect them as human beings (58).
It also seeks to standardise the conduct of clinical trials within the United States of America, Europe and Japan, the principles in the Declaration of Helsinki were incorporated into the International Conference on Harmonisation Good Clinical Practice Guidelines (ICH GCP) (5) (59). GCP is a set of globally recognized ethical and scientific requirements that must be observed throughout the lifecycle of a clinical trial (60).

Today, the Nuremberg Code, Declaration of Geneva, ICH CGP and Declaration of Helsinki provide the bedrock of best practice guidelines, allowing research to be conducted ethically and morally in the medical setting. To expand upon this by formally harmonising and regulating medical research conduct throughout the European Union (61), the European Directive 2001/20/EC was established.

2.5 European Directive 2001/20/EC

The core objective of the European Directive 2001/20/EC is to protect human research subjects and to safeguard public health (62). However, it was the duty of each member state to formally implement EU 2001/20/EC and members states could adopt the rules set out in the directive they saw fit. In 2005, an amendment to the original directive was published, namely the European Directive 2005/28/EC (63).

The amendment outlined specific guidance to Good Clinical Practice procedures in regards to investigational medicinal products for human use (63). On the 16th April 2014, the European Commission Regulation (EU) No 536/2014) came into force. This new regulation superseded the original directive 2001/20/EC and the amendment 2005/28/EC (64). It is now a legal requirement that researchers abide by the principles outlined in the regulation in order to engage in lawful and ethical clinical trial practices.

2.6 Informed Consent

It is a requirement of the Directive 2001/20/EC that those who are unable to consent to medical research due to capacity issues must be afforded special protection by each member state (61). This includes minors. The importance of informed consent and protection of minors was further strengthened in Regulation (EU) No 536/2014. The
Regulation explicitly states that the guidance set out in relation to informed consent in Directive 2001/20/EC must be adhered to by all involved in medical research (64).

Research subjects must provide a written informed consent and in the event whereby a subject has literacy issues due to age or issues with literacy, appropriate methods of recording informed consent must take place. According to the Regulation, it is the responsibility of each member state to determine the legally designated representatives of both minors and incapacitated persons (64).

2.7 Informed Consent Form

The informed consent form is classed as an Essential Document. According to ICH GCP essential documents are defined as;

“documents which individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced”(5).

It is a legal and ethical requirement that study subjects receive and sign the form, or, in the case of consenting to neonatal research, that those responsible for proxy consent receive and sign the form. The objective of the form is to provide information regarding the trial and trial procedures to the parents/guardians of the study subject.

The consent form must be written in a language that is understandable to parents of all ages. It must be presented using non-medical, scientific or technical language. The contents of the form must include (but are not limited to) the following: the purpose of the trial, the aspects of the trial that are experimental, reasonably expected benefits, alternative procedure(s) that may be available to the subject, trial intervention(s), randomisation, and the fact that refusal to take part in the trial will not in any way alter the infants clinical care (5).

Investigators must be aware of their duty to parents who may fall into the category of vulnerable such as parents with reading difficulties (partial or total illiteracy) or parents who do not speak English. Ireland is fast becoming a multinational country with more
parents of international backgrounds than ever presenting themselves to the maternity hospital setting. In order for researchers to adhere to the governing principles of medical research involving humans, they cannot exclude subjects because of language or readability problems. Kuthning et al. (65) states:

“**Illiteracy is a critical problem that affects all corners of our earth; it has no boundaries and exists among every race and ethnicity, age group, and economic class**”.

If it is not feasible to provide a translated informed consent form to non English speaking parents then a translator must be involved in the informed consent process. In the case where parents may be partially or completely illiterate, the Investigator must ensure that he/she spends enough time speaking to the parents about the study. In these cases, the consent form must also be signed by an independent witness.

### 2.8 Informed Consent in Ireland – A General Overview

On the 01st May 2004 the EU Directive 2001/20/EC was transposed into Irish Law by the Minister for Health and Children, Mr Micheál Martin, namely S.I. No. 190/2004 (66). Previous to this, clinical trials in Ireland were governed by the ‘Control of Clinical Trials Acts 1987 – 1990’ (67). It is both an ethical and legal obligation of researchers to protect the rights, well being and confidentiality of those who volunteer to take part in medical research.

For those unable to consent themselves (a minor or a person deemed incompetent) consent can be given on their behalf. According to the regulations set out in 2004 a child is defined as a person aged 16 and under (66). For this age group a “**person with parental responsibility**” can consent on behalf of the child. “**Person with parental responsibility**” means a natural or adoptive parent, a guardian, a person who has acted in *loco parentis* to a child or a person having charge or control over a child, where such person is actively involved in making decisions affecting the child's welfare (66).

In neonatal research proxy consent to a research study must be given by the parent(s) or guardian(s) of research participants. If parents are married it is deemed best practice to
have both parents sign the informed consent form. Previously if parents of the newborn infant were not married only the mother’s signature was a legal requirement.

On the 06th April 2015 the Children and Family Relationships Act 2015 was published (68). The act includes an amendment to the Guardian of Infants Act 1964 (69). The amendment serves to strengthen the rights unmarried fathers have to their newborn infant. However a mother’s signature remains a prerequisite of neonatal research participation if the father of the newborn infant has not been formally named a legal guardian.

An update to S.I. No. 190/2004 was published in 2006. This amendment, outlines additional requirements relating to informed consent, specifically that it must be obtained from study subjects prior to their participation in a clinical trial (70).

2.9 European Legislation for informed consent in neonatal research

Dalla-Vorgia et al. (2001) published the paper “Overview of European legislation on informed consent for neonatal research” (42). The authors presented a summary of the regulations which currently govern informed consent in neonatal research. They focused on 10 European countries; Denmark, Finland, France, Germany, Greece, Ireland, Norway, Spain, Sweden and the United Kingdom. Results highlighted that most countries have similar, if not the same informed consenting process. Proxy consent is permitted in all countries, either by parents or legal guardians.

In some countries consent to neonatal research can be given from one parent, however in Denmark and Germany if custody of the infant is shared by both parents’ or legal guardians then both must provide written consent. In France and Sweden it is deemed best practice to obtain consent from both parents prior to the initiation of a research study and the case of consent to treatment for emergency research a waiver of consent is generally acceptable as part of emergency care. A waiver of consent in that situation is not permissible in Ireland and Denmark.

In general, it is a requirement in the ten countries that there must be a potential direct benefit for the newborn infants who enter into a research study. However research that is
of no direct benefit to newborn infants is permissible with the stipulation that the research study involves no more than a minimal risk to the newborn infant (42).

2.10 Research Ethics Committees

The 1975 revision to the Declaration of Helsinki stipulated that research involving human subjects should be approved by an independent research ethics committee (71). The function and responsibilities of research ethics committees was further harmonised across Europe with the publication of the EU Directive 2001/20/EC (61). According to this Directive an ‘Ethics Committee’ is an independent body whose function is to protect the rights, safety and wellbeing of human subjects involved in clinical trials.

Ethics Committees consist of healthcare professionals and lay members who oversee the ethical conduct of a clinical trial (61). In all jurisdictions it is a legal requirement that Investigators seek approval from either their local or national Ethics Committee. It varies between members states as to whether local or national approval must be sought. Regardless of the member state and its own regulations pertaining to ethics committees, Investigators must seek permission from the committee prior to initiating any type of research study.

2.11 Conclusion

Since the end of World War 2, informed consent in clinical and non therapeutic research has become a highly controlled and regulated aspect of human experimentation. Extra protection has been afforded to those classed as vulnerable. This includes newborn infants as well as minors and those who are responsible for consenting on their behalf. Audits and inspections are carried out by regulatory agencies to ensure compliance with Good Clinical Practice procedures and applicable regulations.

In Ireland the Health Products Regulatory Agency is responsible for such inspections. All clinical trials must also have an independent trial monitor who will oversee all aspects of the trial protocol including adherence to informed consent procedures.
The clinical trials which took place during World War 2 serve as a stark reminder of the importance of informed consent for all trial participants including those consenting on behalf of their loved ones. Sadly, examples of historical unethical research practices are still coming to light. As recently as 2014, a newspaper published an article describing unethical clinical trials involving almost 300 children residing in care home’s in Ireland (72). The article outlined the fact that it was suggested that informed consent was not sought from parents of these children.

While positive steps have been implemented legislatively on a worldwide basis in relation to informed consent in clinical research, it is important that past atrocities remain in memory to serve as a reminder to all, of the potential horrors clinical research can inflict on human beings. Adult, minor and proxy consenters involved in the consenting process must be treated with equal respect as that of a medical patient.
Chapter 3: Original Research

Title: Perceptions of Parent(s) and Clinicians regarding the informed consent process in neonatal research in Ireland.

3.1 Background information

Informed consent is a core aspect of medical research involving humans. Apart from situations involving emergency research, it is a legal and ethical requirement that informed consent be obtained prior to any procedures taking place. Proxy consent must be sought from parents or guardians for any type of research which involves their newborn infant. For the remainder of this chapter I will refer to parents and guardians as parents.

Parents are usually approached with information about a neonatal study before or shortly after the birth of their baby. This can be an incredibly emotional and stressful time for parents, particularly if their infant is born premature or ill. According to Mason et al. (2000) questions have arisen as to whether the process of obtaining informed consent from parents for neonatal research leads to valid consent (14).

McKechnie et al. (2006) reinforces this point highlighting that consent obtained from parents during times of extreme emotional pressure can fall below the expected requirements needed for informed consent to be considered valid (73). In Ireland minimal research has been completed to assess the validity of consent obtained in the neonatal period from parents of newborn infants.

In its own guidelines the Health Service Executive (2013) states:

“Consent is the giving of permission or agreement for an intervention, receipt or use of a service or participation in research following a process of communication about the proposed intervention” (6).
The purpose of this study is to explore the communication exchanged between parents and clinicians during the informed consent process in neonatal research, from an Irish hospital setting. As a result two questionnaires were developed including one questionnaire to be completed by parents and the other by clinicians. The questionnaires were drafted in a manner which allowed for various styles of replies from parents and clinicians. This included answers with a yes/no, free text answers and answers based on the likert scale.

**3.2 Aim and objectives of the study**

The aim of this study was to gather as much information possible from parents and clinicians regarding their views and experiences of the informed consent process in neonatal research from an Irish hospital setting, thereby allowing one to identify the strengths and weaknesses of the consenting process. This will allow the neonatal community to explore and ultimately improve upon this process.

My research objectives were as follows;

1. To explore into the communication exchanged between parents and clinicians during the informed consent process to neonatal research, from an Irish hospital setting;

2. To identify and discuss positive and negative experiences and opinions of the process, as described by those involved;

3. To produce guidelines for clinicians to act as a guide for best practice procedures when gathering informed consent from parents; and

4. To identify methods to increase the informed consent experience for all those involved.

**3.3 Inclusion Criteria**
The table below describes the inclusion criteria for parents and clinicians. Only those who fulfilled the inclusion criteria were asked to complete the questionnaires.

**Table 4: Inclusion criteria - parents**

<table>
<thead>
<tr>
<th>Inclusion Criteria – Parents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parents of infants born at &lt; 37 weeks GA.</td>
</tr>
<tr>
<td>Parents of infants that had been admitted to the neonatal intensive care unit of the Cork University Maternity Hospital (CUMH) after birth.</td>
</tr>
<tr>
<td>Parents who had been approached by clinicians/researchers information about a neonatal research study antenatally or after the birth of their infant.</td>
</tr>
<tr>
<td>Parents who were attending the neonatal clinic with their infant after discharge from the hospital.</td>
</tr>
</tbody>
</table>

**Table 5: Inclusion criteria - clinicians**

<table>
<thead>
<tr>
<th>Inclusion Criteria – Clinicians</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinicians currently employed in a hospital Ireland.</td>
</tr>
</tbody>
</table>

3.4 Methods

*Questionnaire Development and data collection*

Overall, two questionnaires were developed for this study;

**Questionnaire 2:** A questionnaire for clinicians entitled: Clinicians Perceptions of the Informed Consent Process in Neonatal Research.

Two information leaflets were developed in conjunction with the questionnaires.

**3.5 Parent questionnaire**

The parent questionnaire was developed with the assistance of Dr. Kieran Doran, senior law lecturer, University College Cork (UCC) and Professor Eugene Dempsey a consultant neonatologist based in the Cork University Maternity Hospital (CUMH). The input provided to me from Doran and Professor Dempsey was fundamental to ensuring that the content in the questionnaire reflected the sensitivity of the subject matter, namely sick newborn infants admitted to the NICU. As a result of this collaboration the questions and layout of the questionnaire were considered sensitive and appropriate for the vulnerable cohort.

The questionnaire included both structured and semi structured questions. This was to allow answers to be varied. Some answers had to be yes/no, some were based on the likert scale and some were free text. This was to maximise the variety possible responses, thus ensuring the highest content and quality of replies. It was our hope that this approach would also increase the likelihood of identifying novel information relating to parents views and experiences of the informed consenting process.

The parent questionnaire contained a total of 26 questions divided into three sections; background information, parent’s own experience of the informed consent process and finally the questionnaire sought information relating to the specific research study parents were asked to enrol their baby to.

**Section 1 - Background information**

This section looked for basic demographic information from respondents. Questions related to gender of respondent, marital status, level of education and gestational age of their infant at birth. It was necessary to obtain basic background information from
respondents to able to locate and correlate any trends resulting as a result from the data acquired from the completed questionnaires.

Section 2 - Parents experience of the informed consent process

The aim of this section was to gather as much information possible from parents relating to their views and experience of the informed consent process. A wide range of questions were incorporated in this section. Questions with likert scale answers, free text answers and yes/no answers were included. The aim of section two was to gather a general overview including both positive and negative experiences, parents had of the informed consent process. We also endeavoured to seek out the preferences parents had in relation to different aspects of the informed consent process in neonatal research.

Questions with yes/no answers sought to gather information general information relating to the uptake of consent, the availability of information leaflets, the amount of neonatal studies parents were asked to consent too and finally, any issues parents had relating to their level of comfort about discussing concerns with researchers.

Questions using the likert scale had a set range of five different answers, starting at “strongly disagree” and finishing at “strongly agree”. The aim of the scale was to rate parents level of agreement to various statements. Questions explored parents views of the timing of consent, their level of understanding of information received, the voluntariness of consent and their level of concern regarding their infants participation in the study.

The goal of the questions with free text answers was to extrapolate any information relating to the level of comfort parents had about relaying concerns to researchers and describing reasons for refusing consent.

Section 3 - Research project

This section related to the research study for which parents were asked to consent. The main goal of section three was to assess parent recall of information received at the time
of consent and also to assess the validity of consent based on questions included in this section. Parents were asked to include any details they could recall about the study their newborn infant took part in. I also sought their views in relation to audio recording the consenting process and their feelings on a waiver of consent. Finally, parents were asked based on their experience of informed consent in neonatal research, would they take part in future studies?

3.6 Clinicians questionnaire

The clinician’s questionnaire consisted of 22 questions divided into two sections. The design and format of the questionnaire was similar to the parent questionnaire. The questionnaire included various types of questions designed to maximise the strength and diversity of responses. Questions with yes/no answers, questions based on the likert scale and questions with free text answers were all incorporated.

For questions with likert scale type answers two different five point scales were used; scale one allowed respondents to rate their level of agreement to the importance of various statements (starting with “very important” and ending with “unimportant”, scale two rated the level of agreement respondents had with various statements starting with “strongly disagree” and ending with “strongly agree”.

Section 1 – Background

Section one was designed to explore into the experience clinicians had of the informed consent process in neonatal research and also their views relating to various features of this process. Questions designed to gather information related to the clinicians background, experience with GCP and informed consent training were also included.

Section 2 – Consenting process

The goal of this section was to explore into the personal viewpoint clinicians have of the informed consent process within neonatal research. I sought to examine their approach to the consenting process including how much time they typically spend with parents
during the consenting process, their views of parents understanding of information received during the consenting process, their views relating waiving of consent and the necessity of signed consent forms.

3.7 Research setting

The majority of the study took place exclusively in the Cork University Maternity Hospital, Wilton, Cork. The CUMH is the second largest maternity hospital within the EU. It caters for approximately 9,000 live births per annum with roughly 15% of the babies entering the Neonatal Intensive Care Unit.

This included recruitment of parents and clinicians, data storage, data entry and data analysis.

3.8 Ethics approval

I submitted an application to the Research Ethics Committee of the Cork Teaching Hospitals (CREC) on the 12 December 2014. The following documents were included in the application:

1. CREC Cover letter
2. Parent questionnaire
3. Parent information leaflet
4. Clinicians questionnaire
5. Clinicians information leaflet
6. CREC application form

These documents can be located in appendix A of this dissertation

Permission to begin the study was granted from the committee on the 17th December 2014. No queries or issues arose from the committee in relation to the application. Recruitment for the study began in February 2015.
In the end of April I had the opportunity to distribute my anonymous questionnaire to approximately 25 clinicians who were attending a neonatal training seminar conducted by Professor Eugene Dempsey. To allow for the inclusion of the questionnaires completed by these clinicians I submitted a letter to the CREC on 06 May 2015.

At this time I specifically requested permission to access clinicians based outside of Cork. While this request was granted by the committee on the 22 May 2015, the approval letter specifically granted me approval for clinicians working in Cork, Kerry and Limerick, thus excluding a number of clinicians recruited at the neonatal training seminar. To rectify this I submitted a new letter and amendment request form to the committee on the 15th June 2015. This request was granted by the CREC on 25th July 2015.

There were no further issues in relation to the ethical aspect of this study.

3.9 Recruitment

I recruited two separate groups to this research study; a parent group and a clinician group.

**Group 1 recruitment**: Parents of infants admitted to the NICU in the CUMH and subsequently discharged.

**Group 2 recruitment**: Clinicians presently working in a hospital environment.

3.9.1 Recruitment of parent group

For this portion of the study I recruited parents attending the neonatal clinic of the CUMH. Infants who attend this clinic can be both new (post discharge from the hospital) or follow up appointments (up to approximately 2 years of age). I was provided with online access to the weekly appointment clinic lists to locate the infants attending clinic and to cross check their eligibility for this study.
A total of five clinics take place on a weekly basis. This number may decrease depending on the availability of the consultant neonatologists. The clinics are based on the first floor of the CUMH. The consultants will see between approximately five and 15 patients per session and each session typically can last between two and three hours. Parents who attend the clinics will check in at reception and wait to be called by the nurse, where their newborn infant will be weighed. After this parent(s) and their baby will return to the waiting area while they wait to be called into see a doctor.

I approached parents with my questionnaire while they were waiting for their clinic appointment, and began recruitment in February 2015 in order to allow adequate time for data entry as well as analysis. Recruitment was completed at the end of May 2015.

3.9.2 Recruitment of clinician group

For this portion of the research study I recruited a total of 36 clinicians. Approximately 11 clinicians, based in the CUMH were asked to complete the questionnaire during a weekly teaching session in the CUMH. The remaining clinicians completed the questionnaire during a teaching seminar in Dublin.

3.10 Recruitment challenges

The biggest challenge I experienced related to recruitment of the parent cohort. At times it proved difficult to successfully locate and meet with parents attending the neonatal clinic. Parents are given a set clinic appointment time and upon arrival to the hospital, check in to the clinic and wait in the waiting area to be called to see the doctor.

Parents were approached while they were in the waiting area of the clinic. Occasionally parents did not attend their clinic appointment or, more frequently arrived to the clinic at incorrect times thus were not in the waiting room when I called into meet with them.

Parents often arrived to their clinic appointment with their baby’s sibling(s). If a lone parent arrived with more than two siblings it may not have been feasible to ask them to complete the questionnaire.
Finally, I chose not to approach parents whose infant was discharged from the neonatal unit with a serious illness.

I did not experience any major hurdles with regard to recruitment of clinician cohort bar receiving an approval letter from the CREC limiting my contact with clinicians to Cork, Kerry and Limerick. However once I submitted a further amendment this issue was resolved without delay.

### 3.11 Data collection

#### Parent group

Of the 49 of parent(s) I approached to complete the questionnaire, none declined. In a few cases both parents completed the questionnaire together but it most circumstances one parent completed the questionnaire whilst the other looked after their infant (and sibling(s)). It was documented where parents completed the questionnaire together. In just one case a couple (mother and father) completed a questionnaire separately. I gathered a total of 49 completed questionnaires however I excluded 6 from data analysis as mothers were more than 37 weeks into their pregnancy.

#### Clinician group

In total 36 clinicians based in an Irish hospital setting completed the questionnaire.

### 3.12 Statistical plan

All data analysis was performed using the statistical programme IBM SPSS statistics version 22.
Chapter 4: Results

4.1 Parent questionnaire

A total of 49 parents (both mothers and fathers) completed the parent questionnaire. Six mothers and were excluded from the analysis portion of the study as they did not meet the inclusion criteria of <37 weeks gestational age at birth. The gestational age of the excluded women ranged from 37 to 40 weeks.

Parents approached to take part in neonatal research whilst their newborn baby was an inpatient in the NICU but declined consent sections of the questionnaire which were relevant to them.

Section 1 of questionnaire:

Background

In total 8 fathers and 33 mothers completed the questionnaire independently. Two questionnaires were completed by parents jointly. In the analysis portion of the study 43 questionnaires in total were included.

Approximately 77% of parents who completed the questionnaire were married, 19% cohabiting and 5% were single parents. The gestational age at birth of mothers ranged from 25 weeks to 36 weeks GA.
Figure 1: Gestational age in weeks at birth

Figure 1 outlines the minimum and maximum gestational age of babies born. The minimum gestational age at birth was 25 weeks and the maximum gestational age at birth was 36 weeks.

A total of 8 parents attended secondary school level education and 32 attended third level education. Of a set of parents who completed the questionnaire together, one attended secondary school level education and one attended third level education although it is not clear who completed which level.

Section 2 of questionnaire:

In this section of the questionnaire parents were asked a series of questions related to their recall and experience of the informed consent process.

When asked if they could recall who had approached them with information about a neonatal study 41% (n=14) were approached by a consultant, 32% (n=11) by a junior
doctor and 26% (n=9) stated ‘other’. Some parents who completed the free text section wrote that they were approached with information to a neonatal study from various clinical and research staff including registrars, nurses, research nurses, researchers and students.

In one case a mother stated she was approached by a consultant, junior doctor and research nurse at different times prior to consenting. Another mother was approached by a consultant along with a junior doctor with information about a neonatal study and a third mother was unsure of who had approached her with information about a neonatal study. This mother chose not to consent her newborn infant to the study.

*Parent views of antenatal consent versus postnatal consent*

Parents were asked a series of questions relating to their views of being approached with information about a research study either antenatally or postnatally and for their individual experiences of either approach.
A total of 33% (n=14) of parents were approached with information about a neonatal study prior to the birth of their baby, 63% (n=27) were approached with information after the birth of their baby and 5% (n=2) were approached both before and again after the birth of their baby.
Parents were asked if they would rather be approached with information about a neonatal study before the birth of their baby. 59% (n=24) of parents agreed or strongly agreed (34% and 24% respectively) to this statement, 33% (n=13) remained neutral and the minority of 10% (n=4) disagreed or strongly disagreed (5% and 5% respectively).

**Figure 3: Five point scale measuring parents preferences to antenatal consent.**
Parents were subsequently asked if they would rather receive information about a neonatal study after the birth of their baby. 40% (n=17) agreed or strongly agreed (21% and 19% respectively), 33% (n=14) remained neutral and 26% (n=11) disagreed or strongly disagreed (19% and 7% respectively).

*Parent understanding of information received about the study*

92% (n=38) of parents received an information leaflet detailing the study for which they were asked to consent their newborn baby into. Parents were asked to rate their level of agreement to a series of statements about to their experience of the informed consent process;

**Statement 1.** *The information I received about the research study was clear and I fully understood it***
86% (n=36) of parents agreed or strongly agreed (57% and 29% respectively) that they had clear understanding and full comprehension of the research study.

Consent

A total of 83% (n=33) of parents gave consent for their newborn baby to take part in a neonatal study. Parents who declined were asked if they could recall their reason. This free text question was completed by a total of five parents.

Parent 1: was approached with information about a study postnatally while his wife was in the high dependency unit in the CUMH. Once the trial was explained to his wife she remained unsure of the full process and therefore was not comfortable going ahead with the study.

Parent 2: refused consent as she was hoping to be discharged from the hospital that day.

Parent 3: traumatic time for them as parents and difficult to make decisions about their newborn infants welfare at such a time.

Parent 4: outlined illness severity at the time of the consent for a reason for refusal.

Parent 5: parents had concerns over the effect participation in the study would have on their very premature baby.

Parents who gave consent for their infant to take part in a neonatal study were asked to elaborate on the reason why. A combined total of 96% (n=32) of parents agreed or strongly agreed (24% and 73% respectively) that they allowed their infant participate as they want to help babies born in the future.

A combined total of 72% (n=28) of parents agreed or strongly agreed (39% and 33% respectively) that their baby’s healthcare would directly benefit from participation in the study.

A combined total of 71% (n=27) of parents disagreed or strongly disagreed (48% and 26% respectively) that they felt obligated to take part in the study.
A combined total of 82% (n=31) of parents disagreed or strongly disagreed (50% and 32% respectively) that they felt pressure to take part in the study.

When asked about their decision to enrol their newborn infant to a neonatal study 60 % (n=25) of parents made the decision alone. Those who did have assistance with decision making specified in free text who helped them; answers included consultants in the NICU, doctors from the research team, husbands, fathers, partners, research nurses, nurses and midwives.

85% (n=29) of parents received a copy of the consent form after they had signed it.

In the following section parents were asked to rate their level of agreement to various statements relating to the consent process and neonatal study.

The results are outlined below.

Statement 1

“I knew my baby’s consent was entirely voluntary and that I could withdraw from the research study at any stage”.

- 90% of parents agreed or strongly agreed (41% and 49% respectively) to statement one.

Statement 2

“I had no concerns for my baby’s clinical care if I decided not to take part in the research study”.

- 83% (n=34) of parents agreed or strongly agreed (39% and 44% respectively) to statement two. Two parents discussed any fears had in relation in relation to refusing consent with researchers.

Statement 3

“I felt being asked to participate in a neonatal research study added extra stress at this time in my life”.
The majority of parents (78%) (n=32) strongly disagreed or disagreed (27% and 51% respectively) to statement three.

19 parents were asked for consent to more than one neonatal study. Discussion regarding alternative treatment for non consenting babies was discussed with a total of 8 parents.

Statement 4:

“Researchers should have guidelines to follow which would recommend situations when it is not advisable to approach parents for consent to neonatal research”?

85% (n=33) of parents agreed or strongly agreed (59% and 26% respectively) to statement four.

Section 3 of questionnaire:

Research Project

This section focused on parent recall of details of the research studies parents were asked to consent to their newborn infant to. A total of 60% (n=22) of parents had recollection of certain details of the study they were asked to consented their infant to. In the free text section parents included brief statements to reflect recollection of the studies such as ‘brain activity’, ‘brain monitoring’, ‘breast milk research’ ‘breast milk for preterm infants, NIRS and CO2 monitoring in resus’, ‘collection of stool samples’, ‘CPAP’, and ‘effect of the use of CPAP for the parents’.

When asked if they would recommend having the informed consent process audio recorded a total of 6 parents stated yes with the majority (29) saying no.

Parents were then asked to choose from a list outlining the various types of neonatal studies which are ongoing in the CUMH. The aim of this question was to choose the type of research which most described the study their infant took part in. 16 parents said their infant enrolled to a medical device study, four parents said they enrolled their baby to a
drug study, 19 said they enrolled their baby to an observational study and three parents said they enrolled their baby to a randomised study.

Parents who gave consent for their newborn baby to take part in a randomised study were asked to write down any details they could remember of the randomisation process. This was a free text answer. Three parents completed this question however one parent who completed the question did not tick the relevant box in the previous section. Parent one included the following text ‘daily infusion of infloren with food (tube fed), parent two included ‘ monitors attached to the body and head for a period of 24 hours and repeated again in a few weeks’ and parent three included ‘some kind of monitoring’.

76% (n=28) of parents disagreed with the concept of a waiver of consent. Finally, 87% (n=33) would take part in future studies based on their experience of neonatal research within the CUMH.

4.2 Clinicians questionnaire

Section 1 of questionnaire:

Background

The questionnaire for clinicians was completed by 36 clinicians; 25 of clinicians were senior house officers, 7 were specialist registrars and 4 were registrars.
Figure 5: Overview of clinical position of doctors completing the questionnaire

7 clinicians were specialist registrars, four were registrars and 25 were senior house officers.

A total of 12 clinicians had previous experience in the acquisition of informed consent in neonatal research. Of these, three had obtained consent to an interventional clinical trial, 6 to a non interventional clinical trial and three to both interventional and non interventional neonatal studies.

**Informed consent training**

In this section clinicians were asked to rate their agreement to various statements relating to their opinions of informed consent.

43% (n=15) of clinicians had received training in the acquisition of informed consent.
Figure 6: Rate of importance of informed consent training.

75% of clinicians rated informed consent training as very important, 22% rated informed consent training as important and 3% rated informed consent training as moderately important.

Clinicians were then asked if it should be an internal hospital policy that all clinicians involved in neonatal research receive study specific informed consent training. A total of 89% (n=32) of clinicians strongly agree or agree (50% and 39% respectively) to the statement.

*Good Clinical Practice*

63% (n=22) of clinicians stated that they were familiar with GCP, 39% (n=14) had previously received training in GCP and 86% (n=30) rated training in GCP as either very important or important (43% each respectively).
Consenting Process

86% (n=31) of clinicians prefer to approach parents for consent to a neonatal study antenatally. Additionally 72% (n=26) of clinicians strongly agree or agree that approaching parents prior to the birth of their child leads to a greater uptake of consent (6% and 67% respectively).

In relation to postnatal consent a small minority (11%) of clinicians strongly agree or agree that approaching parents after the birth of their child leads to a greater uptake of consent (3% and 33% respectively).

81% (n=29) of clinicians believe parents do not fully understand the information they received at the time of consent. However, 52% (n=15) of clinicians stated they would proceed to allow parents consent their newborn baby to a study upon their insistence. A free text section allowed clinicians to document their reasons for this;

Clinician 1: stated the belief that if parents had fully understood the study they would agree, therefore if every attempt is made to explain the study to parents and they somewhat understand, the clinician would accept consent.

Clinician 2: noted that parents should be allowed to enrol their infant if they ask questions which reflect the information provided.

Clinician 3: although this clinician stated yes to allowing parents consent, they further clarified that this would depend on the study characteristics and further explanation may be required.

Information Leaflets and consenting procedures

67% (n=22) of clinicians read through the information leaflets they provide to parents during the consenting process. Clinicians were asked roughly how much time they spend with parents during the consenting process. Results are in figure 7 below:
Figure 7: Time clinicians spend with parents during the consent process.

73% (n=19) of clinicians spend less than 20 minutes with parents during the consenting process and approximately 27% (n=7) spend between 20 and 40 minutes.

77% (n=20) of clinicians believe they spend enough time with parents to obtain valid informed consent and 32% (n=8) take contemporaneous notes during the consenting process.

90% (n=29) of clinicians are not in favour of audio recording the consenting process. 41% (n=13) of clinicians stated they approach parents at various stages throughout a study to ensure a continuous consent. 83% of clinicians strongly agree or agree that a signed consent form should be a prerequisite for all types of neonatal research (39% and 44% respectively).

Randomised trials and waiver of consent
A total of 6 clinicians had previously obtained consent to a randomised controlled trial. Clinicians were then asked for their opinion in relation to parental comprehension of the randomisation process.

**Figure 8: Do clinicians believe parents understand the randomisation process?**

In summary approximately 39% (n=14) disagreed, stating a belief that parents do not understand the randomisation process when explained to them at the time of consent, 33% (n=12) remained neutral and approximately 28% (n=10) agree, believing that parents do understand the randomisation process when explained to them at the time of consent.

To conclude clinicians were asked for their opinion in relation to a waiver of consent in neonatal research.
In summary approximately 25% (n=9) disagreed, stating a belief that a waiver of consent is not appropriate in neonatal research, 19% (n=7) remained neutral and approximately 56% (n=10) agree that a waiver of consent is appropriate in certain types of neonatal research.
To conclude clinicians were asked to specify the type of neonatal research for which they believe a waiver of consent to be appropriate. Results are summarised in the table below.

<table>
<thead>
<tr>
<th>Neonatal Study</th>
<th>Yes (%)</th>
<th>No (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interventional study involving a drug</td>
<td>6</td>
<td>94</td>
</tr>
<tr>
<td>Interventional study involving a medical device</td>
<td>6</td>
<td>94</td>
</tr>
<tr>
<td>Non interventional/observational study</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Emergency research</td>
<td>19</td>
<td>81</td>
</tr>
</tbody>
</table>
4.3 Discussion of study results

The Parents of newborn infants who are admitted to the NICU have been described in the literature as vulnerable (74) (14) (33). A number of studies have been completed which explore into the perceptions parents have of the informed consent process in neonatal research (31) (40) (29). However, only a handful of studies exploring into the perceptions clinicians have of the informed consent process have been completed. This Irish based study sought to investigate into the perceptions that both parents and clinicians have of the informed consent process in neonatal research. The study also sought to gather as much information possible relating to their views and experiences of this delicate process.

As described earlier, two questionnaires were developed for this research study. One questionnaire was given to parents and the other was given to clinicians. The questionnaires included questions and statements of a similar design and content. This was to allow for clear analysis and reporting of conflicting and/or crossover results. For example, both groups were asked for their thoughts in relation to the timing of consent. 72% (n=26) of clinicians agreed that approaching parents with information about a study antenatally leads to a greater uptake in consent from parents. A total of 59% (n=24) of parents said they would prefer to be approached with information about a neonatal study antenatally. These results highlight that both groups have a preference toward antenatal consultations/obtaining consent antenatally.

It is of interest to note that despite the expressed preference to antenatal consultations as described by both groups, in this study a total of 29 parents from the parent cohort were approached with information about a neonatal study after the birth of their baby. This was this is despite the fact that many clinicians in the clinical cohort of the study expressed a preference to antenatal consultation. There may be several reasons as to why despite a majority preference to antenatal consultations, postnatal consent was sought more often than antenatal consent. Mothers/unborn may have been severely ill prior to birth thus making it unethical to approach for antenatal consent. Capacity to consent may have been compromised due to the severity of illness for mother and/or
unborn and finally, there may not have been enough time to obtain consent antenatally from parents. This tends to be the primary reason.

It would be helpful to parents of newborn infants and to the neonatal research community to further explore what factors clinicians take into consideration when making a decision about when to approach for consent, and to establish in what circumstances parents believe that they should or should not be approached for consent, and when. This information could hopefully assist with the establishment of a general consensus for clinicians as to the most appropriate time to approach parents with information about a study. This in turn may help to increase the overall numbers of parents consenting to neonatal studies.

Consent to neonatal research

There is a positive uptake of consenting parents to neonatal research studies within the CUMH. Of the 43 parents included in analysis portion of the study, 34 (79%) consented to their baby taking part in neonatal research study. A further five parents from the group excluded from the analysis portion also gave consent. In total of 39 parents out of a possible 49 permitted their baby’s inclusion to a neonatal study. When asked for details about who approached them with information about a neonatal research study five parents were unsure or could not recall who had approached them with information about a neonatal research study. The remaining parents gave a written description of who approached them with information. Overall the majority of parents could recall the specific clinical role of the person who approached them for consent.

A breakdown of the roles of clinical staff responsible for obtaining consent from parents and the correlating numbers of parents who consented can be found in table 7 on the next page:
Table 7: Parent description of clinical staff who approached them for consent to a neonatal study

<table>
<thead>
<tr>
<th>CUMH research staff</th>
<th>Number of parents who consented</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consultant neonotologist</td>
<td>15</td>
</tr>
<tr>
<td>Junior doctor</td>
<td>8</td>
</tr>
<tr>
<td>Research nurse/nurse</td>
<td>2/2</td>
</tr>
<tr>
<td>Researcher</td>
<td>3</td>
</tr>
<tr>
<td>Consultant and junior doctor</td>
<td>2</td>
</tr>
<tr>
<td>Consultant, junior doctor and nurse</td>
<td>1</td>
</tr>
<tr>
<td>Student</td>
<td>1</td>
</tr>
<tr>
<td>Unsure/cannot remember</td>
<td>5</td>
</tr>
</tbody>
</table>

These results show that consultant neonatologists working in the CUMH are heavily involved in the informed consenting process in neonatal research. One must question if parents find the extra contact with consultants a comfort during this difficult period in their lives?

Interestingly this study found that the 10 parents who refused consent to a neonatal research study had been approached with information about a neonatal study a junior doctor not a consultant. This study showed that the majority of consent was obtained by a consultant, a fact that should be taken into consideration. It must be noted that 39 of 43 parents agreed that their consent was entirely voluntary and they were aware of their right to withdraw their baby from a study at any stage. Results indicate that the vast majority of parents felt no coercion from clinicians and consent was voluntary.

These results reflect a positive number of parents consenting to neonatal research studies. Consultant involvement during the consenting process should to be further increased. Parents/guardians should be afforded the opportunity to meet with consultants at some stage during the informed consenting process in neonatal research.
To ensure neonatal research studies are conducted in an ethical fashion and for consent to be considered valid it is essential that consultants ensure junior research staff receive adequate training in informed consent procedures. Research needs to be completed which explores into the validity of consent obtained by junior doctors, including research into the numbers of parents who consent/refuse consent to neonatal studies when approached by non consultant clinical staff.

The parent questionnaire contained a ‘free text’ comment section that parents were asked to complete. Parents gave positive and negative reflections of their consenting experience. They also made recommendations to the process for future parents. One mother described how within 24 hours of being admitted to the hospital she was asked to take part in two studies and approached with information about four studies antenatally. She felt bombarded and was very worried about the welfare of her extremely preterm unborn baby. She recommended that consultants be present during all meetings between parents and clinicians regarding neonatal research studies.

On a similar note another parent suggested the appointment of a liaison nurse who would be available at all times during the consenting process. It was also suggested that a separate room be made available for parents to engage in discussions about participation to research studies with research staff (away from general staff and population).

From these results it would seem that consultant availability and support during the consenting process is essential for both parents and junior research staff. Consultant support may offer comfort to parents at such a difficult period of their lives. It may also assist them in their decision making process whilst affording consultants the opportunity to oversee the consent process junior research staff take part in and ultimately, oversee that a valid informed consent is obtained by junior research staff from parents.

Some negative feedback from parents include one mother who believes discussing research participation after a traumatic labour is not appropriate; however she expressed no issue with antenatal consent provided mum is well. An interesting comment which emphasized the vulnerability of parents of newborn infants admitted to a NICU was from a father. While he praised the staff in the NICU it was his belief that parents do not
receive adequate guidance from hospital staff regarding the transitioning period of babies being a fulltime inpatient in the NICU to being discharged and at home on a full time basis. It is appreciated that this comment does not reflect the informed consent process or research participation however it is an important statement reflecting the need for increased home care guidance for parents of babies who are an inpatient in the the NICU. It is essential that comments of this nature are not ignored if we are to improve the experience parents in the hospital setting.

One of the objectives of this study was to explore into the reasons why parents consent or refuse consent to neonatal research. When asked about their reasons for allowing their baby enrol into a neonatal study 97% (n=32) of parents stated their desire to help babies born in the future as a reason for giving consent. This altruistic intention has been expressed by parents as a motivating factor in giving consent to neonatal research in previous studies (26, 28, 30).

A total of 72% (n=28) of parents believed that their baby's healthcare would directly benefit from taking part in a neonatal study. It is a clinician's duty to ensure that clinical care of patients/study subject precedes research procedures in all circumstances. Previous studies have shown that those who participate in clinical trials can have a better outcome than those who decline by virtue of their participation (75). However it is essential that despite this proven fact consent to research must remain entirely voluntary.

In this study 71% of parents agreed that they did not feel obliged and 82% did not feel pressurised to take part in a neonatal study. These complimentary statistics highlight the element of voluntariness and of no coercion within this cohort. However a minority of parents did feel obligated and pressurised to give consent, thus rendering it impossible to refer to their consent as ‘informed’ or valid.

Parents and clinicians were asked if they would like to have the informed consent process audio recorded. The majority in both groups said no. It is a documented legal requirement of clinical research that written consent be obtained from research subjects (including those consenting on behalf of others). However, written consent alone does not provide
evidence that full comprehension of a research protocol has taken place. While the majority of parents and clinicians in this study expressed that they would not like the consenting process to be audio recorded, it should be noted that audio recording the informed consent process could prove to be a useful tool for both clinicians and parents to monitor consent. It would allow clinicians to subsequently review the consenting process they took part in and if necessary hold further meetings with parents (if they feel this is required after review of the audio recording). In turn, parents could use the audio recording as a tool to help them with recall of information received during the consenting process. If audio recording of the consenting process is to be conducted appropriately it is essential to obtain consent from parents for the audio recording and from the local research ethics committee.

A waiver of consent remains a controversial and ongoing subject in research. In certain circumstances a waiver of consent will be permitted by a research ethics committee (76), thus allowing investigators enrol research participants into a study without their written consent. In the US Federal Law permits a waiver of consent to a research study provided three conditions are met:

1. the research must involve no more than a minimal risk to study participants;
2. the waiver or alteration cannot not adversely affect the rights and welfare of the participants; and
3. it would not be possible for the research to be carried out without the waiver or alteration (77).

In this study 57% of clinicians agree that a waiver of consent is appropriate in certain types of neonatal research. However when presented with specific types of neonatal research for which a waiver of consent could be applied to (interventional drug trials/medical device trials, non interventional/observational research and emergency research) the vast majority of clinicians were opposed to a waiver of consent for all types of neonatal research with the exception of 50% (n=18) believing a waiver of consent to be acceptable in the case of non interventional/observational research.
76% (n=28) of parents expressed opposition to a waiver of consent in neonatal research. A total of 8 parents were in favour of waiving consent. It is interesting to note that the 8 parents who were in favour of a waiver of consent to neonatal research had previously given consent to a neonatal research study whilst their newborn was an inpatient in the NICU. While this study did not specifically seek information from parents as to exactly why they are in favour or against a waiver of consent, it would have been worthwhile to have enquired from these 8 parents who had previously taken part in the consenting process, why they were in favour of a waiver of consent to neonatal research, having themselves taken part in the consenting process.

Considering the contentious and varying opinions the medical and ethical community have in relation to a waiver of consent, it is suggested that further exploration into this sensitive area of informed consent be conducted, with parents who are at the heart of the process.

The study sought to investigate into the amount if time clinicians spend with parents during the consenting process. 58% of clinicians spend less than 20 minutes in total with parents during the consenting process. A total of 76% of clinicians believe they allocate enough time with parents to acquire informed consent. It must be noted that the time it takes to acquire informed consent will vary from parent to parent. Consequently, it is essential that clinicians delegate as much time as they feel is necessary to obtain a valid informed consent from parents. It could be argued that a time frame of less than 20 minutes is inadequate to fully inform parents of a sick newborn infant about, for example a randomised, controlled clinical trial.

Parents who refused consent to a neonatal research study were asked if they could recall their reason for doing so. Statements relating to refusal of consent included the severity of illness of either mother and/or baby. One parent refused consent as she was hoping to be discharged from the hospital that day and one set of parents expressed concerns about the effect the study procedures would have on a very premature baby.

This study endeavoured to find out if being asked to participate in neonatal research added extra stress to parents. The majority of parents (78%) (n=32) did not feel that being
asked to participate in neonatal research studies added extra stress to their lives. While these are encouraging figures it is suggested that further research be carried out in an effort to further minimise extra stress which some parents may feel as a result of being asked to participate in neonatal research studies.

The majority of clinicians in this study do not continue to monitor consent for validity once obtained and do not make contemporaneous notes during the consenting process. It is therefore suggested that a consenting guideline be made available for clinicians to follow which incorporates other important aspects of consenting process such a checklist to ensure validity of consent and, due to the litigious nature of research, a policy on note taking during the consenting process.

**Information Leaflets**

The majority of parents in this study (93%) could recall receiving information leaflets about the study they were asked to consent their baby to and 85% (n=36) stated a clear understanding of the information contained in the leaflet. These results highlight a majority of parents receiving information leaflets and having clear comprehension of the information in the leaflet. All research related documentation which parents receive should be reviewed by a national ethics committee. It is of vital importance that researchers ensure information leaflets are drafted using language readable and understandable to all. Currently, it is common practice (and in most cases a requirement) to provide information leaflets to study participants during the consenting process. It must be noted that parents in this study who said they did not receive an information leaflet may not have had correct recollection of the consenting process as it may have been two years since their baby was in the NICU. Also depending on illness severity, parents may not recall receiving an information leaflet about a neonatal research study due to the trauma they were experiencing at that time.

In an effort to assess recall of study information, parents were asked to write down any details they could remember about the study which they were asked to consent their baby to. In the ‘free text’ section parents included brief statements to reflect recollection of the studies. Statements included ‘brain activity’, ‘brain monitoring’, ‘breast milk
research’ ‘breast milk for preterm infants’, ‘NIRS and CO2 monitoring in recus’, ‘collection of stool samples’, ‘CPAP’, and ‘to study brain development in very premature babies’. Although brief, the majority of descriptions given by parents did reflect the various research studies ongoing within the NICU of the CUMH at that time.

However two sets of parents exhibited a lack of understanding for a research study they took part in. The first set of parent described the study as the ‘effect of the use of CPAP for the parents’. The other set of parents described the study as the ‘use of breathing monitors in addition to stethoscope following birth’. The research study they were referring to was in fact a RCT involving End Tidal CO2 monitoring. Newborn infants in this study were randomised to either quantitative or qualitative monitoring arms. Again it must be noted that a period of up to two years may have passed since these parents took part in the consenting process for that RCT. Both parents had consented to the trial. It is impossible to say if at the time of giving consent parents had full comprehension of the trial procedures or not.

In this study 66% of clinicians read through information leaflets with parents during the consenting process. The majority of parents who took part in this study stated that they had full comprehension of the information contained in the leaflets. However it remains essential that clinicians take the time to read through information leaflets with parents as the amount of time which clinicians delegate to the consenting process may be difference between informed consent and just consent.

In an attempt to determine the area which caused the greatest difficulty in understanding the information received during the consenting process parents were asked to choose from a list of possible reasons. One parent stated a language barrier as a reason for her difficulty in understanding information received during the consenting process, four parents had difficulty understanding the words used by the doctor when describing the study to them and three parents had difficulty understating the information provided in the information leaflet.

*Good Clinical Practice*
According to ICH GCP (5);

“The investigator should be aware of, and should comply with, GCP and the applicable regulatory requirements”.

This study produced surprising and in some cases concerning results in relation to clinicians awareness of GCP. In total 62% of clinicians were familiar with GCP however only 38% of clinicians had received GCP training. A total of 12 clinicians who took part in this study had previously acquired consent to neonatal research studies from parents. Of these 12 clinicians, 6 were familiar with GCP and only five had received training in GCP.

These results are interesting. The overall aim of GCP is to protect rights, safety and well-being of trial subjects and also to ensure that clinical trial data is credible (5). GCP is a very well established guideline which in 1994 was transposed into Irish Law thus making it an offence to conduct oneself in a manner which is not in keeping with GCP guidelines. It is essential that investigators ensure that researchers/clinicians who are acting as co-investigators receive training in GCP if a research study is to be conducted to applicable GCP law. It should also be noted that while a total of 85% of clinicians rated GCP training important, only 62% of the clinicians stated that they were familiar with it. It is suggested that for hospitals which conduct research, a policy enforcing GCP training to all new appointees should be made mandatory.

**Randomised trials**

Clinicians were asked if they were of the opinion that parents tend to fully understand the randomisation process when explained to them. 39% (n=14) agree that parents do not fully understand the randomisation process when explained to them and 29% (n=10) believe they do. The remainder of clinicians remained neutral on the subject.

Parents were asked if they had given consent to a randomised study and if so, to write down any details of the randomisation process they could recall. Three parents had enrolled their baby to a randomised study and provided details. However the details they gave did not provide any information as to the randomisation process for which their
baby took part in. It is impossible to say if this is because parents did not have an understanding of the randomisation process when explained to them at the time of consent or if they simply could not recall the details of the process at the time of completion of the questionnaire.
Chapter 5: Conclusion and Future Direction

The last 40 years has witnessed significant advances in neonatal care (78). The health of our future generation of newborns is directly intertwined with the performance of clinical research in which infants participate (78). The informed consenting process of research involving newborn infants raises many ethical issues. Clinicians involved in the informed consenting process must ensure that they adhere to the core ethical principles which govern research with human subjects. It is a legal and ethical duty of clinicians to ensure a valid informed consent has been given from the parents of newborn infants.

One of the goals of this study was to systematically explore into the perceptions parents and clinicians have of the informed consenting process in neonatal research. It became clear from the literature review that in the last 30 years a far greater number of studies which explore the perceptions parents have of the informed consenting process have been complete, with minimal studies completed to explore the perception clinicians have of the process.

*Literature review and original research study*

Many results noted in my original research study entitled “Perceptions of parent(s) and clinicians regarding the informed consent process in neonatal research in Ireland” support the results found in my literature review. Overall parents are very supportive of neonatal research and have expressed altruistic reasons for allowing their newborn infants to take part. This includes parents wanting to help future generations of sick, newborn infants. Parents also expressed a belief that their baby’s healthcare would directly benefit from taking part in a research study.

Parents are aware of their own vulnerability during the neonatal period. They also acknowledged fellow parents vulnerability during this time. The majority of parents who took part in my study had consented to a neonatal research study and did not express regret of their decision. However parents who refused consent gave reasons such as the traumatic nature of their lives at that time and the inability to completely understand the study when explained to them. Parental confusion surrounding research protocols was
noted in my literature review. Additional correlating results between my literature review and questionnaire based study include parental opposition to a waiver of consent in neonatal research.

Clinicians believe a waiver of consent is acceptable in the case of non interventional/observational research.

On a positive note, the majority of parents who took part in my study did not feel coerced by clinicians/researchers to take part in neonatal research studies.

During my literature search it was surprising to find only two studies available which explored into the perceptions clinicians have of the informed consent process in neonatal research. Both studies were interview based studies. My original study involved clinicians and parents completing a questionnaire.

The results of the published studies and those of my original study had similar themes. For example parents in both the published studies and from my cohort both reported that alternative treatment for their newborns was not discussed during the consenting process. However for one study reported in the literature review the ability to withdraw from the study at any time was not overly discussed with parents during the consenting process. The results of my original study highlighted that the vast majority of parents were aware of their right to withdraw from a study at any time.

**Ethical and legal issues of informed consent in research**

The main focus of this chapter was to provide the reader with an overview of the ethical and legal issues of informed consent in research. This included examples of unethical conduct by researchers in the past. Unfortunately, as highlighted in the Tuskegee Syphilis Study when the core ethical principles which govern research involving human subjects are overlooked and ignored by researchers the results can be in devastating for those research subjects.
The regulations investigators must adhere to have become increasingly demanding. National Ethics Committees are now taking responsibility for the ethical conduct of research toward its study subjects. This includes reviewing and approving all documentation that study subject/proxy consenters will receive. This step ensures further adherence to the principles that govern human research. However remains the responsibility of clinicians involved in research to adhere principles as outlined in the groundbreaking publication by Beauchamp and Childress (79).

5.1: Future Direction

In essence the process of informed consent is one of the main contributors of upholding ethical conduct throughout the lifecycle of a research study (80). The results of the research undertaken to complete this dissertation make suggestions regarding how to improve the informed consenting process for both parents and clinicians.

Parents felt strongly that clinicians should have set guidelines to follow which would advise them of when, and in what situation, that they should not approach parents with information about a neonatal research study. One mother, approached with information about four separate neonatal research studies antenatally expressed how she felt bombarded whilst in the hospital. It is essential that clinicians minimise any further stress to parents where possible. Guidelines to assist clinicians in the consenting process including advising when to not speak to parents about neonatal research should be made available to clinicians and researchers throughout Irish hospitals.

Results from the questionnaire study highlighted an increased need for consultant support during the consenting process for both parents and clinicians. One parent recommended that a consultant be present during all meetings between parents and clinicians regarding neonatal research. Another parent suggested the appointment of a liaison nurse and the availability of a consultation room for consenting discussions between parents and clinicians. The amount of consultant support given during the consenting process should vary in respect of the type of research study for which parents are asked to consent their newborn infant to. For example it would be highly recommended that a consultant be available during the informed consenting process to a
RCT involving preterm infants however, for non emergency observational research an appropriately trained junior doctor would be suitable.

It is recommended that clinicians involved in neonatal research attend informed consent training seminars hosted by senior consultants with expertise in the acquisition of informed consent and finally, mandatory training in GCP should be introduced to hospitals nationwide to ensure clinicians involved in research have awareness of GCP and its applicable procedures.

It is recommended that clinicians involved in neonatal research attend informed consent training seminars hosted by senior consultants with expertise in the acquisition of informed consent and finally, mandatory training in GCP should be introduced to hospitals nationwide to ensure clinicians involved in research have awareness of GCP and its applicable procedures.
Appendix 1

A. CREC cover letter

12th December 2014

Professor Michael Molloy,
Chairman,
Clinical Research Ethics Committee of Cork Teaching Hospitals,
Lancaster Hall,
6 Little Hanover Street,
Cork

Re: Perceptions of Parent(s) and Clinicians regarding the Informed Consent Process in Neonatal Research.

Dear Professor Molloy,

I am presently in my final year of an MSc in Healthcare Ethics and Law at the Royal College of Surgeons. I am also a clinical trial coordinator employed by University College Cork. I am currently based in the Cork University Maternity Hospital (CUMH). I would like to undertake a research study that would examine the perceptions parent(s) and clinicians have of the informed consent process in neonatal research in Ireland.

To complete my research study I have enclosed the following documents for the attention of the Committee:

- Questionnaire 1: A questionnaire for parents entitled Parental Perceptions of the Informed Consent Process in Neonatal Research and an accompanying Information Leaflet. (x 8 copies)
- Questionnaire 2: A questionnaire for clinicians entitled Clinician’s Perceptions of the Informed Consent Process in Neonatal Research and an accompanying Information Leaflet. (x 8 copies)
- Ethics Application Form - Form 1 (x 8 copies)
- CV of Chief Investigator (x 1 copy)

With the permission of the Ethics Committee I hope to give the two questionnaires and accompanying information leaflets to parents and clinicians that have taken part in neonatal research in Cork. Questionnaire 1 and information leaflet will either be posted to parents of infants who previously had been approached to take part in a research study whilst their infant was an inpatient in the neonatal intensive care
unit of the CUMH or, I will approach parents upon discharge to give them the documents to either complete or take home and post back to me should they want to take part. Only parents of infants who were discharged from the neonatal intensive care unit will receive the documents. Questionnaire 2 and information leaflet will be given to clinicians based in the CUMH who may or may not have experience in the informed consent process in neonatal research.

The purpose of this study is to further explore into the communication process between parent(s) and clinicians during the informed consent process in neonatal research.

It is our hope that by gathering as much information possible from parents and clinicians regarding their own personal experiences of the informed consent process in neonatal research, we can explore the pitfalls currently being experienced during the informed consent in neonatal research and hopefully to produce guidance for clinicians to assist them when gathering informed consent from parents to hopefully increase the experience had by all.

Should you have any queries, please do not hesitate to contact me at 087 9696229

Kind regards,

Niamh O’Shea,
Department of Paediatrics & Child Health,
UCC.
Questionnaire for Parent(s)

Parental Perceptions of the Informed Consent Process in Neonatal Research
Please tick the boxes as appropriate

Background Information

1. Are you Male or Female? Male ☐ Female ☐

2. Marital Status: Single ☐ Cohabiting ☐ Married ☐

3. How many weeks gestation were you at the time of the birth of your baby? __________

4. Highest level of education attended: Secondary Level ☐ Third Level ☐

Your Experience of the Informed Consent Process

5. Who approached you with information about the research study?
Consultant ☐ Junior Doctor ☐ Other (please specify) ______________

6. Were you approached with information about the research study before or after the birth of your baby? Before ☐ After ☐

7. If a research study was to commence shortly after the birth of your baby, would you rather be approached by a doctor seeking your consent for your baby to take part in the study before the birth of your baby?
Strongly Disagree ☐ Disagree ☐ Neither Agree nor Disagree ☐ Agree ☐
Strongly Agree ☐

8. If a research study was to commence shortly after the birth of your baby, would you rather be approached by a doctor seeking your consent for your baby to take part in the study after the birth of your baby?
9. When the doctor approached you for consent, did you receive an information leaflet about the research study which explained the study to you? Yes □ No □

10. Please indicate how you agree with the following statement “The information I received about the research study was clear and I fully understood it”. 
   Strongly Disagree □ Disagree □ Neither Agree nor Disagree □ Agree □ Strongly Agree □

11. If you experienced difficulty understanding the information received during the informed consent process, can you please tick the appropriate box to outline the reason? 
   There was a language barrier □
   I had difficulty understanding the words used by the doctor when he/she was explaining the study to me □
   I had difficulty understanding the information provided in the Information Leaflet □

12. Did you give consent for your baby to take part in the study? Yes □ No □
   If no, can you recall your reason why you decided not to consent your baby to the study?

13. If yes to Q12, please tick the box(es) which most describe your reasons for allowing your baby to take part in the research study.
   I want to help babies born in the future: Strongly Disagree □ Disagree □ Neither Agree nor Disagree □ Agree □ Strongly Agree □
   I felt my baby’s healthcare would directly benefit from taking part: Strongly Disagree □ Disagree □ Neither Agree nor Disagree □ Agree □ Strongly Agree □
I felt obligated to take part in the study: Strongly Disagree □ Disagree □
Neither Agree nor Disagree □ Agree □ Strongly Agree □

I felt pressure to take part in the study: Strongly Disagree □ Disagree □
Neither Agree nor Disagree □ Agree □ Strongly Agree □

Other (please outline):

________________________________________________________________________
________________________________________________________________________

14. Did you have help from anyone when making your decision about enrolling your baby in the research study? Yes □ No □
   If yes, please specify: _____________________________________________________

15. Did you receive a copy of the consent form once you had signed it? Yes □ No □

16. Please indicate how you agree with the following statement “I knew my baby’s consent was entirely voluntary and that I could withdraw from the research study at any stage”. Strongly Disagree □ Disagree □ Neither Agree nor Disagree □ Agree □ Strongly Agree □

17. Please indicate how you agree with the following statement “I had no concerns for my baby’s clinical care if I decided not to take part in the research study”. Strongly Disagree □ Disagree □ Neither Agree nor Disagree □ Agree □ Strongly Agree □

   If you disagreed with the above statement did you relay these issues to the researcher? Yes □ No □
   If no, can you please explain why: ____________________________________________

________________________________________________________________________
18. Please indicate how you agree with the following statement “I felt being asked to participate in a neonatal research study added extra stress at this time in my life”. 
Strongly Disagree ☐ Disagree ☐ Neither Agree nor Disagree ☐ Agree ☐ Strongly Agree ☐

19. Were you approached to take part in more than one research project? 
Yes ☐ No ☐

20. Were alternative treatment options for your baby discussed should you decide not to take part in the research? Yes ☐ No ☐

21. Please indicate how you agree with the following statement “Researchers should have guidelines to follow which would recommend situations when it is not advisable to approach parents for consent to neonatal research”? 
Strongly Disagree ☐ Disagree ☐ Neither Agree nor Disagree ☐ Agree ☐ Strongly Agree ☐

Research Project

22. Can you remember any details of the research study you were asked to consent your baby to? Yes ☐ No ☐
If yes, can you outline any details you recall here? ________________________________________________________________________

23. Would you recommend having the informed consent process audio recorded? 
Yes ☐ No ☐

24. Can you please tick the box which most describes the study your baby enrolled in to? 
A. My baby enrolled into a study that used a medical device ☐
B. My baby enrolled into a study and received a drug as part of that study ☐

Parents Questionnaire Version 1.0 Page 4 of 5
C. My baby enrolled into a study that was observational only (i.e. my baby did not receive any type of intervention but was monitored by the doctor/investigator) ☐
D. My baby enrolled into a study and received a randomly allocated treatment ☐

If you ticked D, can you please write down any details you remember of this process?

25. Would you have preferred to have had your baby automatically enrolled to the research study after birth without seeking your consent (a process known as a waiver of consent) on the premise that your consent is sought after your baby has started the research study? Yes ☐ No ☐

26. Based on your experience with the research study you took part in, would you take part in future studies? Yes ☐ No ☐
If no, please explain why:

Do you have any further comments?

Thank you!
C. Parent information leaflet

Research Questionnaire Project, Parent(s) Information Leaflet

Introduction:

You are invited to take part in a questionnaire based research project. This aim of the project is to determine the perceptions of parent(s) and doctors regarding the informed consent process in neonatal research. This project is being undertaken by a student of the Royal College of Surgeons, Dublin. The questionnaire should take approximately ten minutes to complete.

Student Name: Niamh O'Shea, Final Year MSc in Healthcare Ethics and Law, RCSI.

Supervisors: Professor Eugene Dempsey, Consultant Neonatologist, Cork University Maternity Hospital and Dr Kieran Doran, Solicitor, Senior Healthcare Ethics Lecturer, University College Cork.

Title of Project: Perceptions of Parent(s) and Clinicians regarding the informed consent process in neonatal research.

What is the aim of the project?

The aim of the project is to gather as much information possible from parent(s) and doctors regarding their views of the informed consent process in neonatal research. This information will be collected using two questionnaires specifically designed for parent(s) and doctors. We would like to identify the general experiences and opinions parent(s) and doctors have of the informed consent process. To do this we are inviting you to complete the enclosed questionnaire. We hope to use information gathered from the questionnaires to identify new methods of improving the whole area of the informed consent process involving neonatal babies for parent(s) and doctors.

Consent

In the past you have been asked to take part in neonatal research while your baby was an inpatient in the Cork University Maternity Hospital (CUMH). We have developed a questionnaire to find out what your feelings were about the whole experience of the informed consent process. Our goal is to improve the consenting process for parent(s) and doctors in the future. With this in mind we would like to invite you to take part in this research questionnaire project. You do not have to take part in this project, it is entirely your decision. If you decide to take part in this project we ask that you complete the attached questionnaire and post it back to the Cork University Maternity using the enclosed stamped and addressed envelope. Doctors working in the Cork University Maternity Hospital are also being asked to take part in this project.

The questionnaire we are asking you to complete is completely anonymous. Data from the questionnaire will be saved to an encrypted laptop which is stored in a secure, swipe access office within the CUMH. The questionnaires will be stored in a locked cabinet located in a secure, swipe access office. Only the research student and her supervisors will have access to returned questionnaires. Data that may be reported in scientific journals will not include any information that identifies you as a participant in this project.
D. Clinicians questionnaire

Questionnaire for Clinicians


Please tick the boxes as appropriate

**Background Information**

1. Please state your current professional position
   - Consultant
   - Specialist Registrar
   - Registrar
   - Senior House Officer

2. Have you ever acquired informed consent for a neonatal research study? Yes ☐ No ☐

   *If yes to Q2 can you clarify the type of research studies(s) you have obtained consent for?*

   - An interventional clinical trial
   - A non-interventional/observational clinical trial
   - Both

3. Have you ever received training in the acquisition of obtaining informed consent?
   - Yes ☐ No ☐

4. How important would you rate informed consent training for clinicians obtaining informed consent in neonatal research? Very Important ☐ Important ☐ Moderately Important ☐ Of Little Importance ☐ Unimportant ☐

5. Please rate how you agree with the following statement: “It should be an internal hospital policy that all clinicians involved in neonatal research receive study specific informed consent training” Strongly Disagree ☐ Disagree ☐ Neither Agree nor Disagree ☐ Agree ☐ Strongly Agree ☐
6. Are you familiar with Good Clinical Practice (GCP)? Yes □ No □

7. Have you ever received GCP Training? Yes □ No □

8. How important do you think receiving Good Clinical Practice training is (please tick appropriate statement)?
   Very Important □ Important □ Moderately Important □ Of Little Importance □
   Unimportant □

   Consenting Process

9. Would you prefer to approach parent(s) for consent to neonatal research before or after delivery of their baby?
   Before…… □
   After…… □

10. Would you agree that approaching parents for consent to neonatal research before the birth of their baby leads to a greater uptake in consenting parent(s)?
    Strongly Disagree □ Disagree □ Neither Agree nor Disagree □ Agree □
    Strongly Agree □

11. Would you agree that approaching parents for consent to neonatal research after the birth of their baby leads to a greater uptake in consenting parent(s)?
    Strongly Disagree □ Disagree □ Neither Agree nor Disagree □ Agree □
    Strongly Agree □

12. In your opinion do you think parent(s) fully understand the information received from the clinician at the time of consenting? Yes □ No □

   If no, would you proceed to allow them consent their baby to the research study if they insisted? Yes □ No □

   If yes to Q 12, can you please give your reason(s)?

   ____________________________________________________________

   ____________________________________________________________

Clinicians Questionnaire  Version 1.0  Page 2 of 4
13. Do you read through study information leaflets with the parent(s)? Yes ☐ No ☐

14. Roughly, can you state how much time you spend with parents when consenting for neonatal research? Less than 20 minutes ☐ 20 minutes to 40 minutes ☐ 40 minutes to an hour ☐ Over an hour ☐

15. Do you feel you allocate enough time with parents to ensure you receive a fully informed consent? Yes ☐ No ☐

16. Do you make contemporaneous notes whilst consenting parent(s) to neonatal research? Yes ☐ No ☐

17. Would you like to have the informed consent process with parents audio recorded? Yes ☐ No ☐

18. Once consent is obtained and the study commenced, do you continue to monitor consent received? i.e. do you approach parent(s) at different stages throughout the duration of the study to ensure continuous consent? Yes ☐ No ☐

19. Do you agree with the following statement: “A signed consent form should be a prerequisite for all types of neonatal research” Strongly Disagree ☐ Disagree ☐ Neither Agree nor Disagree ☐ Agree ☐ Strongly Agree ☐

20. Have you obtained consent for a randomised, controlled trial? Yes ☐ No ☐

21. Would you be of the opinion that parents tend to fully understand the randomisation process when explained to them at the time of consent? Strongly Disagree ☐ Disagree ☐ Neither Agree nor Disagree ☐ Agree ☐ Strongly Agree ☐
22. Do you agree with the following statement “A waiver of consent is appropriate for certain types of neonatal research”.

Strongly Disagree ☐ Disagree ☐ Neither Agree nor Disagree ☐ Agree ☐

Strongly Agree ☐

If you agree or strongly agree to Q22 can you please tick the type of neonatal research where you believe a waiver of consent should be allowed?

Interventional neonatal research with a drug.................. ☐
Interventional neonatal research with a medical device..... ☐
Non Interventional/observational neonatal research....... ☐
Emergency neonatal research.................................... ☐

Do you have any further comments?

________________________________________________________________________
________________________________________________________________________

Thank you!!
Research Questionnaire Project

Information Leaflet for Clinicians

Introduction:

You are invited to take part in a questionnaire based research project. This aim of the project is to determine the perceptions of parent(s) and clinicians regarding the informed consent process in neonatal research. This project is being undertaken by a student of the Royal College of Surgeons, Dublin. The questionnaire should take approximately ten minutes to complete.

Student Name: Niamh O Shea, Final Year MSc in Healthcare Ethics and Law, RCSI.

Supervisors: Professor Eugene Dempsey, Consultant Neonatologist, Cork University Maternity Hospital and Dr Kieran Doran, Solicitor, Senior Healthcare Ethics Lecturer, University College Cork.

Title of Project: Perceptions of Parent(s) and Clinicians regarding the Informed Consent Process in Neonatal Research.

What is the aim of the project?

The project aims to gather as much information possible from parent(s) and clinicians regarding their views of the informed consent process in neonatal research. This information will be collected using two questionnaires. The first questionnaire will be completed by parent(s) who have been approached to take part in neonatal research while their infant was an inpatient in the neonatal unit of the Cork University Maternity Hospital (CUMH). The second questionnaire, which we are asking you to complete, is for clinicians based in the CUMH. We would like to review the answers from completed questionnaires to identify the positives and negatives experienced during the informed consent process by both parent(s) and clinicians. We hope to use the information provided from parent(s) and clinicians to help identify new methods of improving the whole area of the informed consent process involving neonatal babies.

The questionnaire we are asking you to complete is completely anonymous. Data from the questionnaire will be saved to an encrypted laptop which is stored in a secure, swipe access office within the Cork University Maternity Hospital. The questionnaires will be stored in a locked cabinet located in a secure, swipe access office. Only the research student and her supervisors will have access to returned questionnaires. Data that may be reported in scientific journals will not include any information that identifies you as a participant in this project.
F. CREC application form

Form 1 - Ethics Application Form

UNIVERSITY COLLEGE CORK
Clinical Research Ethics Committee of the Cork Teaching Hospitals

PROTOCOL SUBMISSION FORM

All items must be completed as indicated; incomplete applications will be returned. A protocol application must include:

1. Protocol Submission Form (pages 1-4) – Original and seven copies. Original must be signed by the Chief Investigator. Hand written forms will not be accepted.
2. Consent Form (the standard Ethics Committee format) – Eight copies.
4. Details of insurance policies in place to cover the study.
5. Curriculum Vitae of Chief Investigator (2 page document only) - One copy.

The complete application package must be received in the Ethics Committee office by the appropriate deadline in order to ensure review the next month. The Ethics Committee office is located at Lancaster Hall, 6 Little Hanover Street, Cork. The telephone number is (021) 4901901 and fax number is (021) 4901919.

Chief Investigator

Name of Chief Investigator: Professor Eugene Dempsey
Appointment: Professor of Neonatology
Department: Department of Paediatrics and Child Health
Office Address: Ground Floor, Neonatal Unit, Cork University Maternity Hospital, Wilton, Cork
Telephone No.: +353 21 4920525

Protocol Details

Protocol Number:
Protocol Title: Perceptions of Parent(s) and Clinicians regarding the Informed Consent Process in Neonatal Research.
Site(s) of Performance: Cork University Maternity Hospital

Co-investigators

Only the co-investigators listed may perform the procedures indicated on this protocol. They may NOT amend the protocol.

Names & Appointments:
Dr Kieran Doran, Solicitor, Senior Healthcare Ethics Lecturer, School of Medicine, University College Cork, Room 2.48 Brookfield Health Sciences Complex, College Road, Cork City, (021) 4901513.
Ms Niamh O Shea, Masters Student in Healthcare Ethics and Law, Royal College of Surgeons and Clinical Trials Coordinator, University College Cork.
Is this protocol part of an active or pending externally funded project:  Yes [ ] No [X]  

If yes, complete the following:

<table>
<thead>
<tr>
<th>Category</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Names of Agency/Sponsor:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Address of Agency/Sponsor:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Title of Grant Proposal:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Does the Chief Investigator personally gain financially from this study: Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Are there any additional cost implications for the hospital management beyond standard of care: Yes [ ] No [ ]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>If yes please specify:</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**SPECIAL CONSIDERATIONS**

<table>
<thead>
<tr>
<th>Category</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is this study is part of a multi-centre project:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Does this study involve laboratory/clinical procedures NOT part of ordinary management: Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Does this study involve the clinical experimental use of radiation or radioisotopes: Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Does this study involve the use of biohazardous or infectious radioisotopes: Yes</td>
<td>No</td>
<td></td>
</tr>
</tbody>
</table>

If yes, please explain:

Are human subjects from the following **special population(s)** involved in this study: **Tick where appropriate**

- Infants (<1 Year) [ ]  
- Children(1-17 years) [ ]  
- Elderly (>59 years) [ ]  
- Pregnant Women [ ]  
- Prisoners [ ]  
- Mentally Disabled [ ]  
- Mentally Retarded [ ]  
- None of these [X]  

No investigator shall recruit from a student group where he/she, or any of the co-investigators, have material influence over the assessment of academic performance of that student group.
**Preceded Study Description** For each of the categories below, please select the items(s) which best describe(s) your study. You may tick up to two items for each category.

### Type of study:
- Behavioural-Social
- Diagnostic
- Preventive
- Other: ____________________________

### Organ System(s):
- Not Applicable
- Dermatologic
- Haematologic
- Ophthalmologic
- Renal
- Cells, blood, other body fluids or tissues only
- Other: ____________________________

### Type of Disorder:
- Not Applicable
- Infectious
- Metabolic/Endocrine
- Traumatic
- Other: ____________________________

### Type of Drug/Device:
- Not Applicable
- Anti-asthma/allergy
- Anti-inflammatory/Anticonvulsants
- Cardiovascular/Antihypertensive
- Contrast Media
- Hormones
- Sedatives/Antidepressants/Tranquilizers
- Analgesics
- Anticoagulant
- Biologicals/Vaccines
- Chemotherapeutic Agents
- Dermatologics
- Immunosuppressives
- Anaesthetics
- Anti-infectives
- Blood Components
- Contraceptives
- Diagnostics
- Vitamins
Purpose of Investigation:

Informed consent is central to all medical research involving humans. It is both a legal and ethical requirement that informed consent be obtained for medical research. For research that involves the participation of newborn infants, proxy consent is sought from the parents/guardians of the potential study participant. According to Mason et al. (2000) questions have arisen as to whether the process of obtaining informed consent from parents for neonatal trials leads to valid consent. Between January 1997 and September 1998 the Euricon study took place. The Euricon study was an international study involving nine EU countries. The aim of the study was to assess the validity of consent in neonatal trials and to seek to improve the consent process. Results showed that only 59 parents out of 200 had given a valid informed consent for their baby take part in neonatal research. In Ireland there has been minimal research completed which assess the validity of consent in neonatal research. According to Health Service Executive guidelines “Consent is the giving of permission or agreement for an intervention, receipt or use of a service or participation in research following a process of communication about the proposed intervention”. The purpose of this study is to further explore into the communication exchanged between clinicians and parent(s) during the informed consent process in neonatal research from an Irish hospital setting. We hope to gather as much information possible from clinicians and parent(s) regarding their views/experiences of the informed consent process in neonatal research.

Procedures to which humans will be subjected:

This is an anonymous questionnaire based research study. The questionnaires have been completed using the Likert Scale to gather as much information possible from participants taking part.

I have enclosed the following documents for approval:


Subjected to the committee's approval, I will either post the parental questionnaire and information leaflet to parents whose newborn baby was an inpatient at the neonatal intensive care unit (NICU) of the Cork University Maternity Hospital (CUMH), or give them the questionnaire upon discharge to either complete or take home and post back to me. I will only post the questionnaire and Information Leaflet or approach parents whose infant has been discharged from the NICU. I will include a stamped and addressed envelope to allow parent(s) return the questionnaire to me with minimal difficulty. I will hand out the clinicians questionnaire and information leaflet to clinicians based in the CUMH, where I myself am based as a clinical trials coordinator. I will personally collect the questionnaires once completed.

Data will be collected for this study on a completely anonymous basis. All data from the questionnaires will be saved to an encrypted laptop which is stored in a secure, swipe access office within the Cork University Maternity Hospital. The questionnaires will be stored in a locked cabinet located in a secure, swipe access office. Data will be destroyed appropriately at the end of the study.
Potential benefits to subjects and/or society:

It is our hope that by gathering as much information possible from parents and clinicians regarding their own personal experiences of the informed consent process in neonatal research, we can further explore into the current pitfalls as described by them of informed consenting in neonatal research. Our overall aim is to produce guidance for clinicians to assist them when gathering informed consent from parents to hopefully increase the experience had by all.

Potential risks to subjects and precautions taken to minimise risk:

This anonymous questionnaire based research study poses minimal risk to subjects. The anonymous data collected will be stored in compliance with all data protection regulations. This includes storing the electronic data to an encrypted laptop which will be stored in a secure, swipe access office within the Cork University Maternity Hospital. All returned questionnaires will be stored in a locked cabinet located in a secure, swipe access office. Data will be destroyed appropriately at the end of the study.

Alternative procedures, if any, available to subjects:

This is a completely voluntary research study. Parents and clinicians are under no obligation to take part. This is highlighted in the information leaflets that they will receive.

Subjects:

What is the total number of subjects to be studied? 200

How will subjects be chosen? (Inclusion and Exclusion Criteria) Inclusion Criteria: Clinicians must be currently working in the CUMH. Parents whose baby was previously an inpatient in the NICU and the baby must have been discharged home.

If there be payment to subjects? Yes ☐ No ☒

If Yes how much?

Methods used to ensure confidentiality of data:

Data will be collected for this study on a completely anonymous basis. All data from the questionnaires will be saved to an encrypted laptop which is stored in a secure, swipe access office within the Cork University Maternity Hospital. The questionnaires will be stored in a locked cabinet located in a secure, swipe access office. Data will be destroyed appropriately at the end of the study.
Declaration of the Chief Investigator

I certify that the protocol and method of obtaining informed consent as approved by the Ethics Committee will be followed during the period of this research project. Any changes of protocol, PI or consent will be submitted for Ethics Committee review and approval prior to implementation. Any adverse reactions will be promptly reported to the Ethics Committee office. This research will be carried out only by the approved Chief Investigator and co-investigators. All records of this research will be maintained as required by the Department of Health & Children.

Signature Chief Investigator:

Print Name:

Date: (dd/mm/yyyy):

[Signature]

[Name]

[Date: 12.12.14]
# Appendix 2 - CASP qualitative checklist

## Screening Questions

1. Was there a clear statement of the aims of the research?  
   ![Yes] ![Can't tell] ![No]

   **Hint:** Consider
   - What was the goal of the research?
   - Why it was thought important?
   - Its relevance

2. Is a qualitative methodology appropriate?  
   ![Yes] ![Can't tell] ![No]

   **Hint:** Consider
   - If the research seeks to interpret or illuminate the actions and/or subjective experiences of research participants
   - Is qualitative research the right methodology for addressing the research goal?
Detailed questions

3. Was the research design appropriate to address the aims of the research? □ Yes □ Can’t tell □ No

HINT: Consider
- If the researcher has justified the research design (e.g. have they discussed how they decided which method to use)?

4. Was the recruitment strategy appropriate to the aims of the research? □ Yes □ Can’t tell □ No

HINT: Consider
- If the researcher has explained how the participants were selected
- If they explained why the participants they selected were the most appropriate to provide access to the type of knowledge sought by the study
- If there are any discussions around recruitment (e.g. why some people chose not to take part)
5. Was the data collected in a way that addressed the research issue?  
☐ Yes  ☐ Can’t tell  ☐ No

HINT: Consider
• If the setting for data collection was justified
• If it is clear how data were collected (e.g. focus group, semi-structured interview etc.)
• If the researcher has justified the methods chosen
• If the researcher has made the methods explicit (e.g. for interview method, is there an indication of how interviews were conducted, or did they use a topic guide)?
• If methods were modified during the study. If so, has the researcher explained how and why?
• If the form of data is clear (e.g. tape recordings, video material, notes etc)
• If the researcher has discussed saturation of data

6. Has the relationship between researcher and participants been adequately considered?  
☐ Yes  ☐ Can’t tell  ☐ No

HINT: Consider
• If the researcher critically examined their own role, potential bias and influence during
  (a) Formulation of the research questions
  (b) Data collection, including sample recruitment and choice of location
• How the researcher responded to events during the study and whether they considered the implications of any changes in the research design
7. Have ethical issues been taken into consideration? □ Yes □ Can't tell □ No

HINT: Consider
- If there are sufficient details of how the research was explained to participants for the reader to assess whether ethical standards were maintained
- If the researcher has discussed issues raised by the study (e.g., issues around informed consent or confidentiality or how they have handled the effects of the study on the participants during and after the study)
- If approval has been sought from the ethics committee

8. Was the data analysis sufficiently rigorous? □ Yes □ Can't tell □ No

HINT: Consider
- If there is an in-depth description of the analysis process
- If thematic analysis is used. If so, is it clear how the categories/themes were derived from the data?
- Whether the researcher explains how the data presented were selected from the original sample to demonstrate the analysis process
- If sufficient data are presented to support the findings
- To what extent contradictory data are taken into account
- Whether the researcher critically examined their own role, potential bias and influence during analysis and selection of data for presentation
9. Is there a clear statement of findings?  
☐ Yes  ☐ Can’t tell  ☐ No

HINT: Consider
- If the findings are explicit
- If there is adequate discussion of the evidence both for and against the researchers' arguments
- If the researcher has discussed the credibility of their findings (e.g., triangulation, respondent validation, more than one analyst)
- If the findings are discussed in relation to the original research question

10. How valuable is the research?

HINT: Consider
- If the researcher discusses the contribution the study makes to existing knowledge or understanding e.g., do they consider the findings in relation to current practice or policy?, or relevant research-based literature?
- If they identify new areas where research is necessary
- If the researchers have discussed whether or not the findings can be transferred to other populations or considered other ways the research may be used
References

5. Use ICoHoTRfRoPfH. ICH Harmonised Tripartite Guideline for Good Clinical Practice E6(R1). 1996.
47. Snowdon C, Elbourne D, Garcia J. “It was a snap decision”: Parental and professional perspectives on the speed of decisions about participation in perinatal randomised controlled trials. Social science & medicine. 2006;62(9):2279-90.
54. The Nuremberg Code (1947) 1996-12-07 08:00:00. 1448 p.
78. Diekema DS, editor Ethical issues in research involving infants. Seminars in perinatology; 2009: Elsevier.