Online Research involving Young People with Cancer: An Exploration of Guidance, Policies and Regulations Governing Internet-mediated Research.

Johanna Linnea Caroline Kempe

A thesis presented for the degree of Master of Philosophy

University College London
Great Ormond Street Institute of Child Health
Louis Dundas Centre for Children's Palliative Care

Declaration

I, Johanna Kempe, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Acknowledgements

I wish to acknowledge the feedback and advice from Professor Bluebond-Lanager, Dr Henderson and Dr Jones. Second I wish to thank the Raisa Gorbachev Foundation and Marie Curie Cancer Care for supporting this research through the Lebedev studentship, and the Louis Dundas Centre for Children's Palliative Care for hosting the studentship. I also wish to say a special thanks to the Health Research Authority for providing the data that was used for the document analysis.

I wish to thank my wonderful friends from the Institute of Child Health, I appreciate your support and will miss the lunches in the ICH cafeteria and the park during the summer months. I want to acknowledge the amazing support and encouragement from my fiancé Graham and my family despite the distance.

I'm forever grateful for the reassurance from all my friends, who have all helped and supported me while conducting the research for this thesis. A special mention to David Moulds and Devin Johnson for the political commentary and life coaching, Hanna Isotalus for the cat videos, Jordana Peake for the immense support, Sally Isted for the Sunday Roasts and gorgeous chocolate cakes. In addition, a special mention to the 'Baby Jags' for all the jokes.

Last but not least, a special thanks to Dr. S. Lupin-Lee for the laughs.

Abstract

Background: Internet-mediated research methodologies are increasingly used to study young people with cancer at any stage during the illness trajectory. Researchers are increasingly debating the ethics of these methods. Despite this limited attention has been given to the actual ethical issues that arise during the study. Furthermore, few studies have explored the types of ethical conflicts that research ethics committees (RECs) identify in relation to this type of research.

Objective: The aim of the thesis is to explore ethical issues by 1) identifying the ethical conflicts researchers report in Internet-mediated research and 2) exploring the content of REC documentation and compare the ethical issues arising in Internet-mediated versus offline research.

Methods: Chapter 1: A review of the literature outlining the development of ethical guidelines and critiques of the current system. Additionally, the chapter outlines the debate on ethical issues in Internet-mediated research involving young people with life-limiting or life-threatening conditions.

Chapter 2: A systematic review of original English language research describing Internet-mediated research involving young people with cancer and young cancer survivors (aged 13-25) to explore the methods employed and what ethical issues arose during the study.

Chapter 3: A document analysis of REC documentation associated with applications for Internet-mediated research and offline research with young people with malignant or non-malignant conditions to explore what impact if any Internet-mediated methodology has on REC appraisal and practice.

Chapter 4: A discussion of the findings of the thesis, the implications for research and an exploration of directions for future research.

Results: While few studies reported on ethical issues arising over the course of the study researchers tended to highlight privacy and prevention of harm. This was replicated in the chapter 3 whereby we identified few ethical issues unique to Internet-mediated research. This contrasts with the extensive literature on these methodologies indicating unique ethical considerations.

Implications: There is misplaced emphasis in the literature on the need for additional ethical guidelines specifically developed for Internet-mediated research. The novel findings of this study contribute to the discussion over the ethics of Internet-mediated research with young people with life-limited and life-threatening conditions and how RECs are practically applying guidelines.

Table of Contents

List of tables

List of figures

Funding note

This research was supported by the Lebedev studentship, through the Raisa Gorbachev Foundation and Marie Curie Cancer Care. The studentship was hosted by the Louis Dundas Centre for Children's Palliative Care at UCL Great Ormond Street Institute of Child Health, University College London. The study was registered at ICH R&D under project code 15PP18.

Ethical approval

The following study was deemed to be exempt from UCL REC ethical approval. The study was exempt as the study consisted of a literature review using published data and an analysis of anonymised information from a public body.

Chapter 1

Introduction

1.1 Research ethics – general background

The study of ethics attempts to understand and evaluate the morality of decisions and actions (Ivanov and Oden, 2013). Ethics thereby provide a formalised framework that guides behaviour. In research, ethical guidelines form a code of conduct and dictates professional boundaries (Douglas, 2003). Ethics and morals are closely linked concepts, and these two concepts are often conflated (Ivanov and Oden, 2013; Swift, 2006). However, Madge (2007) argued that ethics is influenced by moral values, suggesting that there is a distinction between ethics and morality. Halse and Honey (2005) supports this distinction, as they emphasise that morals can be conceptualised as an individual's beliefs, biases (e.g. religious/spiritual convictions) and sociocultural norms. The purpose of this thesis is to explore formalised frameworks that researchers conduct their research within, meaning that the emphasis throughout this thesis will be on ethical conflicts that can arise during the research process. Ethics can refer to both the philosophical frameworks and the practical application of ethical principles to a context. The purpose of this thesis is to explore the practical application of ethical guidance within the context of clinical online research involving young people with life-limited and life-threatening conditions.

1.2 Background to the development of ethical guidance for research

Modern ethical guidelines and legislation around human subjects research originates as a response to the atrocities committed by Nazi doctors during the Second World War in the name of "scientific advancement" and "research" (Guta et al., 2013) and the subsequent Nuremberg trials and the Nuremberg Code (Abebe and Bessell, 2014). The atrocities were committed on concentration camp prisoners and civilians before and during the Second World War and included for example high-altitude experiments, freezing experiments, malaria experiments, bone, muscle and nerve regeneration experiments, bone transplants, seawater experiments, typhus and other vaccine experiments, sterilisation experiments and incendiary bomb experiments (Abebe and Bessell, 2014). During the Nuremberg trials in 1946-1947 a panel of American judges prosecuted 23 doctors and administrators for the organization of and participation

in war crimes and crimes against humanity through these medical experiments and procedures in the so-called Doctors' Trial.

Following the Doctors' Trial, Dr Leo Alexander submitted six points defining legitimate medical research to the American Council for War Crimes together with four additional points outlined following the verdict at the Doctor's trial. The ten principles were drafted into the Nuremberg Code and included informed consent, minimal harm, proportionality of risk to benefit and right to withdraw from research participation (Saginur, 2014).

1.3 Ethical violations post-Nuremberg and their influence on ethical governance

Despite the development of the Nuremberg Code, a number of studies conducted in the following decades have subsequently been considered unethical clinical research (Saginur, 2014). These studies include those violating the principles of consent (e.g. the Tearoom sex study by Humphreys, 1970), the principle of informing participants of the true purpose of the study and debrief (e.g. the obedience studies by Milgram, 1978) and any lasting effect participants may have of research participation (e.g. the Tuskegee syphilis study by e.g. Schuman et al. 1955 and Cadwell et al. 1978), protection from harm (e.g. the Little Albert study by Watson & Rayner, (1920) and Willowbrook hepatitis studies by Krugman (1971)), rules regarding storage of human tissue or other research data (e.g. Henrietta Lacks and the HeLa cells (Lucey et al. 2009)) in addition to the transparency and accuracy of research findings (e.g. the Summerlin Mouse Affair (Resnik, 2014) and the MMR study by Wakefield (Leask et al. 2010)).

1.4 Research ethics committees (RECs)

Out of these studies arose the Belmont Report, the Beecher paper (1966) and the establishment of the first institutional review boards (IRBs) to protect human participants in clinical research. After a shift in attitudes towards the role of ethics in clinical research since the 1960s; IRBs and research ethics committees (RECs) have become a significant part of the ethical review process in many countries (Saginur, 2014). The shift in attitude went from initial academic and societal resistance to the governance of research to an approach which sees ethical approval as central to the process of setting up a study and a crucial way in which researchers can share liability from any harm done to participants during the research process (Beecher, 1966; Saginur, 2014).

The review system of clinical research in the UK has undergone several structural and operational changes; from no RECs in 1966 to over 80 RECs for clinical research in 2016 (Health Research Authority (HRA), 2016; Hedgecoe, 2009). Due to the revelation of past unethical research in the 1980s there were increasing calls for regulation and public oversight for RECs (Wilson, 2011).

Juritzen (2011) suggested that RECs have been set up on the assumption that researchers are uncontrollable and dangerous. One way of ensuring oversight of research and to protect the public from the danger of unethical clinical research has been the increased bureaucratisation of the process of starting up and designing a research study. This includes the establishment of procedures for seeking consent, assent, debrief, oversight of the research by study sponsors, training of researchers in areas such as good clinical practice and data protection, requirements of institutions who carry out research to have policies for allowing participants to seek help from mental health organisations, or seek other recourses through insurance policies. The increasing bureaucratisation of research ethics and influence of RECs in the UK research environment has led several academics to call the current ethics review system an 'ethics industry' (Hedgecoe, 2009; Wilson, 2011). Wilson (2011) also cites the distancing from clinical autonomy by increasing the involvement of the judicial system and the government as contributing to the emergence of the "ethics industry".

1.4.1 Criticisms of RECs

RECs have been criticised by researchers for acting as gate-keepers, and hindering research (Kreicbergs et al. 2004, Hinds et al. 2007). Other critics have focused on the lack of transparency (Ashcroft and Pfeffer, 2001) and an increasing bureaucratization (Klitzman, 2012). For example, in the UK most of the documents associated with the ethical appraisal process (e.g. meeting minutes) are confidential, and other documents (e.g. ethical review forms completed by REC members prior to meetings) are destroyed following meetings (HRA, 2016) hindering transparency of the process. There are also several reports of inconsistent decision-making processes without due process for researchers (Burris, 2008). These critiques have lead some researchers to claim that the ethical review process is focusing more on the ethics of documentation rather than the ethics of research (Klitzman, 2012). There are several suggestions that the lack of adherence and conformity to ethical guidelines creates a system more interested in

complying with documents and institutional norms in contrast to engaging in a process involving compliance with ethical governance (Allen 2008; Jennings 2010).
Stark (2006) observed three IRBs in the USA and found that IRB members often attempted to judge the ethical merit based on a poor grasp of the methodology involved, overestimation of the dangers, and a reliance on personal anecdotes rather than research. Furthermore, some IRB members judged the ethical merit of some studies solely on spelling and grammatical errors. Shah et al. (2004) interviewed chairmen of IRBs and found that they had a biased view of risk associated with different medical testing methods. The authors found that the IRB chairmen overestimated the risks associated with the tests, meaning the perceived risk did not correspond with the actual risk of the medical testing methods. A number of studies report tense relationships between REC members and researchers (Davey 2009; Lidz and Gaverich 2013; Tilley 2008). However, despite the guidelines and training, studies suggest that REC members may have limited knowledge of national ethical guidelines (Guillemin et al., 2012) or they do not refer to it (Guillemin et al., 2010). Guillemin et al., (2012) interviewed Australian REC members and found that members tended to rely more on personal experience or the chair's experience and knowledge of ethical guidelines. Furthermore, anecdotal reports suggest that REC members sometimes rely on personal or professional ethical frameworks when appraising the ethics of research (Egan et al., 2016).

1.5 The use of the Internet in research

In 2007 there were approximately 1.24 billion Internet users world-wide (James and Busher, 2009), which increased to an estimated 3 billion in 2014 according to the International Telecommunication Union (2014) and it is likely there are even more today. Purcell (2011) states that at least 93% of US adolescents (aged 12-17 years) and 90% of young people (aged 18 to 29 years) use the Internet, compared to 84% of adults (30-49 years). The Oxford Internet Institute surveyed 2,657 respondents in 2013 and found that 100% of UK 14 to 17 year olds classify themselves as an Internet user (Blank, 2013). The Internet can be defined as an interconnected system of networks that use the same communication protocol (e.g. the Internet protocol suite) to transfer information between hosts (Luppicini, 2013). Increased use and access has led to a growing proportion of activities moving online including online banking, shopping and communication (Kosinski et al., 2013). In turn this has caused new research questions to emerge and different types of research methodology to be adapted to suit the new environment (Wiles

et al., 2013). Internet-mediated research can be defined as research studying online behaviours e.g. communication (Zahedi et al., 2011), social support (Malik and Coulson, 2011) and social networks (Bouvier, 2012) in addition to research conducted using online methodologies, e.g. web-based survey (Eaton et al., 2010), interviewing using video communication programmes such as Skype (Hanna, 2012) and online ethnography (Torres et al., 2010).

While the literature is divided as to whether Internet-mediated research methodology is as valid and reliable compared to 'traditional' methodology (Davis et al., 2004; Ayling and Mewse, 2009) researchers have reported several advantages of using online methodology. The Internet has been utilised to access hard to reach populations (Ritterband and Palermo, 2009) such as young people (Levine et al., 2011), homeless individuals (Guadagno et al., 2013) and individuals with palliative care needs (Elwell et al., 2011). The Internet has also been harnessed to provide mass online psychological interventions cheaply and efficiently to adolescents who would have otherwise been excluded from such interventions due to cost or their living too far away from face to face services (Henderson et al., 2012). For the purpose of this thesis the term "offline research" will be used to denote research that does not take place within an online context (Orgad, 2009). In contrast "Internet-mediated research" or "online research" will be defined here as research using the Internet or Internet technologies to obtain data and will be used interchangeably.

1.5.1 The ethics of Internet-mediated research

In addition to the debate over the validity of Internet-mediated methodologies there has been an increased debate as to what constitutes 'ethical' online research. Rodham and Gavin (2006) argued that the ethical decision-making process that researchers engage is not affected by the online versus offline environment where the research takes place. The authors suggested that Internet-mediated research raises no more and no different ethical concerns compared to traditional, offline research. However, other researchers argue that modifications should be made to account for potential new ethical challenges arising in Internet-mediated research not covered by other guidance (Hair and Clark, 2007; Wilson, 2011; Buchanan and Hvizdak, 2009; Henderson et al., 2013). Buchanan and Ess (2009) surveyed American IRBs with open-ended and closed questions, and of the 334 respondents (44% response rate), almost 50% agreed that Internet research was an area of concern or importance. The majority of

respondents (62%) reported that they did not have any separate guidelines or checklists for reviewing Internet-based research protocols, and a few boards were not aware of specific guidelines (such as e.g. the AoIR guidelines). A majority of IRBs (74%) did not provide training that dealt with issues surrounding Internet-based research. Despite this, 42% of respondents reported that there was sufficient regulatory documentation to support decision-making (Buchanan and Ess, 2009).

An analysis of the open-ended questions revealed that some IRBs relied on IT departments to advise on what the members called "IT related issues" (Buchanan and Ess, 2009). In addition, 38% of IRBs tended not to review privacy policies associated with commercial and/or third party software. Buchanan and Ess (2009) noted that 9% of IRBs required or encouraged their members to undergo training on Internet-mediated research ethics; in contrast 60% of IRBs required or encouraged members to undergo training on offline research ethics. It should be noted that the survey was carried out with American IRBs, and there are differences between the review processes in the USA and in Britian. For example in Britian the researchers are present during the meeting when their ethical application is reviwed, which is not always the case in the rest of the world. The debate on ethical issues normally centres on issues around informed consent, privacy and the private-public debate.

1.5.1.1 Informed consent

Scherer et al. (2007) argued that three criteria must be met for consent to be considered informed. Firstly, a participant must be given sufficient information to make a decision knowingly, secondly the consenter should have the competency to make the decision and thirdly the consent must be provided without coercion (Scherer et al., 2007). The General Medical Council states that informed consent relates to a respect for patient autonomy and is the basis of trust between a health care professional and patient (2008). In addition to enabling the participants to make an informed choice regarding participation, informed consent provides legal protection for institutions and researchers against litigation (Burgess, 2007). The principle of consent is underpinned by the moral philosophical notions of self-determination and autonomy (Freer et al., 2009). A legal requirement to obtain consent to medical treatment has been established by case law in US, while informed consent in research has been established through ‘best practice’ (Freer et al., 2009). Informed consent is also an important part of the European data protection laws and under the new General Data Protection Regulation (GDPR) valid

consent is required for lawful processing of data (article 7). While research is exempt (article 83) if certain conditions are met, Borghi et al., (2013) argued that there is still legal uncertainty as to how consent should best be obtained.

The traditional definition of informed consent therefore implies that consent to participate in a study can only be given after sufficient information is provided. Coons (2012) argued that a basic consent form includes information on the rights of study participants (such as right to withdraw participation), the study purpose and procedure, duration and, risks and benefits. In the face of increased regulation and standardisation the information required has increased. This has led both 'traditional' and 'online' researchers to question whether "information by volume" leads to better informed consent (Coons, 2012).

Secondly, informed consent requires competency to understand the information that is provided. Sin (2005) noted that competency is assumed in most adults, and it is only when participants are perceived as atypical or impaired that competency is questioned. In research with children and young people, legal guardians are required to provide informed consent while the young person can provide assent, a type of informal agreement without legal standing (Spriggs, 2010). In the UK, a young person under the age of 16 years can provide consent to treatment in their own right if they are deemed Gillick competent (Hunter and Pierscinek, 2007). Gillick competency is established by determining a young person's ability to understand what the treatment or advice involves (Hunter and Pierscinek, 2007). Gillick competency was established by Gillick v West Norfolk & Wisbech Area Health Authority and Department of Health & Social Security (Hunter and Pierscinek, 2007). Hunter and Pierscinek (2007) noted that the competency decision is very subjective and at the discretion of the practitioner, and they therefore warned against attempting to use Gillick within research, citing lack of appropriate training for researchers. However, researchers within Childhood Studies argue that children and young people should be conceptualised as active agents capable of understanding and interpreting information (James et al., 1998) and therefore having competency to consent to research (Punch, 2002).

Competency is also related to how the information is presented. Freer et al. (2009) found that parents who received a verbal explanation of a study recruiting neonates had a better understanding of the study compared to participants who only received a written consent form. Rowbotham et al. (2013) found that an interactive consent procedure (involving video and text) improved understanding of a chemotherapy neuropathy study.

Third, The final part of the definition argues that consent must be voluntary, indicating that the participant should participate of their own free will, and that participation can be withdrawn at the participants discretion (Coons, 2012).

In both traditional and online research there is an ambiguity surrounding the meaning of informed consent (Borghi et al., 2013), but unlike traditional research the individual participant is not always the consenter (Hewson and Buchanan, 2013). Hudson and Bruckman (2004) conducted a study into participant's reactions to being studied in online forums, and found that forum members did not want to be studied. Instead of individual participants, webmasters, moderators or other gate-keepers are often asked to provide consent. It can be argued that only asking gate-keepers for informed consent does not remove responsibility to prevent potential harm to participants.

Vayena et al. (2013) argued that traditional applications of informed consent are inappropriate as the models are too inflexible to use with evolving technology, and the transition of data from personal to a commodity that can be sold, shared or altered by different users makes traditional notions of informed consent obsolete. The architecture of the Internet means that it is difficult for data to completely disappear indicating that a traditional notion of 'right of withdrawal' might become meaningless and difficult to enforce for researchers using certain types of methodology, such as 'big data'. McNamara (2013) argued that it is difficult to guarantee 'voluntary' consent, as consent can be implied by providing data, and some types of data might be collected automatically, such as IP addresses. Taken together, it suggests that online researchers need to revaluate the current application of informed consent.

1.5.1.2. Privacy

Privacy is a debated ethical and legal concept (Joinson et al., 2007), in part this is related to the changing value of information where online data has become a commodity that can be owned and used (Joinson et al., 2007). Privacy laws aim to give individuals control over their own data and personal information (Lindsay et al., 2007) and in the EU personal data protection is a fundamental human right (Article 8 of the EU Charter of Fundamental Rights). In the UK/EU privacy is currently regulated by EU Data Protection Directive 95/46/EC but the directive will be superseded by the General Data Protection Regulation (GDPR) in 2017 (Borghi et al., 2013).

In the absence of individual informed consent, online researchers are to some extent required to put additional emphasis on protecting individual privacy and anonymity compared to traditional researchers (Dias, 2003). Dias (2003) argued that while researchers could (and should) investigate online resources without obtaining consent; they need to ensure that participant's privacy is protected. This protection could be implemented by replacing usernames with pseudonyms, and removing other identifiable information (e.g. URLs, location names and specific ages). While both traditional and online researchers collect identifiable data, it is possible to collect a significant amount of personally identifiable data using online methods without an individual being aware of it (Frankel and Siang, 1999). More significantly the information can be linked (Frankel and Siang, 1999) and it might therefore be possible to identify a person's offline identity (Hewson and Buchanan, 2013). There is a debate on the extent to which different types of information can be linked and de-anonymised (Frankel and Siang, 1999; Lindsay et al., 2007). de Montjoye (2015) analysed meta-credit card data and found that knowing four spatial and temporal data points such as time of transaction was sufficient to name 90% of a sample of 1.1 million people. Zimmer (2010) discussed privacy issues with reference to the 'Tastes, Ties, and Time'' (T3) Facebook study by Lewis et al., (2008). Lewis et al., (2008) conducted a four-year study of 1,700 Facebook profiles from an 'anonymous' US college. Due to the terms of the authors grant, they were required to published the database online. While the data set was not publically available the codebook was, and taken together with comments made by the research team, such as mentioning the unique method for determining how undergraduates are housed and unique majors, the college was identified within days (Zimmer, 2010). Despite the fact that all information was anonymised in line with current ethical guidelines, the identification of the college was done without accessing the data itself. While none of the participants were identified, it could be argued that their privacy was at risk of identification. Additionally, Bobicev et al., (2013) developed an Authorship Attributor software, and successfully linked 75-80% of 6,000 messages of 100-150 words with the authors on two online in vitro fertilization (IVF) support groups. The accuracy score increased to 97.9% on messages with at least 300 words, leading the authors to question the anonymity of pseudonyms in online forums.

These studies show that traditional concepts of privacy, anonymity and identifiable data might not translate to the online context. Zimmer (2010) noted that even trivial information can become identifiable if aggregated as the combination is unique to

an individual. The studies indicate that researchers and RECS/IRBs may be required to re-evaluate of what is meant by privacy and identifiable information within the context of Internet-based research. Additionally, they raise questions about the move towards publishing data online, meaning that online researchers may have to balance their obligations towards their participants and obligations to uphold scientific transparency standards.

Another ethical issue associated with Internet-based research, which is not as salient for traditional research, is the illusion of privacy. An online space can be perceived as private, despite being public (for example, Facebook profiles, blogs and online forums) and it can change the way researchers are expected to carry out their ethical responsibilities (Woodgate, 2008). Further, conflicts can arise if different stakeholders advocate opposing stances (Hudson and Bruckman, 2004), for example a moderator or webmaster may see the online forum as a public space but the individual user may perceive the same space as private. Hewson and Buchanan (2013) argues that, to fulfil ethical responsibilities, researchers need to respect participants' privacy expectations. Other ethical frameworks argue that a researcher observing activity on an open-access forum has to fulfil a lower privacy requirement compared to a researcher observing a password protected forum (Wu et al., 2011; Zimmer, 2010).

Within the online qualitative research community, a debate has emerged surrounding whether to publish quotations from online text sources. For example Battle (2010) argues that the risk of harm to participants is too high and quotations should never be published. Other researchers suggest splicing quotations, and making sure they do not link back to the original source (Henderson, 2012; Rodham and Gavin, 2006) while others are in favour of publishing quotations as long as the individual poster has given consent (Brownlow and O'Dell, 2002).

It is important to note that these privacy and data protection laws mainly apply to Western-countries. The Oxford Internet Institute noted that many African countries have weak privacy and data protection laws (Taylor, 2013). First, conducting online research in countries with weak legal frameworks increases the risk of data and participant exploitation (Taylor, 2013). Second, it increases the risk of unethical research practices and thirdly it highlights issues sounding the application of Euro-centric ethical guidelines to non-European countries (Ocholla, 2011), such as increased risk of cultural insensitivity and inappropriateness.

1.5.1.3. Private versus public space online

The distinction of what constitutes private versus public space online is less clear compared to 'traditional' research, as online space is both public and private at the same time (Madge, 2007; Hewson and Buchanan, 2013). King (1996) argued that when participants perceive the space to be private, it would be unethical and immoral for the researcher to treat the space as public. While the Internet is public in the sense that the information might be accessible, the illusion of privacy creates a perceived private place (Eysenbach and Till, 2001), meaning that the Internet can be public and private at the same time. It could therefore be that the traditional private-public dichotomy is better theorised as a continuum (Ess and Jones, 2002; Bruckman, 2002) for online research. This continuum would mean that the line between private versus public sphere is blurred when using the Internet in research (Lomborg, 2012). Bruckman (2002) posits that using this continuum requires researchers to make a trade-off between protecting participant privacy and the quality of the reported result. The more information that is published the greater the risk that the participant can be identified (even if the identification only occurs within the studied online community).

While this trade-off might occur when using traditional methods as well, it can be argued there is greater relevance of this issue to online research. Conflicts can arise when stakeholders advocate different stances on whether online space is public or private (Hudson and Bruckman, 2004). It could be that a moderator or webmaster (who bears legal responsibility) sees the online forum as a public space whereas the users perceive the same space as private. Hewson and Buchanan (2013) argues that to fulfil ethical responsibilities researchers need to respect participants' privacy expectations. Other ethical frameworks argue that a researcher observing activity on an open-access forum has to fulfil a lower privacy requirement compared to a researcher observing a password protected forum (Ess and Jones, 2002). Scenarios such as these challenge a researcher's moral compass, as the two ethical stances represent two different ethical frameworks.

There are some limitations of arguing that the "publicness" of the Internet is similar to the "publicness" of conducting research in a public real space (such as a library or public square; Zimmer 2010). Zimmer (2010) argues that the analogy of a public square is flawed, as a researcher conducting traditional research in a public real space will observe random interactions which might be less likely to occur online. Similarly, a traditional researcher cannot observe all participants at once, but will need to select which participant to include in the study (Zimmer, 2010). In contrast a researcher can study all

group members in an online forum at once. The information gathered from traditional research in a public space is more likely to be imprecise and limited to observable traits (Zimmer, 2010). In comparison, a study of social networking site profiles can collect information ranging from name to sexual orientation to country of birth without interacting with the participants. To collect the same information within an offline research context would likely require interaction between the researcher and participant.

A number of studies on online forums have found that there is a high degree of personal disclosure, even in online forums classified as open-access- websites for which one does not register to view posts and message threads (Coulson and Greenwood, 2012) and the same studies have linked the high level of disclosure to perceived anonymity (Coulson and Greewood, 2012; Malik and Coulson, 2011). For example, Coulson and Greenwood (2012) investigated three online forums used by family members who had children with cancer and found a high degree of personal discourse. The authors argued this occurred because the participants assumed they would be anonymous. Joinson (2001) compared levels of self-disclosure in face-to-face versus synchronous Internet discussions and found that there were significantly higher levels of disclosure in the Internet discussions. In a follow-up study, Joinson (2001) found no difference in the level of personal disclosure between a face-to-face and video-based Internet discussion, indicating that anonymity can facilitate personal disclosure. Since perceptions of anonymity can affect the level of personal disclosure, online researchers need to reflect on how participants may perceive their environment. However, online anonymity has no widely accepted definition. Keipi et al. (2014) argued that the Internet offers three levels of anonymity for users; visual anonymity, pseudo-anonymity and full anonymity. Keipi et al. (2014) define visual anonymity as i) situations were physical characteristics are hidden from other users and ii) situations where there is no direct visual feedback between users. In contrast, pseudo-anonymity can be defined as situations where users use avatars or other profiles (Keipi et al. 2014). Full anonymity is only possible when users remain unidentifiable after interacting (Keipi et al. 2014).

In addition, the private-public debate has legal implications, for example the protection of personal identification is not as stringent under the GDPR if the data is already publically available (Article 83.2c). In addition, informed consent is required when the behaviour takes place in a private space but not when the behaviour takes place in a public space (Markham and Buchanan, 2012). In light of the implications of this debate, researchers should reflect on where on the private-public continuum their study is

best placed. Instead of viewing the private versus public sphere as a dichotomy, Nissenbaum (2010) suggested that researchers should focus on the contextual norms of the space from which the data is taken.

1.5.1.4. Prevention of harm

While the responsibility to prevent harm is a general ethical and moral obligation that underlies ethically sound research with human subjects, what constitutes harm is rarely defined (Kuhlau et al., 2008). It can be difficult to apply this principle, as the meaning of harm is context-dependent. It can be defined as emotional distress that impacts functioning (Ahuja, 2015). However, the harm that a researcher needs to prevent and what preventative measures to take are therefore not always apparent (Kuhlau et al., 2008). King (1996) argued that psychological harm/distress and feelings of being violated can occur when participants have discovered that their conversations have been used without their explicit consent (King, 1996). Additionally, psychological harm can occur if the participants could be identified either by external individuals or other group members, or if participants are asked about sensitive information. However, disclosure of sensitive information does not automatically mean that the participant has suffered harm (Ben-Ze'ev, 2003). Regardless of the situation, the researcher is ethically and morally responsible for preventing harm to participants at every stage of the research process (King, 1996). Kuhlau et al., (2008) distinguished between intentional and unintentional harm, where intentional harm is an action that will cause harm to a participant, while unintentional harm might create a risk of harm. A researcher's moral and ethical obligation could therefore include an awareness of the potential risks of harm, and an awareness of the potential consequences.

One reason there is a debate regarding publishing quotations from online qualitative research is that these quotes can be inserted into a search engine and the participant can be identified. As mentioned there are various ways of handling this information (including not publishing quotes and splicing) but it could be argued that with the evolving and increasing searchability of the Internet, researchers should not publish any quotations since it could be possible to identify participants by their quotations in the future. This could therefore cause the participant future harm, and the researcher would not be able to carry out their moral and ethical responsibilities. However, Kuhlau et al. (2008) argued that researchers cannot be held morally responsible for unforeseeable use of their research. Regarding publishing verbatim quotations, this

means that a researcher can be held morally and ethically responsible for ensuring participants are protected from harm (that is, it is not possible to trace their quotations using the present technology) but is not possible to hold researchers morally responsible for harm that results from future technological developments or improvements.

Unlike traditional face-to-face research it might be more difficult to identify harm and distress to participants during the online data collection as researchers might not have been trained to pick up on non-audio-visual cues of distress (Fox et al., 2007). Fox et al. (2007) found it to difficult assess distress in a synchronous focus group and Childress and Asamen (1998) questioned the feasibility to deal with participants dealing with a psychological crisis during web therapy sessions. This would mean that the suitability of using an online research methodology compared to traditional research depends on the level of potential risk of harm to participants.

1.6 Research involving young people who have cancer

There are several reports of palliative care researchers facing unique ethical conflicts e.g. issues surrounding informed consent from participants with fluctuating physical and cognitive capacity (Vig et al., 2010; Gysels et al., 2013). In addition, Beecham et al. (2016) found that researchers tended to perceive the ethical review process itself as a barrier to research. While there is a debate in the literature as to whether ethical concerns differ for research with adults versus young people (Arnold, 1992), gaining ethical approval for research with young people can be challenging (Wagener et al., 2004). The challenges of conducting research with young people relates to issues of consent, recruitment and the protection of participants, in addition to issues around research design and patient privacy (Angell et al., 2010). The ethical concerns that are highlighted in research with young people are often influenced by how vulnerability and maturity are conceptualised (Jamieson and Milne, 2012; Bluebond-Langner and Korbin, 2007; Tisdall, 2012). There has been increasing concern and debate about research involving vulnerable participants (Lasanga, 1997). Vulnerability can be conceptualised in various ways; Fisher (1993) defined vulnerability as one of various traits associated with individuals who cannot protect their own rights and welfare. A potential participant can be considered vulnerable when their circumstances (e.g. age, physical or psychological impairment, illness) impairs their ability to provide consent, increases the risk of susceptibility to deception, invasions of privacy or being forced to participate against their will (Fouka and Mantzorou, 2011).

For the purposes of this thesis the following definitions will be used for the terms 'malignancy', 'life-limiting condition' and 'life-threatening condition'. Malignancy is a concept often associated with cancerous tumors and tends to be used as an indicator of the degree of metastasis to local and/or distant locations (Jaaskelainen et al. 1986). In contrast, non-malignancy refers to non-cancerous conditions (Jaaskelainen et al. 1986). A non-malignant condition can be either life-limiting or life-threatening. A life-limiting condition can be defined as an illness "for which there is no reasonable hope of cure" (Fraser et al., 2011). This means that the young person is likely to die from the illness before reaching adulthood, examples include cystic fibrosis and Batten disease. In comparison, a life-threatening condition is an illness for which curative treatments exist but there is a risk that the treatment may fail (Fraser et al., 2011). Examples of life-threatening conditions include renal diseases and cardiac anomalies.

In contrast, a chronic illness can be defined as an illness that lasts longer than three months, there is no spontaneous recovery and rarely a cure available (Stanton et al., 2007). Other definitions tend to emphases a disruption to typical activities (e.g. attending school) of frequent hospitalisation (Mokkink et al., 2008) or a condition that requires a young person to take regular medication or use special equipment (Van Cleave et al., 2010). Examples of chronic illnesses include rheumatoid arthritis, chronic pain, diabetes and asthma. While there is overlap between these three concepts, the focus of the thesis will be limited to life-limiting and life-threatening conditions as these clinical populations have different illness trajectories compared to young people with a chronic illness.

1.7 Aims and objectives

Despite the extensive debate about ethical issues in Internet-mediated research, limited research has explored the practical implications the debate has had on research and RECs. Furthermore, few studies have explored what type of ethical issues arising from research involving young people with life-limiting or life-threatening illnesses. This is despite the recognition that young people receiving palliative care face a unique illness experience (Taylor et al., 2008; Woodgate, 2008) compared to other age cohorts.

The central aim of this thesis is to explore ethical issues by 1) identifying the ethical conflicts researchers report in Internet-mediated research and 2) exploring the content of REC documentation and compare the ethical issues arising in Internet-mediated versus offline research.

The structure of this thesis is:

Chapter 2: A systematic review of original English language research describing Internet-mediated research involving young people with cancer and young cancer survivors (aged 13-25). The aim of this chapter was to explore the methods employed and what ethical issues, real or hypothetical, arose during the conduct of the research.

Chapter 3 a document analysis of REC documentation associated with applications for Internet-mediated research and offline research with young people with malignant or non-malignant conditions. The aim of this chapter was to explore what impact, if any, Internet methodology has on REC appraisal and practice.

Chapter 4: A discussion of the results of this thesis and an exploration of future directions for further research and a discussion of the limitations of the thesis.

Chapter 2

Internet-mediated research with teenagers and young adults with cancer: A systematic review of ethical issues and how they are addressed.

2.1 Introduction

Young people with cancer are more likely than any other cancer patients to use the Internet (Dutton et al., 2013) and an increasing number of studies have been conducted using Internet-mediated methodologies with this group (Whelan and Fern, 2008; Wiles et al., 2013). Online technologies such as mobile apps, social media and message boards can be used both in research and recreationally at any stage in the illness trajectory of young cancer patients (Majeed-Ariss et al., 2015). Previous research has described how Internet-mediated technologies can be applied to the prevention of cancer (Lana et al., 2014), diagnosis of cancer (Robinson et al., 2014; Dekker et al., 2014), in support of patients or caregivers during active treatment primarily through measuring symptoms (Baggott et al., 2012), giving psychosocial support (O'Conner-Von, 2009) or medical advice (Stinson et al., 2013; Ruland et al., 2009, Lewis et al., 2005), during transition from active treatment (Sansom-Daly et al., 2012) and in cancer survivorship and follow-up (Ashley et al., 2011; Bartlett et al., 2012; Moody et al., 2015).

Methodologies used in previous studies include interventions delivered via Internet-based platforms (Fasciano et al., 2015; McLaughlin et al., 2012; Keim-Malpass and Steeves, 2012), mobile-based symptom capture tools (Jibb et al., 2014), synchronous and asynchronous focus groups (Fox et al., 2007; Nilsson et al., 2014; Tates et al., 2009; Zwaanswijk et al., 2007), and analysis of conversational data from online forums (Donovan et al., 2014; Elwell et al., 2011; Han et al., 2014). To date there has been no systematic overview of the types of Internet-mediated methods used in research involving young people with cancer (Zebrack et al., 2006; Fernandez and Barr, 2006).

There is no consensus on what constitutes good practice for conducting Internet-mediated research involving young people (Henderson et al., 2012). Rodham and Gavin (2006) argued that the online environment in which the research is conducted does not affect the types of ethical issues a researcher may face and these may be the same as the issues arising offline (e.g. consent seeking may be a contentious issue in both arenas). This would suggest that ethical dilemmas are similar in a “novel” online context to those

in offline context (Rodham and Gavin, 2006). However, using guidelines developed for offline research in an online environment may be unsuitable due to the rapid technological advancements (Hair and Clark, 2007) over the last decades. New technologies may raise ethical conflicts that are not adequately covered by currently accepted guidelines (Zimmer, 2010) (e.g. geographical tagging of online content). To date there has been limited systematic overview of the types of ethical issues that arise in Internet-mediated research involving young people with cancer. In addition, few reviews have explored how these ethical issues influence study methodology.

2.1.1 Aim and objectives

There are two aims to this systematic review. First, to describe the types of Internet-mediated research methodology conducted involving young people (aged 13-25) with cancer. Second, to review and describe ethical issues described in the reporting of these studies.

2.2 Methodology

2.2.1 Eligibility criteria

2.2.1.1 Study criteria

All included studies were published after 2007. This year was selected as almost 50% of Americans had broadband access at home (Horrigan, 2009) and 51% of UK households had home access to broadband (ONS, 2008). All studies were required to use an Internet-mediated platform as either the main (e.g. online focus groups) or underlying technology (e.g. mobile-based technology). Additionally, studies were included if they used an Internet of Things technology. The Internet of Things is the colloquial term used to describe objects (e.g. watches, glasses) communicating with other objects (e.g. smartphones, laptops) and the Internet via wireless connections (Whitmore et al., 2015).

All studies were required to have gone through peer-review, therefore theses, dissertations, conference proceedings, and abstract-only texts were excluded. Other systematic reviews were also excluded, although their reference sections were searched for additional articles. All studies were required to have been published in English. There were no other restrictions on study characteristics.

2.2.1.2 Participant criteria

Studies were included if the participants were aged between 13 to 25 years old, or if the median age of participants fell within this range. This age range was selected as it is reflective of current clinical practice of treating teenage and young adult patients as a group to aid their transition from paediatric to adult oncology services (Kelly, 2008). Participants were required to be in active treatment or remission. Screening and prevention studies were excluded. Studies which involved patients and family members and/or caregivers were included; however, studies aimed exclusively at family members and/or caregivers were excluded.

2.2.1.3 Article search and screening

The search terms were developed in consultation with a health librarian. Four databases were searched: PubMed, Web of Science and Embase and PsychInfo (through Ovid). The search terms used can be found in appendix A. The first and second author independently screened all titles and abstracts using a standardised screening protocol. Titles and abstracts not fulfilling the eligibility criteria were excluded.
The first author retrieved the full texts of the eligible articles and they were hand searched for further references. In addition, the first author searched systematic reviews which were retrieved in the original search for any further relevant articles.

2.2.1.4 Data extraction and analysis

Due to the heterogeneous nature of the studies, it was decided that a meta-analytical approach to synthesis would not be appropriate. Furthermore, the lack of randomised controlled trials and the lack quantitate treatment effect meant that a narrative synthesis was deemed more appropriate (DerSimonian and Laird, 1986; Feldman et al., 2004). We adopted a narrative approach, meaning that the synthesis relied on the use of text to summarise and explain the findings (Popay et al., 2006). A key feature of narrative synthesis is the emphasis on a text-based approach which aims to ‘tell a story’ of the findings from the studies.

To ensure that the data was reliability extracted from each study, a standardised extraction form was developed. It was developed by the first author and piloted on five papers by the first and second author. Minor changes were made to the extraction form post-pilot. The information extracted from each eligible paper related to study setting, sample characteristics, ethics, methodology, result, patient engagement and stakeholder

involvement (see appendix B). All data was extracted by the first author and a pool of 20% was extracted by the second author to ensure consistency of extraction. Following the pilot, the first author extracted information from all the eligible studies using the standardised extraction form. The first author then synthesised the extracted data into a cohesive narrative by exploring the relationship and themes between and within the studies. The synthesized narrative was then examined in the wider context of ethical issues associated with research involving young people with cancer. The studies included in the final review were not critically appraised for the risk of bias. As a result, no studies were excluded at this stage of the analysis.

2.3. Results

The systematic review protocol was registered with International Prospective Register of Systematic Reviews (PROSPERO) on October 7th 2015 (registration number: CRD42015026295).

2.3.1 Study selection

The search was carried out on September 3rd 2015. A total of 3,060 articles were identified, and after removing duplicates (n = 66), 2,994 titles and abstracts were screened by the first and second author. Of these, 2,972 articles were identified as not meeting the inclusion criteria and excluded from further analysis. Twenty-two full-text records were included following the first round of screening. These and the excluded systematic reviews (Abogunrin and Martin, 2013; Brier et al., 2015; Bender et al., 2015; Madhavan et al., 2011; Mo et al., 2009; Scott et al., 2003; Valsecchi et al., 2008) were hand searched for any remaining references. Thirty-two articles were identified from the hand search as fulfilling the eligibility criteria. Therefore a total of 54 full-text records were assessed for inclusion in the systematic review. After closer examination 43 papers were excluded due to i) insufficient information regarding participant age (n = 7), ii) not being primary research (n = 10), iii) not containing an Internet-mediated methodology (n = 12), iv) primary clinical population did not have a cancer diagnosis (n = 7), v) participants being too old (n = 5) or vi) too young (n = 2). Eleven papers were included in the final synthesis (see flow diagram in figure 1).

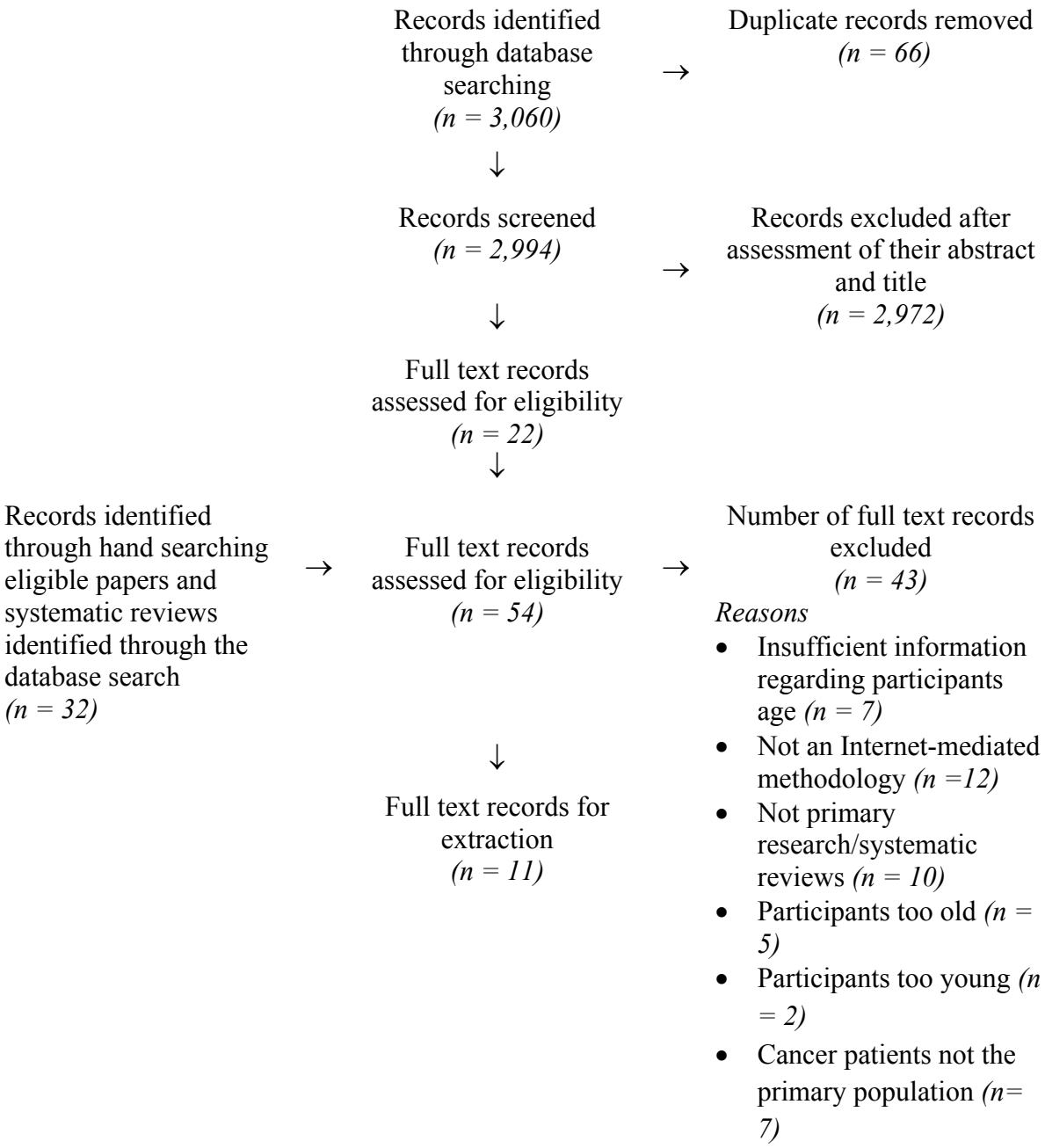

Figure 1: Adapted PRISMA flow diagram illustrating the article selection process.

2.3.2 Sample characteristics

Three of the studies focused on cancer survivors, four on cancer patients during treatment and two studies recruited a mixed population. The remaining two studies did not report any demographic information. Table 1 outlines the diagnoses and age ranges of each of these studies grouped per the study methodologies identified.

All studies excluded patients with cognitive impairments and those who did not have a high proficiency in the native language (English, Spanish or Dutch). None of the studies included in this review recruited patients who were in the palliative stage of their illness trajectory.

Table 1: Demographic characteristics of the studies.

Methodology	Authors	Participant type	Diagnosis	Age range	Median age	Ethnicity
Website-based interventions	Ewing et al., (2009)	Patients in active treatments and siblings	Not reported	Not reported but in range	Not reported but in range	Not reported
	Huang et al., (2014)	Survivors	Acute lymphoblastic leukaemia (ALL)	10-16 years	Fit4Life group 13 years Control 13 years.	Whole cohort n = 34 Hispanic n = 3 White n = 1 African American Fit4Life group n = 17 Hispanic n = 2 White Control n = 17 Hispanic n = 1 White n = 1 African American
	McLaughlin et al., (2012)	Survivors	Not reported	18-29 years	Not reported but in range.	n = 12 Hispanic n = 1 Asian/Pacific Islander n = 1 Native American

Methodology	Authors	Participant type	Diagnosis	Age range	Median age	Ethnicity
Online focus groups	Nilsson et al., (2014)	Survivors	n = 31 central nervous system (CNS) tumours n = 32 Hodgkin's lymphoma n = 20 Rhabdomyosarcoma n = 19 neuroblastoma n = 18 osteosarcoma n = 14 Ewing/Ewing-like sarcoma	16-24 years	21 years.	Not reported
	Zwaanswijk et al., (2007)	Mix of parents, patients in active treatment and survivors	Patients n=3 leukaemia n=2 brain tumours n=1 lymphoma n=1 soft tissue sarcoma Survivors n=10 leukaemia n=2 brain tumours n=3 lymphoma n=1 bone tumour	Patients 8-17 years old Survivors 8-17 years at diagnosis	Patients 11.6 years Survivors 15.5 years	Not reported.

Methodology	Authors	Participant type	Diagnosis	Age range	Median age	Ethnicity
Clinical feasibility studies of symptom capture tools	Baggott et al., (2012)	Patients in active treatment	n = 6 leukaemia/lymphoma n = 3 bone tumour n = 1 sarcoma/other	13-21 years	18.2 years	n= 3 Hispanic white n = 1 non-Hispanic white n = 1 African American n = 5 other/not specified
	Macpherson et al., (2014)	Patients in active treatment	n = 10 ALL n = 5 Acute myeloid leukaemia (AML) n = 16 Hodgkin lymphoma n = 6 Non-Hodgkin lymphoma n = 21 sarcoma n = 2 brain tumour n = 12 solid tumour NOS	13-29 years	Adolescents 15 years Young adults 21.5 years	n = 57 White/Non-Hispanic n = 4 Hispanic n = 3 Asian/Pacific Islander n = 7 African American n = 1 other/not specified

Methodology	Authors	Participant type	Diagnosis	Age range	Median age	Ethnicity
	Stinson et al., (2013)	Patients in active treatment	Whole cohort n = 17 ALL n = 5 AML n = 5 Ewing's sarcoma n = 5 Non-Hodgkin's Lymphoma n = 7 osteosarcoma n = 3 Rhabdomyosarcoma n= 5 diagnosis not specified	8-19 years old	Whole cohort 13 years old. Phase 1a 13.9 years Phase 1b 13.4 years Phase 2 13.2 years	Not reported
	Wu et al., (2011)	Patients in active treatment	n=13 leukaemia n=11 lymphoma n=10 sarcoma n=4 brain tumour n=2 diagnosis not specified	13-20 years	Not reported	n = 30 White n = 1 Asian n = 2 Native Hawaiian n = 3 African American n = 2 American Indian n = 2 ethnicity not specified

Methodology	Authors	Participant type	Diagnosis	Age range	Median age	Ethnicity
Online discussion forums	Donovan et al., (2014)	Not reported	Not reported	Not reported but in range	Not reported but in range	Not reported
	Elwell et al., (2011)	Not reported	Not reported	Not reported but in range	Not reported but in range	Not reported

2.3.3 Summary of studies

From the eleven papers, we identified four Internet-mediated methodologies: website-based interventions, online focus groups, clinical feasibility studies of symptom capture tools and online discussion forums. Table 2 summarises the study characteristics of the 11 studies.

Table 2: Study characteristics.

Methodology	Authors	Aim	Procedure	Outcome measure(s)
Website-based interventions	Ewing et al., (2009)	The aim of the study was to investigate website utilization among families of young people with cancer.	Participants were enrolled onto the website and assigned passwords and usernames. After enrolment participants were offered an in-home training session where research staff provided instructions including e.g. how the participants should log onto the website. If required, families were provided with laptops and Internet access for the duration of the study.	Website utilisation • Number of times participants logged onto the website • what sections of the webiste participants visited. The researchers also conducted post-intervention telephone interviews with carers to evaluate barriers to website use.
	Huang et al., (2014)	The aim of the study was to test a website-based weight management intervention among ALL survivors.	The experimental group received a six-month website-based weight management intervention with telephone support (including calorie reduction goals, and activity goals). The control group received monthly informational leaflets relating to nutrition, physical activity and genera health, in addition to telephone support from health coach during the first study month. In study month 2 to 4 the control group received monthly calls from the health coach only	Primary outcome • weight change • BMI Secondary outcomes • Behavioural measurements (e.g. physical activity level, calorie intake), • physiological measurements (e.g. blood pressure, blood glucose levels) • psychological measurements (e.g. negative mood).

Methodology	Authors	Aim	Procedure	Outcome measure(s)
	McLaughlin et al., (2012)	The aim of the study was to explore how self-rated social support influenced use of a social networking site.	Participants were asked to complete a battery of social support and QoL measures. After completing the measures, participants were given access to a social networking site. The log files automatically collected records of the participants did on the site while logged in.	The study had seven outcome measures which were correlated with participants' log files: • social support, • bridging social capital, • bonding social capital, • depressive symptoms, • survivorship self-efficacy, • family interaction • QoL
Online focus groups	Nilsson et al., (2014)	The aim of the study was to explored fertility issues among cancer survivors.	Participants were invited to participate in closed online synchronous focus groups.	Participant discourse on fertility issues
	Zwaanswijk et al., (2007)	The study explored participants' preferences regarding the information exchange and decision making with the healthcare professionals among parents and patients.	Participants were invited to participate in closed online asynchronous focus groups.	Participant discourse on information exchange and decision-making.

Methodology	Authors	Aim	Procedure	Outcome measure(s)
Clinical feasibility studies of symptom capture tools	Baggott et al., (2012)	The study aimed to explore the feasibility and acceptability of a mobile-based symptom capture e-diary.	Participants were asked to record daily symptom ratings on an 8 GB iPhone 3GS and pinpointed the location of their pain on a body diagram.	Feasibility was measured by: • dependability of the application assessed by recording system malfunctions. • Reasons for missing data recorded by research staff. • Adherence which was measured by the number of missing entries. exceeded 90% across the 21-day study period. • Usefulness to researchers and clinicians, measured by exploring the content of the diaries. Acceptability was explored in exit interviews with participants.

Methodology	Authors	Aim	Procedure	Outcome measure(s)
	Macpherson et al., (2014)	The study investigated the feasibility and acceptability of a tablet-based symptom capture e-diary.	Participants completed the C-SCAT 24-96 hours after a chemotherapy dose in a chemotherapy cycle. The C-SCAT was designed to be completed in one session. Participants were instructed to select from a pre-existing list including symptoms such as feeling drowsy and pain. Alternatively, participants could enter free text for symptoms listed. In addition to symptom selection, participants also described attempted self-management strategies as a result of these symptoms and the effect of the symptoms on daily activities. Participants were then asked to connect symptoms that were related by drawing arrows between the symptoms and thereby creating a visual representation of their symptom experience. The participants were presented with the image after completing the C-SCAT.	Feasibility was measured through: • Rates of completion, • Reasons for non-adherence, • Number of sessions need to complete the C-SCAT, • Perceived accuracy of the symptom experience image, • Required completion time, • Observable fatigue/frustration and technical problems. Acceptability was evaluated through a 19-item questionnaire, which addressed ease of use.
	Stinson et al., (2013)	The study aimed to develop and test the feasibility of a symptom capture tool.	The participants were allocated to two development phases and one clinical feasibility testing phase. During the development phases (focus groups were conducted with adolescents with cancer using low and high fidelity copies of the application.	Clinical feasibility • Compliance, • perceived satisfaction. Satisfaction The Pain Squad Evaluation Questionnaire contained multiple 4-

Methodology	Authors	Aim	Procedure	Outcome measure(s)
			During the second phase, a new group of adolescents were asked to: • rate pain intensity, • describe location, • duration of the pain, • any pharmacological and non-pharmacological coping strategies employed in response to the pain. While rating their pain, participants played the role of a member of a special investigative unit "Pain Squad". Each completed entry built up to a reward, and three consecutive reports earned the participant a rank promotion. For each promotion participants were shown a badge and a short video clips featuring actors from popular Canadian police TV shows. The members of the research team offered technical assistance over the telephone where required.	point Likert scales where the participants were asked to rate likes and dislikes with the application.

Methodology	Authors	Aim	Procedure	Outcome measure(s)
	Wu et al., (2011)	The study aimed to test the feasibility of the Electronic Self-report Assessment-Cancer Adolescent Form (ESRA-C AF).	Participants were asked to complete the ESRA-C AF in private conference rooms in the presence of their parents and a member of the research team	Feasibility was measured in four ways: • Data completeness, • The acceptability scale (a scale of 1 (low) to 5 (high)), • Time taken to complete the questionnaires, • Assistance required to complete the questionnaires.
Online discussion forums	Donovan et al., (2014)	The study aimed to explore the prevalence of different types support and the prevalence of the different types of support in response to uncertainty in written conversations from an online forum.	The authors randomlly selected 510 message threads from the online forum.	The authors coded the data using four categories; • Informational support • Emotional support • Esteem support • Network support
	Elwell et al., (2011)	The study aimed to explore how information and emotional support was expressed in written conversations from an online forum.	The authors analysed 393 randomlly messages from “Teens Living with Cancer”, an online community with posters from all over the world.	The authors coded for two types of support; • Informational support • Emotional support

2.3.3.1 Website-based interventions

Three of the studies were website-based interventions (Huang et al., 2014; Ewing et al., 2009; McLaughlin et al., 2012). Two of the three online interventions were aimed at survivors (Huang et al., 2014; McLaughlin et al., 2012) while one intervention was aimed at families of young people with cancer (Ewing et al., 2009).

Huang et al (2014) conducted a psychological randomised controlled trial (RCT) to reduce weight among 38 acute lymphoblastic leukaemia survivors (15 males and 23 females, aged 10-16 years). Participants were recruited during attendance at an outpatient clinic and from an electronic database. Half (n = 19) of the 38 participants were allocated to the intervention and the remaining 19 participants were allocated to the control group. The authors found significant group differences in weight maintenance, negative mood and physical activity, with older participants (defined as participants aged 14 years or older) allocated to the intervention more likely to maintain their weight. Participants receiving the intervention also reported significantly lower negative mood scores and increased physical activity. No other significant differences were reported.

Ewing et al., (2009) described the utilisation of an informational website which was part of a larger online intervention. The intervention offered support and information to families of young people with cancer. Of the families that consented to participation in the larger study, two-thirds were randomly assigned access to the study website. Of 21 enrolled families six had at least one family member who used the wesbite during the study period. In total eleven participants (of 51 consented participants) used the website over the six month study period. Of these eleven participants five were caregivers (1 male and 4 females), four were patients (2 males and 2 females, aged 8-13 years) and two were siblings of patients (2 females, aged 13-17 years). The parent discussion group had the largest number of page viewings (88 viewings), followed by the teen sibling discussion group (73 viewings) and the teen patient discussion (44 viewings). The child patient and child sibling discussion groups had the lowest number of page viewings (7 and 5 page viewings respectively). Four website features were most frequently visited: the discussion forums, “Common areas of concern” (78 page viewings), “Previously asked questions” (66 page viewings) and “Connect to Coping” (60 page viewings).

In the post-study interviews caregivers reported five main barriers to using the website: unfamiliarity with computers, being too busy, limited hospital Internet access,

sufficient healthcare staff support and preference for face-to-face interaction. When asked about barriers for use among young people with cancer, caregivers cited unwillingness to focus on their loved one's illness, sufficient offline support, too ill and using computer for other activities (e.g. gaming) as possible barriers. As a result of these findings Ewing et al. (2009) outlined strategies to address computer illiteracy (through training).

McLaughlin et al. (2012) described a study exploring use of a social networking intervention titled LIFECommunity by young cancer survivors over a six-month period. Participants were identified through a hospital-based cancer registry and contacted via mail. Interested participants were asked to return a card indicating their interest and were then contacted by the study team. The website was developed specifically for research on an open source-based platform. Participants were provided with passwords and usernames, meaning that membership was closed to other users.

The authors found that bridging social capital was positively associated with LIFECommunity participation and social support was negatively correlated with site participation. Bridging social capital can be defined as distant and weak connections between individuals (Office for National Statistics, 2016). The authors found that participants with high levels of offline social support (such as e.g. family support) did not participate with LIFECommunity to the same extent as participants who reported low offline social support. Furthermore, the authors found that participants who reported a high level of family interaction interacted less with the social networking site compared to participants who reported low levels of family interactions. Additionally, the authors found that participants with low depression scores, low self-efficacy scores and low quality of life (QoL) scores had higher overall sites participation compared to participants who scored high on these three measures.

2.3.3.2 Online focus groups

Two of the studies reported the result of online focus groups (Nilsson et al., 2014, Zwaanswijk et al., 2007).

Nilsson et al., (2014) conducted synchronous focus groups exploring concerns over fertility among young cancer survivors (n = 134). Eligible participants were identified and recruited through a national cancer registry. The results of the study were the identification of five themes. The first theme was "risk of infertility affects wellbeing". This theme centred on how the risk of infertility influenced everyday wellbeing and how their perceived risk of infertility influenced their everyday wellbeing.

A second theme the authors identified was “dealing with possible infertility”. This theme described different coping strategies used by participants in dealing with possible infertility, ranging from assuming infertility to active investigation. The third theme was “disclosure of possible infertility is a challenge”. This theme captured concern over discussing fertility with a partner primarily due to concerns about the relationship ending. The fourth theme related to the “heredity” of the cancer. It cantered on the perceived risk of heredity and the resulting reluctance to have biological children. The final theme was “parenthood” and it explored reasons for considering adoption as a way of having children due to the perceived physical and psychological cost of pregnancy. The online focus group was conducted on a platform developed by third-party consultants. The authors did not report any details of the website security structure.

Zwaanswijk et al., (2007) conducted an online asynchronous focus groups with 11 parents of patients and survivors, seven patients and 18 survivors. Family members were able to participate individually, meaning that a parent and a young person from the same family did not necessarily participate in the study. Patients still in treatment were recruited from one of two recruitment sites, a tertiary care setting or outpatient oncology service. Eligible participants in the tertiary care centre were approached first by a nurse and invited to participate. In the oncology service, eligible participants were approached directly by a nurse. Survivors were identified from a medical database attached to both wards. They were approached through an invitation letter from the head of Department of Paediatric Hemato-Oncology.

The authors identified three themes from the focus group discussions, “preferences concerning interpersonal relationships”, “preferences concerning information exchange”, and “preferences concerning participation in the decision-making process”. “Preferences concerning interpersonal relationships” centred on the relationship between clinicians and participants. All participants valued an honest communication with the clinicians, with both patients and parents trusting a clinician’s expertise. They also expressed a preference for continuity of care (e.g. consultations with the same clinician) and they did not want every interaction with their clinician to focus on their illness.

“Preferences concerning information exchange” captured all participants’ wish that young patients should be aware of their illness, although the extent of awareness should be tailored to the young person’s ability and need. However, opinion was divided among patients and survivors as to whether the patient should always be present during

consultations. A young person's presence/absence from consultations was dependent on cognitive ability and sociocultural norms.

The third theme focused on the decision-making process. A majority of participants expressed a preference for a collaborative approach to decision-making, although some survivors and patients preferred a passive decision-making role. While some survivors and patients emphasised that the final decision should lie with them, they acknowledged that contextual factors may limit their role. These contextual factors may include age, stage of illness, side effects of treatment or limited knowledge.

The focus groups were conducted on a password secured website, and all participants were issued with unique usernames and passwords. Other than this information, no other details regarding the website security structure was reported. Participants were asked not to mention their own names, addresses or the names of their health care providers.

2.3.3.3 Clinical feasibility studies of symptom capture tools

Four studies explored the feasibility of using mobile-based platforms to collect real-time physiological and psychological symptom data from patients in active treatment (Baggott et al., 2012; Macpherson et al., 2014; Stinson et al., 2013; Wu et al., 2011).

Baggott et al., (2012) conducted a feasibility study of a mobile-based symptom capture e-diary used daily for 21 days. The goal of the study was to determine the suitability of using the e-diary to collect symptoms relating to pain, nausea, vomiting, fatigue, and sleep quality. Ten cancer patients, on active treatment were recruited from a tertiary care setting.

The authors reported high feasibility, with limited technical issues reported and adherence exceeding 90% across the 21-day study period. While the exact content of the diaries was not reported, the authors reported that the eDiary could capture symptom variability over time and symptom variability across participants. In addition, some patients recorded novel symptoms and moods. The final measure was acceptability which was explored in exit interviews with participants. Overall, participants described the application as easy to use, and tended to use positive descriptors when describing the application. Some participants noted that some features were difficult to use. For instance, a participant with mild visual difficulties struggled to read the text on the application.

Macpherson et al., (2014) tested the Computerized Symptom Capture Tool (C-SCAT), a tablet-based iPad application exploring symptoms and symptom clusters in

young people with cancer. After being identified by a member of the research team, 72 participants with a diagnosis of cancer were recruited from in-patient and out-patient settings by a clinician.

The authors found a high degree of feasibility and acceptability. All participants completed the symptom diary in one setting with infrequent technical malfunction. A session lasted on average 25 minutes (SD = 17, range = 2-83 minutes). Furthermore, participants needed minimal help from the research team in completing the C-SCAT and most participants did not display any observable fatigue/frustration. A majority of participants (74%) reported that the final image was an accurate representative of their symptom experience.

Stinson et al., (2013) described the development and feasibility testing of a symptom capture tool for young people with cancer titled *Pain Squad*. Forty-seven patients in active treatment were recruited from a tertiary haematology/oncology care centre. The application had been adapted from a juvenile idiopathic arthritis eDiary and uses a gamified structure to engage young people in daily use of the tool. Participants in the low-fidelity design phase identified four main changes to the original application, including the need to change the theme of the gamified component from a detective agency investigating pain cases to a law enforcement officer. Other changes identified during the low fidelity design phase included clarification of content and changes to the usability of the application. During the high-fidelity design phase another group of participants were presented with a prototype of the application. There was general endorsement of the application, and gamified features were considered appealing.

During the clinical feasibility testing (phase two) fourteen young people were asked to complete a twice-daily pain report for two weeks. Participants were given an iPhone 4S for the duration of the study to complete their participation. During the clinical testing phase the research team had access to the daily reports so they could monitor and respond to potential clinical emergencies. In addition to tracking pain ratings and treatments, the research team would receive an alert if participants rated their pain as moderate-to-severe during two consecutive entries.

The authors reported a mean compliance rate of 81% (SD = 22%). Two participants had low compliance (explained as forgetfulness and medical emergencies). After exclusion of these two participants the average compliance rate increased to 88% (SD = 8%). There were no significant differences in compliance between morning versus afternoon ratings, weekday versus weekend ratings or between study week one and study

week two. In addition, compliance was not dependent on participant characteristics such as gender or initial treatment location (outpatient versus inpatient setting). The authors reported a high level of satisfaction, although 14% found the application difficult to complete and one participant noted that completing the application interfered with other daily activates.

Wu et al., (2011) explored the feasibility of using the Electronic Self-report Assessment-Cancer Adolescent Form (ESRA-C AF) in an outpatient setting. The ESRA-C AF is a battery of netbook-based QoL and symptom questionnaires. The questionnaires addressed health related QoL in young cancer survivors, cancer-specific symptoms, resilience and questionnaire acceptability. In addition to the four questionnaires participants were able to use an open text box to address the two of the most important concerns or issues the researchers should address or anything the participants felt was not covered by the questionnaires.

Data completeness ranged from 99.3% to 100% and 25% of the participants used optional text box to elaborate on their QoL ratings or ask questions. Overall, participants' acceptability score showed an overall average score of 4.18 (SD = 0.91). Average completion time was 30 minutes. Participants requiring more time cited issues relating to the use of the symptom capture tool (e.g. issues with the wireless connection), taking a break for routine clinical care such as a break to have a blood draw. In addition, the authors identified issues with the internal validity of the scale; approximately 67% of participants required clarification of the word "resilience", suggesting that the ESRA-C AF may need modification to increase usability.

2.3.3.4 Online discussion forums

The remaining two studies (Donovan et al., 2014; Elwell et al., 2011) analysed conversation data from social media platforms used by young cancer patients and survivors.

Donovan et al., (2014) explored the types of peer and social support offerred by cancer survivors to others online in response to medical, social and personal uncertainty. The anonymous forum the authors used to sample their messages was open to adolecents with any type of cancer, and the authors reported that the forum had world wide participation. To post members had to register and messages could only be accessed and read with a username and password.

Types of support displayed in the posts on this website were informational support, emotional support, esteem support and network support. Replies frequently contained informational support expressed through sharing their own stories. Emotional support (expressed through empathy) was the second most used type of support. Esteem support was found to be expressed through validation of the poster's (the individual who posted the original message) coping strategies. Network support was present in 24% of replies and tended to contain a sense of belonging. The authors also found that different types of social support tended to co-occur in response to different types of uncertainty (i.e. informational, emotional and network support tended to be used more frequently in reponses to posts containing social uncertainty compared to medical uncertainty).

Elwell et al., (2011) explored how informational and emotional support was expressed among TYA cancer patients and cancer survivors. The authors found informational support was communicated through expert advice (either from an "expert patient" or healthcare professional) personal dislosure and personal experiences (e.g. links to media such as video of treatments). Informational support was often given as a response to uncertainties (e.g. as a reponse to questions about treatment side effects, body image, effect of cancer on ability to live a normal life). Emotional support was often expressed when a poster was coping poorly with their diagnosis through mentioning of God and praying or encouraging positive thinking.

2.3.4 Ethical issues

A majority of the papers did not give special attention outside of the method section of their articles to the ethical issues encountered over the course of setting up or completing their study. A summary of the ethical issues that arose during the course of the studies and the remedies to these issues are summarised in table 3.

Table 3*:* Ethical issues arising in Internet-mediated research.

Methodology	Ethical issue	How the ethical issue arose	Remediation
Website-based interventions	Confidentiality	Participant access	• Participants can be issued with unique usernames and passwords.
	Prevention of harm	Preventing harm and distress	• Drafting of safety management protocols containing a clear procedure for both participant and researcher conduct during the study. • Participants can be advised not to post medical questions as these may not receive a timely reply. • Research team can be notified by programmed alerts when participants posted content. • Researchers can be provided with a summary of daily reports.
Online focus groups	Privacy	Access to focus group website	• Participants can be issued with unique access codes.
	Anonymity	Maintaining participant anonymity	• Participants can select their own screen alias, but the authors can elect to publish fictional names and approximate ages. • Participants can be asked not to mention identifiable information.
	Moderation/prevention of harm	Monitoring of user-generated content	Members of the research team can moderate the discussion and/or posts.

Methodology	Ethical issue	How the ethical issue arose	Remediation
Clinical feasibility studies of symptom capture tools	Privacy	• Providing sensitive information • Secure data storage	• Participants can be asked to provide the data in a private room. • The data can be stored in a password-protected cloud account and be transferred via an encrypted connection. • The application can contain a secure database on the device.
	Prevention of harm	Monitoring of user-generated content	• The research team can draft safety management protocols. • Researchers can receive an alert if participants submitted moderate-to-severe ratings.
Online discussion forums	Consent seeking	Participants did not actively provide consent prior to the study commencing.	• The authors can seek permission from the site administrators. • Some guidelines (e.g. the guidelines from the British Psychological Society) state that consent does not need to be obtained if the online forum does not require a subscription.

2.3.4.1 Privacy

Privacy was discussed in all but one of the research categories (online discussion forums). It was never overtly defined in any of the research studies included in this review but it seems to, in this context, apply to protection of participant data throughout the participation process. In practice the application of privacy as a concept also differed. For instance, Zwaanswijk el al. (2007) viewed privacy as closer to the maintenance of anonymity. For example, online focus groups ensured privacy of participants by enforcing board rules around what information could be discussed during the study. Zwaanswijk el al. (2007) explicitly stated that this measure was taken to ensure privacy and anonymity. They asked participants not to disclose identifiable information. However, elaboration on what constituted "identifiable" information was not given.

In contrast, Nilsson et al. (2014) also reported anonymity and privacy as a concern. They provided little information on how they approached these concerns and in registering for their websites they allowed participants to choose their own screen name, which could be either an alias or their real name. Nilsson et al. (2014) did not clarify how participant anonymity was maintained. Further steps were also taken by two websites based interventions (Ewing et al. (2009), and McLaughlin et al. (2012) and one online focus group Nilsson et al. (2014) to ensure privacy by issuing participants with usernames and passwords meaning they could not be identified offline by others in the study.

Other studies viewed privacy as more akin to confidentiality. Confidentiality can be defined as information shared within a research setting or within the exchange between a researcher and a participant (Jackson et al., 2014). Website-based interventions and clinical feasibility studies of symptom capture tools mostly ensured privacy of participation by removing participants from the public space of the clinic waiting room for their participation (Macpherson et al., 2014). However, in the study by Wu et al., (2011) parents were also present for participation, so privacy within the family group was not achieved and may have influenced the results.

2.3.4.2 Data security

Another salient ethical issue that arose in the reporting of some of these studies was data security. All studies who mentioned this focused exclusively on hardware and software structures to ensure data protection. Of the studies that transmitted information between devices only three studies mentioned steps taken to ensure data protection

(Stinson et al., 2013, Macpherson et al., 2014, Baggott et al., 2012) and only two provided sufficient technical information for the reader to determine the level of encryption during transmission (Stinson et al., 2013, Macpherson et al., 2014). These same studies also cited steps taken to ensure safe storage of data. Data held by Macpherson et al., (2014) was stored on a password-protected Amazon Simple Storage Service (S3) account and it was transmitted via an encrypted connection.

Stinson et al., (2013) stored their pain rating scores on a SQLLite database on the iPhone application when the phone was offline. When the phone was connected to the Internet the data was transmitted over a Secure Socket Layer (SSL) connection. The authors mentioned that the receiving server was located at the tertiary care setting. The server was behind a secure firewall, and a username and password was required to access the data. Neither of the papers provided any other details regarding the measurers taken to ensure the level of encryption. Baggott et al., (2012) also described their procedures for safe transmission and delivery of data, by stating that the participant data was delivered to a secure website. However, they did not provide details regarding the level and type of encryption.

2.3.4.3 Protection of participants from harm

Protection of participants from harm was dealt with in studies by reviewing user generated content prior to allowing posts to become visible to other participants. Studies cited this process as serving one of two functions, moderation of posts to ensure courtesy to others on the board or to determine if there was a clinical need to intervene and engage with participants whose physical or psychological health was at risk. However, this was only described for four studies (Zwaanswijk et al., 2007, Nilsson et al., 2014, Stinson et al., 2013, McLaughlin et al., 2012) out of 7 studies that had user generated content. Further, of the three who did review content prior to posting, it is unclear how often they needed to moderate or provide clinical advice. Overall, this finding would seem to indicate that patient safety was a concern for methodologies with user generated feature, especially when the user generated clinical content.

2.3.4.4 Consent

Consent seeking only seemed to be raised as a salient issue for online discussion forums. Seeking consent during analysis of openly accessible, pre-existing online forums

is considered unnecessary by a variety of ethical guidance on the subject (Markham and Buchanan, 2012; Rodham and Gavin, 2006, Henderson et al., 2012). The driving force behind this argument is the view that conversations which take place on a public forum are no different to conversations which take place in any public place online. Observations of these interactions are subject to the same ethical constraints as offline observations in public spaces (Zimmer, 2010). In this context researchers may have a responsibility to ensure anonymity of poster's comments including taking measures to disguise quotes and avoiding using verbatim text so as to avoid comments being traced back to a website or participant using common search engines (Rodham and Gavin, 2006). From within this ethical framework Donovan et al. (2014) and Elwell et al., (2011) did not request consent from their participants and only one of them (Elwell et al., 2011) cited the relevant guidance (which in this case was the guidance developed by the British Psychological Society) which allowed them to conduct their study without participant consent.

When a subscription is required, as in the case of Donovan et al. (2014), the choice not to seek active consent becomes more controversial (McNamara, 2013). This controversy is rooted in the inaccessible nature of these posts without a subscription, and the privacy that users therefore may expect (Hudson and Bruckman, 2004). Donovan et al. (2014) analysed posts on an online forum which required participants to sign up to terms and conditions agreeing that their posts will be accessible for researchers to read in an agreement termed a "click-wrap agreement". Despite using negotiated consent (Kennedy, 2008) through a click-wrap agreement, steps still need to be taken by researchers to ensure protection of identity of posters to these websites including not reporting usernames of posters, not quoting verbatim quotes, ensuring that quotes which are reported cannot be traced back to the website on which they were posted (Markham and Buchanan, 2012).

2.4 Discussion

In this systematic review we have first explored the types of Internet-mediated methodologies currently used in research involving young people with cancer. Second, we identified and described ethical issues that can occur in this type of research. Eleven papers using Internet-mediated technology in research involving young people with cancer were identified. We categorised the methodologies into four different approaches:

website-based interventions, online focus groups, clinical feasibility studies of symptom capture tools and analysis of conversational data from online discussion forums.

Nine of the papers did not give special attention outside of the method section of their articles to the ethical issues which arose in the conduct of their research. One reason for this finding may be the relative rarity of issues which appeared over the course of the research. Another view may be that this systematic review has found what previous research has also hypothesised, researchers in e-health contexts rarely report on the issues that they have encountered in getting ethical approval for their Internet-mediated studies (Henderson et al., 2013). Regardless, the results of this review suggest that at least in the process of having these studies peer reviewed, there may be a disconnect between the effort currently expended in the generation of ethical guidance specifically for Internet-mediated research and the relatively low frequency where this ethical regulation and safeguards need to be used and be reported upon.

Predictably approaches to the seeking of consent differed between studies, with observational studies of online forums taking a different approach to that of the other studies in this review. Full discussion of the validity of the approach of not seeking consent in the conduct of these research projects is outside the scope of this review (see Shapiro and Ossorio, 2013; Henderson et al. 2012; Markham and Buchanan, 2012). However, the studies who did not seek consent, only one cited an ethical guidance paper which allowed them permission to do so (Elwell et al., 2011). While approaching consent in this way is now seen as the most pragmatic approach to the seeking of consent in Internet-mediated research of this sort, lack of full and proper citation of the relevant papers to support this approach would seem to indicate that it is more of an ingrained approach than one which needs to be continually justified during the peer review process.

Studies also differed on what constituted participant harm and the methods that should be undertaken to protect participants from harm. Again participant harm is a concept that is rarely defined and there is very little consensus within the literature as to what it means (Kuhlau et al., 2008). Henderson et al., (2012) listed a number of approaches to reduction of harm using procedures common to both online and offline methodologies (e.g. creating critical incidents procedures). However, there was not sufficient detail in the reporting of the studies in this review to determine what if any steps were in place for the menu of hypothetical instances of participant harm which may have arisen in the conduct of these projects.

Three groups of participants were systematically excluded from the studies presented here: those with cognitive impairments, those with lower language skills and those receiving palliative care. These exclusions are problematic as they may mean a large proportion of patients who receive care are systematically being ignored by the research designed to improve the patient experiences and care. Cognitive impairment following cranial radiation, neurosurgery and chemotherapy (e.g. methotrexate, cytarabine) is well-documented among acute lymphoblastic leukaemia (ALL) and brain tumour survivors (Mohrmann et al., 2015). Some studies estimate that 33% of 350,000 of US childhood cancer survivors are affected by cognitive impairment (Castellino et al., 2014). Previous studies have found that ethnic minorities have different healthcare experiences compared to ethnic majority peers (Lyratzopoulos et al., 2012; Saunders et al., 2015; Fazil et al., 2015). Systematic exclusion of those without native languages might disproportionately disadvantage these minorities. Especially as research suggests that ethnic minorities have a higher rate of some malignancies than other ethnic groups (Ward et al., 2004). Previous research has also indicated that parents of children receiving palliative care want to be asked to participate in research studies (Crocker et al. 2014) and palliative services are considered one area in which online technologies could improve patient access to good quality, round the clock care which will improve patient choice with regard to decision-making about care and treatment (Nwosu et al., 2014).

The marriage of research ethics and clinical data protection requirements is seen as one of the final frontiers for transition of this research into standard care (McGuire et al., 2016). Data which is held on the Internet requires further protection to prevent it from being accessible to non-researchers (Nosek et al., 2002). For this reason, common approaches to data storage include password protected devices for storage, holding data on secure servers in institutions and encryption of data. An emerging discussion within this debate is data security and storage during transmission of information from the device to the server. Of the studies that transmitted information between devices only two studies provided sufficient technical information for the reader to determine the level of encryption (Stinson et al., 2013, Macpherson et al., 2014). While the reporting of technical information may be outside the scope of most papers it is important that sufficient detail is provided for the reader to determine whether adequate measures were taken and it may be important during the consent process for a participant to be aware of what measures are being undertaken to ensure the security of their data. Further, for these

studies to make the transition to standard care they have to be compatible with data protection regulation within the healthcare system (e.g. adherence to section 251 within the NHS constitution, Department of Health, 2013) and national and/or international legal frameworks (e.g. European data protection laws, de Terwangne, 2013).

The other nine studies in this review did discuss privacy issues however, privacy tended to be conflated with confidentiality or anonymity. The lack of universal definition for privacy within the online sphere and further how to maintain privacy using different methodologies mean that reviewing these studies was not to review like for like. There is an underlying concern within these findings which also suggests that the conceptualisation of privacy, anonymity and confidentiality are conflated despite being three distinct concepts (Wiles et al., 2006).

There are some limitations of the systematic review. It should be stressed that the authors made the conscious decision not to assess the quality of the included papers. Historically reviewers have used summary scores to differentiate between "high quality studies" and "low quality studies" (Vittal Katikireddi et al., 2015). However, more recently reviewers have moved way from this checklist approach towards a focus on biases associated with different domains. The Cochrane Collaboration emphases the importance of assessing the quality of and bias in any study included in a systematic review. The tool recommended by the Cochrane Collaboration, the Risk of Bias Tool (Higgins et al., 2011), was developed to evaluate randomised controlled trials. Only one of the eleven studies in the current systematic review was a randomised controlled trial, meaning that relaying on the Risk of Bias tool to evaluate the bias associated with the eligible studies would have been inappropriate. Furthermore, the psychometric characteristics associated with many risk of bias tool (including the tool developed by the Cochrane Collaboration) have not been fully described (Hartling et al., 2013). For example, Hartling et al., (2013) assessed the reliability of the Cochrane Risk of Bias tool, and found that there was a degree of variability between the risk assessment.

The issue of assessing quality is contentious within narrative-based studies (Collier and Mahoney, 1996). While tools have been developed for the use within narrative-based studies (e.g. the Critical Appraisal Skills Programme (2016)) there is limited information on the validity and reliability of these tools (Hannes et al., 2010). Cohen and Crabtree (2008) conducted a systematic review of published criteria for good qualitative research and found differences in how concepts of researcher bias, validity and

reliability should be applied to text-based research. The authors found that the differences in how these concepts should be applied and evaluated were related to the theoretical framework different authors grounded their analysis. Cohen and Crabtree (2008) further argued that part of the issue with creating an appraisal tool for qualitative research relates to the wide range of qualitative methods available to researchers, and the lack of a unifying ground between the frameworks (Rolfe, 2006; Sparkes, 2001). Given the lack of consensus on what constitutes a high quality in qualitative studies (Dixon-Woods et al., 2004), none of the studies were assessed. Future studies may want to explore the possibility to critically appraise qualitative studies so that it's possible to asses both qualitative and quantitative studies prior to inclusion in a systematic review analysis.

Another limitation of the systematic review is the use of 2007 as the cut off for study eligibility. It can be argued that the 2007 cut off was arbitrary and it may have excluded otherwise eligible papers. In turn this may have increased the sample size, and it may thereby have enabled us to draw stronger conclusions. The Internet has been used in research since the early 1990s and there is a strong argument that ethical issues may have been discussed to a larger extent in the earlier papers. However, 2007 was in part selected due the level of saturation of home broadband in the UK and the USA. Furthermore, it could be argued that by using an earlier cut off year may lead to a more of review of historical ethical issues. Whether the type of ethical issues associated with Internet-mediated research have changed as the research methodology has matured was outside the scope of the current review. Furthermore, Gosling and Mason (2015) argued that conducting online research can best be described as conducting research on a moving target. The authors argue that with rapid and considerable changes in how individuals interact with and consume Internet content makes it difficult for the research to stay relevant. Gosling and Mason (2015) described that researchers are now faced with content and interfaces (e.g. blogs, vlogs, social networking sites) that did not exist a decade earlier. Within the context of the current study and considering how the target population (i.e. young people) consume web content (e.g. accessing information via smartphones) it can be argued that a later cut off point will capture more relevant content. A cut-off of 2007 was therefore seen as balancing the need for a narrow focus with the need for a comprehensive inclusion of relevant studies.

There are a number of directions for future research arising from this systematic review. First, it could be that there are additional ethical issues that arise in research using

Internet-mediated methodology but that these are identified during the ethical review stage and do not make it into a peer reviewed publication of the results of these studies. Future studies should therefore explore the types of ethical issues that research ethics committees (RECs) identify in Internet-mediated research. Previous research exploring the content of REC documentation has focused on issues involving children (Angell et al., 2010) and adults lacking capacity (Dixon-Woods and Angell, 2009), style (Angell and Dixon-Woods, 2009; Angell et al., 2007; Angell and Dixon-Woods, 2008) and the functions of the REC (Angell et al., 2007). However, limited attention has been given to the types of ethical issues RECs identify in studies using Internet-mediated methodologies. Second, future research may want to explore how researchers, RECs and patients can come together to define some of the ethical concepts mentioned in this systematic review. Particularly if all three stakeholders assign the same importance to the ethical concepts of privacy, anonymity and confidentiality that appears either researchers or peer-reviewers do.

The Internet is an instrument of 21st century health care that is likely to become more and more integral to everyday clinical practice. However, conduct of studies into how Internet technologies should develop to meet the needs of patients rarely report on the ethical constraints on what they can do in their research and without this clarity it will be difficult to determine if we need more or less guidance to continue.

A document analysis of Research Ethics Committee communication regarding Internet-mediated research with young people (aged 0 to 25 years) with life-limiting conditions.

3.1 Introduction

Obtaining ethical approval from RECs for research involving young people can be challenging (Wagener et al., 2004; Arnold, 1992). The challenges of involving young people in research relates in part to the historic conceptualisation of young people, in addition to perceived vulnerability and dependency on adults (Tisdall, 2012). Young people have historically been conceptualised as 'human becomings'(Qvortrup, 2009), meaning that young people have not developed the competency associated with the 'gold standard' and the 'end goal' of development; adulthood (Tisdall and Punch, 2012). The definition of young people is therefore related to their status as non-adults, and this vulnerability has underpinned the interaction between young people and researchers for a long time (Gittins, 2004). Young people's perceived vulnerability increases the risk of them being exploited by researchers (Stevens et al., 2010). Previous studies have found that the ethical issues that arise in research involving young people relates to consent, recruitment and the protection of young participants (Angell et al., 2010). Other issues that have been identified have centred on research design and patient privacy in research with young people (Angell et al., 2010). However, there are additional concerns regarding the vulnerability associated with research involving young people with life-limiting conditions (Stevens et al., 2010). These concerns often relate to the sensitive nature of the topic, the emotional burden associated with a life-limiting or life-threatening conditions (Stevens et al., 2010). The concerns accompanying this type of research contributes to a reported difficulty in conducting research with this population and is often expressed through e.g. gate-keeping from RECs (Beecham et al., 2016) and clinicians (Stevens et al., 2010).

Previous literature has explored the content of decision letters. For example, Angell and Dixon-Woods (2009) explored whether RECs identify process errors in decision letters, and found that the REC identified different types of process errors. The authors defined process errors as errors occurring in the paperwork, application process or issues relating to the management of the study which did not have an obvious ethical

basis (Angell and Dixon-Woods, 2009). Angell and Dixon-Woods (2009) argued that the RECs attention to non-ethical process errors is a result of care and attention. Another interpretation offered by the authors was that the REC considers process errors to be a sign of researchers' carelessness or inattention. Angell et al., (2007) examined the ethics/scientific quality boundary in decision letters, and found that RECs did highlight issues relating to scientific quality (e.g. issues around recruitment or methodology) that would have been reviewed during the peer-reviewed process. The authors explained that, while this 'ethical creep' can be seen as the REC overstepping their remit, it could also be that the quality of the science has ethical implications. Both these studies suggest that there is a degree of ethical creep, where the REC may be overstepping their remit.

There is limited consensus on what constitutes good practice for Internet-mediated research (Henderson et al., 2012; Rodham and Gavin, 2006; Hair and Clark, 2007; Zimmer, 2010). For example, researchers have debated how well the concept of privacy and protecting participants' identity translates from offline research to the Internet sphere (Dias, 2003). While both types of research collect identifiable data, Frankel and Siang (1999) noted that it is possible to collect significantly more data online compared to offline. In addition, online data can be linked to a greater extent and quicker in comparison to offline data (Frankel and Siang, 1999; Lindsay et al., 2007; de Montjoye et al., 2015). Zimmer (2010) noted that the unique combination of seemingly trivial information can make participants identifiable in Internet-mediated research.

In contrast to the growing debate in the literature and the effort to draft special guidelines for Internet-mediated research, a recent systematic review (Kempe et al. in preparation) indicated that ethical conflict seems to be relatively rare in practice. Kempe et al., (in preparation) suggested that a reason as to why researchers may not have reported ethical issues in their articles could be that the ethical dilemmas are identified and resolved during the ethical review stage. While previous research exploring the content of REC documentation has focused on issues around involving children (Angell et al., 2010) and adults lacking capacity (Dixon-Woods and Angell, 2009), style (Angell and Dixon-Woods, 2009, Angell et al., 2007, Angell and Dixon-Woods, 2008) and the functions of the REC (Angell et al., 2007) limited attention has been given to the types of ethical issues RECs identify in studies using Internet-mediated methodologies. It is therefore not known what types of ethical issues the RECs identify during the review stage for Internet-mediated research involving young people with life-limiting conditions

nor whether REC refer to the ethical guidelines that have been developed specifically for Internet-mediated research (e.g. the Ethics Guidelines for Internet-mediated Research developed by the British Psychological Society (Hewson and Buchanan, 2013)).

3.1.1 Aim and objectives

The objective of the current study was to analyse the content of decision letters and meeting minutes of two groups of research projects: i) research involving children and young people (under the age of 25 years) with life limiting or life threatening conditions, using internet mediated methodologies and ii) research involving children and young people (under the age of 25 years) with life limiting or life threatening conditions, using non-internet mediated methodologies.

3.2 Methodology

3.2.1 Eligibility criteria

3.2.1.1 Document type

Documents were considered for inclusion if they were generated by a UK-based REC reviewing applications for clinical research. Documents generated by any other type of REC (e.g. a university-based REC) were excluded from this analysis.

Documents considered were both decision letters (summaries of the REC meetings circulated to researchers after the meeting information relating to the discussion, opinion and conditions, if applicable) and meeting minutes for each study were included in the analysis. The opinion is the final REC verdict given by the end of the meeting, which is final until the researcher forms a response (if requested). The opinion which can be favourable, provisional or unfavourable (O'Reilly et al., 2009). A favourable opinion is equivalent to an approval, while a provisional opinion indicates that the REC has identified some ethical issues with the application (O'Reilly et al., 2009). An unfavourable opinion is equivalent to a rejection of the application (O'Reilly et al., 2009).

All included records were given their REC opinion after 2007. This year was selected as 51% of UK households had home access to broadband (Office for National Statistics, 2008) and almost 50% of Americans had broadband access at home (Horrigan, 2009).

3.2.1.2 Population

Studies were included if participants were diagnosed with a life limiting or life threatening condition as defined by the condition's inclusion in the Directory of Life-Limiting Conditions (Hain et al., 2013) if participants were 25 years old or younger, were on active treatment or surveillance following treatment. Studies of caregivers were included, but only if part of the study also focused on the patient for whom they cared (e.g. parent-child dyads).

3.2.1.3 Methodology

Studies were eligible for the group using internet methodologies if any part of the methodology used the Internet as the main (e.g. online surveys, email, online focus groups) or underlying platform (e.g. mobile technologies such as smartphones, social networking sites, social media) in addition to the "Internet of Things" (e.g. Apple watches). The Internet of Things is a colloquial term used to describe objects (e.g. watches, glasses, phones) communicating with other objects and the Internet via wireless connections (Whitmore et al., 2015). Studies employing offline methodologies but fulfilling all other criteria (i.e. age and diagnosis) were included in the comparison group.

3.2.2 Accessing the documents

The search terms (see table 4 and table 5) were derived from a systematic review (Kempe et al, in preparation). These were used to search a database maintained by the Health Research Authority. The database contains individual records of all applications received via the Integrated Research Approval System (IRAS), including title, abstract and REC identification number. The records were screened against the inclusion criteria listed above by the first author and then validated by the second author. Records not fulfilling the eligibility criteria were excluded at this point.

Table 4: Search terms associated population characteristics.

Search terms associated with population
Chronic illness
Teenager
Teenagers
Young adult
Young adults
Life-limiting condition
Life-limiting illness
Life-threatening condition
Young person
Life-threatening illness
Young people
Adolescent
Adolescents

Table 5: Search terms associated methodology characteristics.

Search terms associated with methodology
Online
Internet
internet
Ipad
Mobile applications
Mobile apps
ehealth
Mobile web
Computer
Computers

Search terms associated with methodology
Mobile
cell phone
Smartphone
web
Android
Social networking site
Social networking sites
Text messaging
text messages
e-health
Telemedicine
Laptop
Laptops
IPhone
digital

3.2.3 Analysis

Several researchers argue that written accounts represent patterns of cultural construction (Chambers, 2000) and as such written accounts reflect the settings in which they are created (Hammersley and Atkinson, 1983). By using a combination of thematic analysis and frequency-based content analysis it is possible for researchers to conduct a reflective analysis of documents (Silverman, 2011) to understand the meaning and verify relationships between categories (Altheide, 1987). Previous studies that have studied REC decision letters (e.g. Angell and Dixon-Woods, 2009; Angell et al., 2007; Angell and Dixon-Woods, 2008) have used a combination of manifest content analysis and a thematic analysis of the data. A manifest content analysis focuses on the visible components of the text, and constitutes a relatively shallow interpretation of the data (Downe-Wamboldt, 1992; Kondracki et al., 2002). In contrast, the thematic analysis explores the latent meaning of the data, meaning that the researcher categorizes the data into emerging themes and then interprets the themes in the content of wider research (Braun and Clarke, 2006).

A codebook for analysis was developed *a priori* based on a recent systematic review (outlined in chapter 2) and an exploration of the literature. Decision letters pertaining to offline projects from the Louis Dundas Centre were also accessed and used to inform the development of the codebook, particularly with a view to the structure of the decision letters. The codebook was drafted and revised thirteen times by piloting it on a portion (n = 4) of opinion letters and meeting minutes. The first and second author met four times to discuss the revision of the codebook. The codes and definitions were refined as a result of this pilot. Through the use of indexing codes (i-codes) it was possible to systematically explore the data by indexing sections of text. Thereby the i-codes enabled us to conduct a more categorical and precise coding process. The codebook contained eight groupings of i-codes: Scientific evaluation, Process Errors, Research involving Young People, Ethical Principles, Presence of an Illness, the REC, Administration of the Study and Other (see appendix C for an outline of all codes and definitions).

After indexing the content of the documents, we applied analytical codes (a-codes). The a-codes, or inductive codes, enabled us to capture interpretations that emerged from the text. There were four a-codes; The process behind the decision, Clarity of the RECs recommendations, Relationship between applicant and REC and Conflict. For the purposes of this study we only coded for Conflict as our a-code, as this theme had

not emerged in the previous literature. We defined Conflict as instances of disagreements between the applicants and the REC/individual REC members (see appendix C).

Attributes or descriptive codes were used to capture demographic features in the data. The attributes categorised the letters and meeting minutes based on: the decision given by the REC, methodology (Internet-mediated, which were further categorised into the types of studies found in Kempe et al, (in preparation) or non-Internet studies), the name of the deciding REC, document type (letter or minutes), participant age ranges, participant diagnosis, stage in the malignant illness trajectory and non-malignant illness trajectory (see appendix C).

The final codebook contained 49 i-codes, four a-codes and eight attributes (see appendix C). Once the codebook was finalised, the first author coded all the documents using the final draft of the codebook. All documents were entered into NVivo 10 for Mac where all coding was conducted. It should be noted that studies were not matched on methodology in the analysis (i.e. comparing face-to-face focus groups to online focus group).

Following the open coding a manifest content analysis was used to categorise the surface meaning of the text (White and Marsh, 2006; Rourke et al., 2001) and to calculate the frequency. We situated the content analysis within a factist framework meaning that the data was assumed to be a true index of reality (Vaismoradi et al., 2013; Sandelowski, 2010).

3.3 Results

3.3.1 Returned records

The research summaries website was searched on November 6th, 2015. An outline of the record selection process can be seen in figure 2.

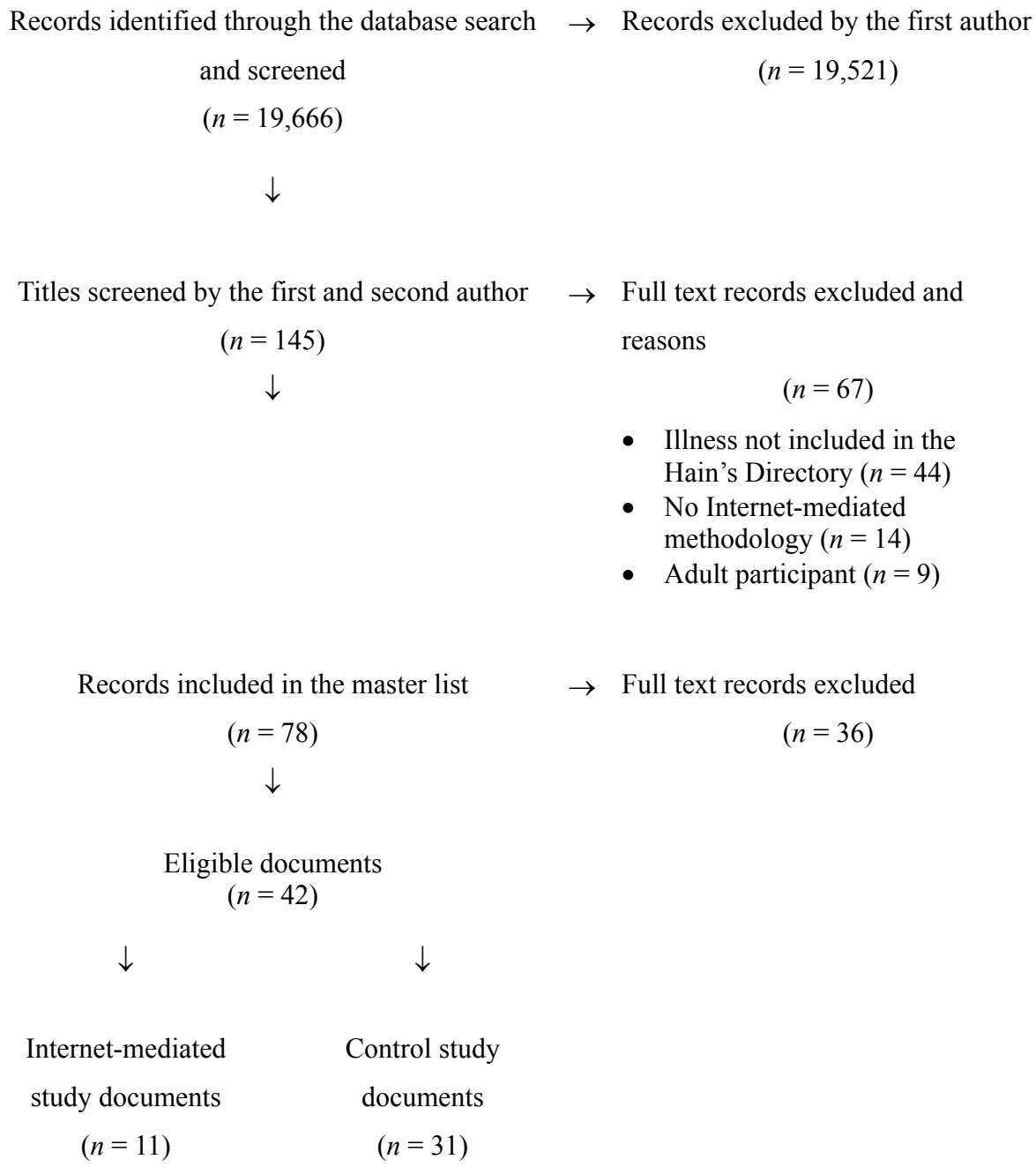

Figure 2: Flow diagram illustrating the record selection process.

3.3.2 Returned characteristics

There were 42 letters included in this study. Eleven decision letters related to applications for Internet-mediated research studies and thirty-one decision letters for non-internet mediated research studies.

An overview of the content of decision letters can be seen in table 6. We found that the content of both the decision letters and meeting minutes were duplicates of each other. Five of the 11 internet mediated studies were applications for Internet-mediated interventions, and three of the studies were clinical feasibility studies of using Internet-mediated methodology. The remaining three records were classified as "other Internet-mediated methodology" and included study methodologies not identified in the systematic review (see chapter 2). The last category included for example a study using Big Data to study a sample with a cerebral palsy population.

Seven of these 11 records were for research involving young people with non-malignant disorders (e.g. cerebral palsy, congenital heart disease). Of the remaining three records, two were applications for research involving young people with malignant disorders (e.g. cancer) and one application for research involving young people with both malignant and non-malignant diagnoses. Seven of the applications received a favourable opinion with conditions, and the remaining four studies received a provisional opinion. On average, it took 28.45 days (SD = 14.33, range = 8-45 days) from IRAS submission to the researchers receiving an ethical opinion.

Of the 31 studies relating to offline research, four were missing the meeting minutes although their decision letters were still included in the analysis. Applications for offline research took on average 23.16 days (SD = 15.35, range = 3-57 days) from IRAS submission to the researchers receiving the ethical opinion. Nine of the records relating to offline research were applications for research involving young people with malignant illnesses (e.g. brain tumours). Eighteen of the applications were for research involving young people with non-malignant illnesses diagnoses (e.g. HIV), the remaining four applications related to young people with both malignant and non-malignant diagnoses. Eighteen of the applications received a favourable opinion with conditions, and thirteen applications received a provisional opinion.

Table 6: Overview of the percentage coverage.

		Internet-mediated studies	Offline studies
Category	**Code**	**Percentage coverage**	**Percentage coverage**
Scientific evaluation	Recruitment	1.31%	13.87%
	Sampling	1.6%	1.11%
	Research question	1%	1.22%
	Procedure	1.7%	0.96%
	Measurements	1.57%	0.99%
	Bias	0.44%	0.87%
	Feasibility	1.99%	1.77%
	Data analysis	2.48	1.47%
	Equipoise	1.39%	0.44%
	Other issues related to scientific evaluation	0.43%	0.76%
Process errors	Procedural violation	0.5%	0.68%
	Missing information	0.69%	0.56%
	Slip-ups	0.89%	0.9%
	Discrepancies	0.83%	1.54%

		Internet-mediated studies	Offline studies
	Code	**Percentage coverage**	**Percentage coverage**
	Other issues related to process errors	0.47%	0.62%
Research involving young people	Responsibility for consent	0.52%	1.02%
	Responsibility for assent	0.32%	0.7%
	Language and adjustments	0.78%	1.04%
	Other issues related to research involving young people	0.56%	0.8%
Ethical principles	Privacy	1.8%	0.82%
	Confidentiality	1%	1.38%
	Anonymity	1.1%	1%
	Harm	1.27%	1.11%
	Voluntariness	0.61%	1.04%
	Consent process	0.86%	1%
	Assent seeking	0.25	0.79%
	Other ethical principles	1.2%	0.8%

		Internet-mediated studies	Offline studies
Category	**Code**	**Percentage coverage**	**Percentage coverage**
The presence of an illness	Interference with clinical care	0.83%	0.65%
	Importance of participation	1.1%	1.19%
	Capacity	-	-
	Burden of participation	0.83%	1.18%
	Other issues related to the presence of an illness	1.14%	0.82%
The REC	Collaborative nature of decision	1.9%	1.02%
	Holding applicants accountable	1.6%	1.8%
	The individual nature of decision	0.66%	0.5%
	Referring to specialist expertise	0.98%	1.11%
	Rituals	0.88%	0.65%
	Administration	2.16%	2.5%
	Further approvals	1.7%	2.75%
	Other issues related to the REC	0.89%	0.37%
Other	Revisions	1.22%	2.57%

		Internet-mediated studies	Offline studies
Category	**Code**	**Percentage coverage**	**Percentage coverage**
Administration of the study	Start & date	0.54%	0.3%
	Funding	0.99%	0.43%
	Suitability of research staff	1.28%	1.3%
	Equipment	0.64%	0.52%
	Sponsor	1.12%	1.02%
Outline of the opinion	Favourable with conditions	3.27%	4.23%
	Favourable without conditions	1.26%	0.2%
	Other issues related to the outline of the opinion	2.36%	2.13%

Note: the percentages in this table are combinations of the percentage coverage from both decision letters and meeting minutes.

The majority of the documents contained text relating to administration, with a minor difference between studies using Internet-mediated methodologies (2.16%) versus offline methodology (2.50%). Examples of administration included:

> "*We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this favourable opinion letter. The expectation is that this information will be published for all studies that receive an ethical opinion but should you wish to provide a substitute contact point, wish to make a request to defer, or require further information, please contact the REC Manager [name], [contact emai]. Under very limited circumstances (e.g. for student research which has received an unfavourable opinion), it may be possible to grant an exemption to the publication of the study.*"
>
> (extract from letter 28, an Internet-mediated study)

The content analysis showed there was a large marginal difference in the percentage coverage for Recruitment between the Internet-mediated methodology studies (1.31%) versus offline studies (13.87%). Content of recruitment discussions in offline studies included examples such as:

> "*[the applicant] explained that she would not be doing a service evaluation and would be approaching participants in order to assess the transition from childhood to adult care. She explained that she was confident of being able to recruit 12 participants and involve 12 carers across the 3 sites. She also stated that a participants' parent's decision to decline involvement, would not limit their involvement. The Committee was satisfied with this.*"
>
> (extract from letter 19, an Internet-mediated study)

> "*The committee noted that the control participants would be siblings and friends of the patient participants and queried if the friends and siblings would be analysed separately.*
> *[the applicant] stated they will have a single control group which will be matched for age, gender and socioeconomic status.*
> *The committee commented that from a psychological standpoint, siblings would exhibit different psychological effects to friends as having a sick*

sibling would affect them. The committee recommended that the researchers avoided using siblings if possible.
[the applicant] will mainly recruit their control participants from outside the family. stated that most families don't have any unaffected siblings, as such they stated they have a youth group they can use to recruit from."

(extract from letter 17, an offline study)

Capacity to consent was not flagged as an issue in either group. Other issues were mentioned very infrequently, for example issues relating to bias (0.44% in Internet-mediated studies versus 0.87% in offline studies) and equipoise (1.39% in Internet-mediated studies versus 0.44% in offline studies).

The REC did not differentiate between ethical issues in the use of Internet-mediated methodologies in research to that of offline research. For example, recruitment and consent have been identified as different in Internet-mediated research compared to non-Internet based research (Fox et al. 2007; Henderson et al. 2012). However, this was not obvious from the text of the decision letters:

"*How will you recruit and consent? At the Out Patients review. Patients who have expressed an interest in doing exercise will be identified. They will be given the information and at least a minimum of one day to consider participating.*"

(extract from letter 53, an Internet-mediated study)

The REC did highlight issues around harm prevention: which seemed to imply that the population studied was considered vulnerable. Measures taken to ensure protection of participants from harm seemed to be around setting up support system and clear boundaries for the research team (e.g. research was to be carried out during office hours only):

"*The committee require an established support system in place at the beginning of the session. 3) The committee request for email interviews to be carried out in office hours only to minimise the risks for vulnerable people*."

(extract from letter 28, an Internet-mediated study)

Interestingly wrapped up in the protection of participants was also protection of their data and security of the websites designed in the research. Despite previous literature treating data protection and physical or psychological harm prevention as separate issues, the RECs did not seem to view these as separate issues. For example:

> "*Care and protection of research participants; respect for potential and enrolled participants' welfare and dignity*
> *The Committee queried the 'mechanics' of the online questionnaire, what was involved and what data protection there are in place for the participant's responses.*
> *[The applicant] informed the Committee that the University of […] has a subsidiary company who have developed a secure web based questionnaire service and that all participants are provided with a unique log in password and it is expected that the participants will access the web based questionnaire once per month and it is expected that the questionnaire will be completed within a +/- 3-week period and If not completed the questionnaire would become locked. Participants will also be sent reminders to complete the questionnaire via one text message. No identifiable data or confidential data will be stored.*"
>
> (extract from letter 28, an Internet-mediated study)

The bulk of the discussion in both the letters and minutes related to the REC flagging what was defined in this study as minor process errors (e.g. spelling and/or grammar). This appeared to form the bulk of their review for both Internet-mediated studies and offline studies and it was not always clear if they requesting corrections to these process errors in study documents such as consent forms and information sheets, or in applications to the REC themselves:

> "*7) Check for typographical and grammatical errors throughout.*
>
> (extract from letter 28, an Internet-mediated study)

> "*The invitation letter requires provision for participants to write their name and phone number.*"
>
> (extract from letter 78, an offline study)

The ethical merits of these process errors are debatable (Angell and Dixon-Woods, 2009). There were instances where the REC did flag process errors that could have ethical merit for instance if the correction would lead to an alteration of the meaning of the text or clarifies inaccuracies in the documents that the participants will see:

> "*The Committee would like to see the Assent Form revised to add the words "to about the study" to point 3*"
>
> (extract from letter 67, an Internet-mediated study)

> "*The Committee would like to see the Invitation Letter revised to correct spelling and grammar*."
>
> (extract from letter 63, an offline study)

However, sometimes the requests were for insertions into the text of these documents which altered the methodology and possible result of the study:

> "*Please make it clear that participants do not have to answer any questions in the questionnaires that they do not feel comfortable answering.*"
>
> (extract from letter 17, an offline study)

We identified mixed evidence suggesting that there are instances where the REC may be more cautious in their appraisal of research involving young people with malignant or non-malignant illnesses in research. In this context the REC flagged an ethical issue (such as informed consent) which required the researcher to re-submit parts of their application documents for a second review:

> "*[…] The Committee noted that the applicant would allow one week for individuals to consider consenting and stated that this may be problematic as the children may forget or be difficult to re-contact. Members advised that if children expressed an interest, the applicant could suggest and agree a time and day to telephone the children to give them further information."*
>
> (extract from letter 17, an offline study)

The RECs did not, contrary to the hypothesis of this study, flag any ethical issues for Internet-mediated research which were particularly unique. Indeed, their overall approach to online research did not show any of the paternalistic approach described in the literature. Rather this was reserved for offline research involving younger children with a life-limiting illness:

> "*3. Please clarify what knowledge of their condition younger children would have. Would they be aware of details such as diagnosis, staging and their treatment pathway? Please confirm that the parents of these young people would be happy with them being asked questions of this nature*."
>
> (extract from letter 29, an offline study)

Within these discussions the REC could be described as gatekeeping. There is ample evidence in the literature across multiple studies (Modi et al., 2014) showing that children are aware of their diagnosis. Discussions of prognosis particularly when the outcome is likely to be poor have been cited as one of the key areas that clinicians and parents were more likely to hesitate to give consent for children to participate (Stevens et al., 2010). However, a growing number of studies indicates that parents would like to be asked to participate in research and allowed to refuse if they felt it not appropriate or too burdensome (Stevens et al., 2010)

> "*The Committee asked for it to be made clearer in the invitation paragraph of the PIS* [participant information sheet] *that if the child does not want to participate in the research then their care will not be compromised*."
>
> (extract from letter 9, an offline study)

There were two instances of conflict between the researchers and the REC. The first instance of conflict was identified in a study using Internet-mediated methodology and centred on the view of one member of the REC committee:

> "*4. A Committee member felt that this study is too invasive and would not consider consenting to their own child being recruited into this study. You replied that this remark is a bit distasteful and that the families she is in touch with would want to get involved in this study.*"
>
> (extracts from letter 19, an Internet-mediated study)

Interestingly the letter identified one REC member in particular within this exchange in contrast to other instances where the REC speaks as a group without singling out any one's member's opinion. It is impossible to determine the reasons for this distancing language from this one instance. It could be that the other REC members did not agree with this view or there could be another reason for the phrasing of this language.

The second instance of conflict was a longer exchange related to a study of patient experience and care during their illness. The Committee expressed some caution about the use of the term "palliative care" as part of one question.

> "*The REC queried whether palliative care was important in the research. [the researcher] replied that it was in the interviews but that she did not want to put people off participating in the study due to the use of the term. [….]*
>
> *Members commented that they were trying to understand the needs of the researchers to support the use of "palliative care". [the applicant] commented that she would like to ask participants whether they felt there was a role for palliative care in their disease. The REC queried whether the term "supportive care" could be used instead. [the applicant] replied that palliative care was used for the final stages of life whereas supportive care led up to that*."
>
> (extract from letter 7, an application for offline research)

The length and detail of this exchange was not replicated in any other document. In the exchange it appears that the term "palliative care" can be contentious and this was revisited over the course of the REC meeting. Given the likelihood for young people who are in the palliative phase of their disease to be excluded from both Internet-mediated (Kempe et al., in preparation) and offline studies (Fernandez and Barr, 2006) it would appear that in this instance the REC may have been hesitant about the introduction of even the term "palliative care".

The REC documents also described rituals of the REC meetings. For both methodology types there seemed to be a ritual of the REC meeting prior to the meeting with the researcher. During this private meeting the REC meet to discuss the ethical issues that arise from the application. The documents analysed for this study only contained references to this private meeting;

"*Other ethical issues were raised in preliminary discussion before your attendance at the meeting*."

(extract from letter 21, an Internet-mediated study)

"*The committee noted in private discussion […]*"

(extract from letter 17, an offline study)

From the documents in this study it is not clear how the private discussion, which took place behind closed doors, affected the outcome of the application.

3. 4 Discussion

This study analysed the content of decision letters and meeting minutes of two groups of research projects: research involving children and young people (under the age of 25 years) with life limiting or life threatening conditions, using internet mediated methodologies and research involving children and young people (under the age of 25 years) with life limiting or life threatening conditions, using non-internet mediated methodologies. There are three salient findings from this study. First, the majority of the content of these documents are taken up with discussion of grammatical and spelling errors in various documents and applications to the REC. While it is legitimate that the REC would wish to ensure the suitability of any information provided to participants, the inordinate amount of time and effort expended on these debates is considered by some to be outside the remit of "ethics" (Angell and Dixon-Woods, 2009). Indeed, the argument could be made that by attaching such importance to these more trivial matters, the RECs are concerning themselves more with copyediting of research documents than with exploration of the ethical implications of their content.

Second, contrary to expectation and despite the extensive literature exploring from both a theoretical (Rodham and Gavin, 2006) and pragmatic (Henderson et al, 2012; Fox et al. 2007) point of view, the ethics of Internet mediated research did not seem to require additional discussion compared to that of offline studies. There are a number of possible explanations for this finding. The majority of homes in the UK have had internet access since 2007 (Office of National Statistics, 2008). Internet use has become commonplace in everyday life and for a multitude of purposes which were unimaginable in the early stages of its development. As its use has become more routine, the uncertainty that RECs may

have expressed in those early days might be less. However, studies were excluded from this analysis and within the small sample presented here there were no effects for age of study found. Additionally, it is outside the scope of the current project to assess how much experience each REC would have had with internet mediated research as a whole. It was not possible to assess if there were individual differences between those RECs for whom appraisals of internet research is a rarity to explore in more detail if there is an experimental effect in REC appraisals of this kind.

Third, and perhaps unsurprisingly, there was some caution experienced on behalf of the RECs included in this study as to the relative vulnerability of the participants included in these research studies. Protection of participants was a frequent code in the discussions. It is well documented that patients receiving palliative care are an understudied group (Fernandez and Barr, 2006) and indeed a population of researchers focused on research in a life limited population cited RECs as one barrier to this research (Beecham et al, 2016). Our analysis supports this view. One source of conflict within the study was the use of the term "palliative care" and caution was expressed as to the vulnerability of patients who are young and may not know their prognosis. We do not know what impact the REC discussions of these issues had on time to approval of these studies, or indeed how legitimate this discussion was based on the content of the protocols.

There are some limitations of the current study. First, this study focused solely on clinical RECs and clinical research. In the context of UK-based RECs this means that studies that the HRA does not consider "research" were not analysed. The exclusion of non-clinical studies may have skewed the result, and by including non-clinical studies it may have been possible to increase the sample size and to strengthen the conclusions of the study. Second, the use of 2007 as the cut off for study eligibility may have skewed the result. As with the systematic review, 2007 was selected due the level of saturation of home broadband in the UK and the USA and to harmonise the findings with the systematic review.

Third, the search method used to locate eligible records was basic, and reflected a limitation of the current HRA filing system. It was not possible to implement a more sophisticated search and as such it is impossible to be sure that there are no other studies which were not returned by these rudimentary search terms which have been overlooked by this analysis. In addition, the Research Summary website is updated daily with new

records meaning that almost immediately new studies which may have been eligible would have been overlooked. Replication of this study is also further hampered as no doubt new studies would have to be included were this study to be conducted today. Future studies may want to use additional avenues to more thoroughly locate eligible records.

The analysis in the current study based only on two types of documents: decision letters and meeting minutes. Both of these documents are authored by the REC, and refer to other researcher authored documents such as information sheets, protocols and consent forms which we did not have access to within this study. By exploring the other documents associated with the applications it would be possible to explore more contextual information and more accurately and independently evaluate the evidence for the RECs claims as to the ethical merits of the studies. Furthermore, it should be noted that the absence of comments do not necessarily equal a lack of attention by RECs to these issues. Furthermore, the analysis relied heavily on qualitative analysis, meaning that there is a degree of subjectiveness inherit in the analysis (Atieno, 2009). The analysis we conducted was therefore only one interpretation of the data, and the degree of rigour of the analysis is limited to the degree of coding reliability which was not calculated. The interpretation of the open coding was to some extent grounded in a content analysis, which categorised the surface meaning of the text (Rourke et al., 2001). However, due to the small sample size we were unable to determine whether there were significant differences in frequency between the two groups. The small and uneven sample size also meant that we were unable to match studies using similar methodology (e.g. comparing an application for a face-to-face focus group study to an application for online focus group study).

Despite being an entrenched part of the ethical review system, the study of RECs and how ethical guidelines are being practically applied has been overlooked by researchers. The findings of this study contributes to the discussion of the ethics of Internet-mediated research and how RECs practically apply the guidelines.

General discussion

The aim of the thesis was to explore ethical issues that may arise while conducting Internet-mediated research with young people with cancer. This was done by 1) conducting a systematic review which identified the ethical conflicts researchers report in Internet-mediated research and 2) exploring the content of REC documentation and compare the ethical issues arising in Internet-mediated versus offline research.

Chapter 1 provided an overview of the development of ethical guidelines for clinical research and how the current review system has been critiqued by researchers. The chapter also described how the penetration of Internet-meditated technologies into everyday life has changed research priorities. Following this, the chapter focused on the debate regarding the uniqueness of the ethical issues arising during Internet-mediated research. The chapter highlighted ethical issues surrounding research involving young people with life-limiting/life-threatening conditions. Chapter 1 highlighted a lack of research on the types of ethical issues (if any) that can arise when conducting Internet-mediated research with young people with life-limiting/life-threatening condition. This is despite the recognition that young people receiving palliative care face a unique illness experience (Taylor et al., 2008; Woodgate, 2008) compared to other age cohorts. The central aim of this thesis was to explore the ethical issues that can arise during the review stage and during research involving young people with life-limiting/life-threatening conditions.

4.1 Ethical issues arising in research involving young people with cancer

Chapter 2 detailed a systematic review of the types of Internet-mediated methodologies used in research involving young people with cancer and the types of ethical issues that arise in this type of research. The types of Internet-methodology currently used in research could be categorized into four different approaches: website-based interventions, online focus groups, clinical feasibility studies of symptom capture tools and analysis of conversational data from online discussion forums. Second, we described ethical issues the authors identified during the course of conducting their research. The salience of ethical issues varied across methodologies. In addition, the ethical issues were rarely defined by the other authors. For example, privacy was

discussed in all but one of the methodology categories however, it was never overtly defined. The lack of an operational definition of for example privacy may explain why the practical application of privacy varied.

Nine of the papers did not give special attention outside of the method section of their articles to the ethical issues which arose in the conduct of their research. We hypothesised that this may be due to researchers in e-health contexts rarely reporting on the issues that they have encountered in getting ethical approval for their Internet-mediated studies (Henderson et al., 2013). This phenomena makes it difficult to assess whether Internet-mediated research require specifically developed guidelines. Regardless, the results of this review suggest the ethical concerns about Internet-mediated research may be overestimated and the emphasis on a generation on new guidance may be misplaced.

4.1.1 Ethical conflicts highlighted by researchers

4.1.1.1 Harm prevention

The authors of the studies included in the systematic review tended to emphasise protection from harm and privacy/confidentiality. Seven of the authors gave special attention to issues around protection from harm. In these studies, user-generated content was reviewed prior to being accessible to other users. The content was reviewed for two reasons. First, it was done for purposes of moderation and second, to engage with participants whose physical and/or psychological health was at risk. However, none of the seven studies stated how often members of the research team were required to moderate or provide clinical intervention. The actual instances of harm in Internet-mediated research is therefore not known (Bessell and MacDonald, 2014). Since the incidences of harm in Internet-mediated research are not well documented, it could be that RECs have a distorted view of the risk (Shah et al. 2004) associated with this type of research. Participants who are studied online are considered more susceptible to harm compared to those studied offline. Given the disinhibiting nature of online interactions (Joiner et al., 2010) whereby discussions that take place online are more likely to escalate to terms that they would not offline, this is considered a very real concern. With the attention given to websites which promote negative behaviours in young people (e.g. websites encouraging anorexia or risk-taking behaviour such as “Neknominate”) there is a concern that young people are especially vulnerable to online persuasion. It may be that the committees that

govern research ethics are cautious in the appraisal of Internet studies in this sphere, and this may be why the authors of these studies emphasised prevention of harm as an ethical conflict.

4.1.1.2 Privacy

Issues of privacy and confidentiality have been heavily debated within the literature on Internet-mediated research methodology (e.g. by Zimmer, 2010). The two concepts have not been consistently defined and they are in some studies used interchangeably by researchers. We identified evidence of this in the systematic review where ten studies used the terms interchangeably. Privacy is a debated ethical and legal concept (Joinson et al., 2007) but in the absence of individual informed consent, online researchers are to some extent required to put additional emphasis on protecting individual privacy and anonymity (Dias, 2003). The protection could be implemented by replacing usernames with pseudonyms, and removing other identifiable information (e.g. URLs, location names and specific ages) as was done in the studies included in our systematic review. These steps reflect how the Internet has increased the interconnectivity and linkage between information (Frankel and Siang, 1999; Hewson and Buchanan, 2013). There is an increased ability to create links between informational units that may not on their own be identifiable but that in an aggregated format are unique to an individual (Zimmer, 2010). For example, Zimmer (2010) described how data linkage techniques were used to de-anonymise an American college in a study of Facebook profiles. Similarly, Bobicev et al., (2013) developed a data miner programme that made it possible to link 75-80% of 6,000 messages of 100-150 words with the authors on two online in vitro fertilization (IVF) support groups. However, the studies included in the review tended to focus on more practical issues surrounding Internet-mediated research e.g. secure data storage (Nosek et al., 2002). We identified no evidence to suggest that ethical issues around privacy raised specific concerns for the researchers during the conduct of their study nor that traditional concepts of what privacy is required to be redefined.

In contrast, the wider debate on ethical issues arising from the use of Internet-mediated research methodology in clinical research has tended to focus on informed consent. Consent has been the cornerstone of research ethics since the Nuremberg code and consent in offline research has become a required component of research practice

(Sin, 2005). However, the translation of consent onto online research has not been direct and researchers have struggled with finding the best way to approach consent in Internet-mediated research (Hudson and Bruckman, 2004). Vayena et al., (2013) argued that the traditional model of consent is inappropriate for Internet-mediated research as the information that participants are consenting researchers to use has transitioned from being personal to becoming a commodity that can be sold, altered or shared indefinitely. Furthermore, the right to withdraw one's data, which is part of the concept of providing consent, cannot be easily translated to some types of Internet-mediated research (such as studies analysing e.g. written text, big data, images or social media) or in cases where data is unknowingly provided (through e.g. using websites that automatically collects and stores data of Internet activity or through IP addresses). The voluntary aspect of informed consent therefore becomes more difficult for researchers to uphold and ensure (McNamara, 2013). The architecture of the Internet means that it is difficult for data to completely disappear indicating that a traditional notion of 'right of withdrawal' might become meaningless and difficult to enforce for researchers using certain types of methodology, such as 'big data'. McNamara (2013) argued that it is difficult to guarantee 'voluntary' consent, as consent can be implied by providing data, and some types of data might be collected automatically, such as IP addresses. Taken together it suggests that online researchers need to re-evaluate the current application of informed consent. Despite extensive debate on how researchers should be best translate a concept central to 'traditional' clinical ethics, informed consent did not appear to be a central issue for the studies included in this review.

4.1.2 Ethical issues identified by ethics committees during the review stage

Following the systematic review, we explored ethical issues identified by RECs reviewing Internet-mediated and offline research with young people with life-limiting conditions. We used the findings from the systematic review to inform the codebook. We identified 11 documents relating to Internet-mediated research applications and 32 documents relating to offline research applications.

The majority of the documents contained administrative text, regardless of the methodology under review. In addition to administrative text, a substantial proportion of the documentation was dedicated to discussing spelling and grammatical errors. While RECs are legitimate in discussing spelling and grammatical errors, the amount of effort

that is currently being spent on these non-ethical issues is seen by some as being outside the REC's remit (Angell and Dixon-Woods, 2009). Instances where the REC oversteps its remit may contribute to a perception of excessive bureaucracy and 'ethical creep' (Angell and Dixon-Woods, 2009). 'Ethical creep' can be defined as instances where a regulatory governance structure continuously expands their remit while at the same time intensifying the regulation of practices that already falls within its remit. While it can be argued that instances of the REC commenting on spelling errors are evidence of nit-picking, Angell and Dixon-Woods (2009) suggested that it may be a result of the REC members wanting to ensure that all of the information presented to participants was correct. REC document tended to focus on procedural errors and rarely engaged with concrete ethical issues. The lack of engagement with ethical issues during the REC meetings may explain in part why researchers do not tend to report ethical issues (Henderson et al., 2013).

4.1.3 The uniqueness of ethical issues in Internet-mediated research

Findings from both the systematic review and document analysis suggests that current Internet-mediated research involving young people may not raise unique ethical conflicts, in contrast to the extensive literature on this topic. With reference to the overall aim of the thesis, it seems the debate on ethical issues has had a limited affect on how researchers and RECs practically deal with research involving young people with life-limiting/life-threatening illnesses. This is evident by the fact that the types of issues identified during the ethical review stage did not seem to differ significantly from issues identified in the published report. Furthermore, there is no evidence that the concerns raised about Internet-mediated research discussed in the literature are necessarily having a significant effect on research practice.

The ethical decision-making process that researchers and RECs engage in is not affected by the online versus offline environment where the research takes place (Rodham and Gavin, 2006). There is therefore a disconnect between the issues emphasised in the literature (e.g. informed consent) and the issues identified during the course of a study (e.g. prevention of harm, participant vulnerability). However, the powerful role of the peer reviewer influence what gets published and this needs to be acknowledged. Hojat et al., (2003) called peer reviewers "gatekeepers of science", describing their influence of a journal editor's decisions, and by extension the direction of a scientific discipline.

The focus on ‘traditional’ ethical issues, such as prevention from harm or participant vulnerability can be traced back to the historic roots of the modern ethics (Saginur, 2014). Although the REC highlighted prevention from harm as an ethical issue they did not clarify why there was a potential risk of harm or how harm was defined. None of the studies in the systematic review stated how many times a member of the research team was required to clinically intervene to prevent harm to a participant. No evidence was for the actual occurrence of negative effects arising from the use of Internet-mediated research. Previous research suggests that REC members overestimate the dangers and the risks of harm associated with studies and clinical interventions (Shah, 2004). Future studies should attempt to quantify the actual occurrences of harm associated with Internet-mediated research, and explore how the actual risks corresponds with perceived risks. This overestimation of risk may contribute to the perception that RECs act as gate-keepers (Gysels et al, 2013; Beecham et al. 2016). Previous research has reported that researchers perceive the REC as barriers to conducting research with palliative care populations (Gysels et al, 2013; Beecham et al. 2016) and we did find that RECs identified issues with palliative care research. It was not possible to determine whether the researchers from the studies in the systematic review perceived the RECs to act as barriers in gaining ethics approval. Future studies should explore the extent of researchers who perceive the REC as barriers. Furthermore, future studies should explore whether the REC are legitimate in emphasising these issues when appraising applications, including for palliative care research.

4.2 Methodological limitations and directions for future research

There are some limitations to the systematic and document analysis that need to be taken into consideration. First, we limited the scope of the systematic review and the document analysis by excluding documents published prior to 2007. By having an earlier cut off year we would have had a larger sample size and more importantly it is possible that ethical issues around Internet research may have been more thoroughly discussed by researchers and RECs. As mentioned in chapter 2 it can be argued that 2007 as a cut-off point may have been too of conservative and it may have limited the sample size of the systematic review and the document analysis. However, it could be that by including papers published prior to 2007 the review and document analysis may have identified more historical issues and not necessarily issues pertinent to more recent research

(Gosling and Mason, 2015). Conducting a comparative review was outside the scope of the current thesis, and may need to be tackled by future studies evaluating the evolution (or lack thereof) of ethical issues in Internet-mediated research involving young people.

Second, both the systematic review (in chapter 2) and the document analysis (chapter 3) relied heavily on qualitative research methodology. While this is not itself a limitation (Galman, 2016; Silverman, 2016) it does mean that we were unable to triangulate the findings. The inherent subjectivenss of the method means that the interpretation presented here is only one interpretation of the data. While steps were taken to ensure transparency of the analytic process and the robustness of the interpretation (e.g. the use of two raters and coders) the limits of the interpretative nature of the analysis needs to be recognised. Furthermore, the reliance on very similar methods of analysis means that we were not able to triangulate our findings. While there are varying definitions of triangulation, Cohen and Manion (2000) define triangulation as an attempt to explain a phenomena from more than one standpoint. The use of mixed methodology in research has limitations including the increased focused on design and methods rather than theoretical issues (Flick, 2017). However, methodological triangulation increases the understanding of the phenomena under study (Bekhet et al., 2012). Future studies should address the issues with triangulation by engaging with researchers and REC members and explore whether similar themes emerge from other sources such as interviews or ethnographic studies of REC meetings.

In addition, the focus of this thesis was limited to clinical research ethics. The UK has two separate review streams for clinical and social science research. Applications for social sciences research tend to go through university-based ethics committees. In contrast, applications for clinical research go through separate ethical committees that were formally based in hospital trusts (Hunter, 2011). The main difference between the two streams is that clinical research is required by law to undergo ethical review; in contrast, social science research is currently undergoing self-regulated and voluntary ethical review (Hunter, 2014). However, funding agencies stipulates that to be eligible for funding, the research is required to go through ethical review. Future research should explore the ethics of social science research using Internet-mediated methodologies, especially in the instances where this type of research involves young people with malignant or non-malignant conditions.

Second, this study has focused on the researchers and RECs view on what

research ethics is and what ethical issues should be raised. A growing number of researchers are calling for participants to become involved in shaping the development of research ethics (e.g. Modi et al 2014). Modi et al. (2014) argued that by involving for example young people in the development of research ethics guidelines it is possible to create ethical guidelines that are better tailored to the research situations and are more relevant to the practical application of ethics. The inclusion of e.g. young people would also ensure that a diverse opinion is represented right at the start of knowledge generation and increase trust between participants and researchers (Modi et al 2014). Future research should more actively engage young people with palliative care needs in the debate on what constitutes ethical Internet-mediated research.

The Internet is becoming increasingly immersed to today's health care, having already become an integral part of everyday life across age cohorts. The integration of technology into everyday life and the health care setting has fuelled the discussion over what constitutes ethical Internet-mediated clinical research. However, a lack of attention has been devoted to describing the type of ethical issues in Internet-mediated research involving young people with life-limiting or life-threatening conditions. While few studies reported on ethical conflicts arising over the course of the studies, researchers tended to highlight privacy and prevention of harm. This was replicated in the study outlined in chapter 3 whereby we identified few ethical issues unique to Internet-mediated research. This contrasts with the extensive literature on these methodologies which indicate that Internet-mediated research has unique ethical considerations. There is therefore a misplaced emphasis in the literature on the need for additional ethical guidelines specifically developed for Internet-mediated research. The novel findings of this study contribute to the discussion over the ethics of Internet-mediated research with young people with life-limited and life-threatening conditions and how RECs are practically applying guidelines.

Abebe, T., & Bessell, S. (2014). Advancing ethical research with children: critical reflections on ethical guidelines. *Children's Geographies*, *12*(1), 126-133.

Abogunrin, S., & Martin, A. (2013). Can the use of social media and mobile apps improve patient knowledge of disease and health outcomes? a systematic review. *Value in Health*, *16*(7), A326.

Ahuja, J. (2015). Liability for psychological and psychiatric harm: the road to recovery. *Medical Law Review*, *23*(1), 27-52.

Allen, G. (2008). Getting beyond form filling: the role of institutional governance in human research ethics. *Journal of Academic Ethics*, *6*(2), 105-116.

Altheide, D. L. (1987). Reflections: Ethnographic content analysis. *Qualitative Sociology*, *10*(1), 65-77.

Anderson, M. (2016). Technology device ownership: 2015. New York: Pew Research Center.

Angell, E. L., Bryman, A., Ashcroft, R. E., & Dixon-Woods, M. (2008). An analysis of decision letters by research ethics committees: the ethics/scientific quality boundary examined. *Quality and Safety in Health Care*, *17*(2), 131-136.

Angell, E. L., & Dixon-Woods, M. (2008). Style matters: an analysis of 100 research ethics committee decision letters. *Research Ethics Review*, *4*(3), 101-105.

Angell, E. L., Jackson, C. J., Ashcroft, R. E., Bryman, A., Windridge, K., & Dixon-Woods, M. (2007). Is 'inconsistency' in research ethics committee decision-making really a problem? An empirical investigation and reflection. *Clinical Ethics*, *2*(2), 92-99.

Angell, E., Biggs, H., Gahleitner, F., & Dixon-Woods, M. (2010). What do research ethics committees say about applications to conduct research involving children?. *Archives of Disease in Childhood*, *95*(11), 915-917.

Angell, E., & Dixon-Woods, M. (2009). Do research ethics committees identify process errors in applications for ethical approval?. *Journal of Medical Ethics*, *35*(2), 130-132.

Arnold, L. E. (1992). A comparative overview of treatment research methodology: adult vs. child and adolescent, psychopharmacological vs. psychosocial treatments. *Psychopharmacology Bulletin*, *29*(1), 5-17.

Ashcroft, R., & Pfeffer, N. (2001). Ethics behind closed doors: do research ethics committees need secrecy?. *BMJ*, *322*(7297), 1294.

Ashley, L., Jones, H., Thomas, J., Forman, D., Newsham, A., Morris, E., ... & Wright, P. (2011). Integrating cancer survivors' experiences into UK cancer registries: design and development of the ePOCS system (electronic Patient-reported Outcomes from Cancer Survivors). *British Journal of Cancer*, *105*, S74-S81.

Atieno, O. P. (2009). An analysis of the strengths and limitation of qualitative and quantitative research paradigms. *Problems of Education in the 21st Century*, *13*(1), 13-38.

Ayling, R., & Mewse, A. J. (2009). Evaluating internet interviews with gay men. *Qualitative Health Research*, *19*(4), 566-576.

Baggott, C., Gibson, F., Coll, B., Kletter, R., Zeltzer, P., & Miaskowski, C. (2012). Initial evaluation of an electronic symptom diary for adolescents with cancer. *Journal of Medical Internet Research: Research Protocols*, *1*(2), e23.

Barak, A., Klein, B., & Proudfoot, J. G. (2009). Defining internet-supported therapeutic interventions. *Annals of Behavioral Medicine*, *38*(1), 4-17.

Bartlett, Y. K., Selby, D. L., Newsham, A., Keding, A., Forman, D., Brown, J., Velikova, G., & Wright, P. (2012). Developing a useful, user-friendly website for cancer patient follow-up: users' perspectives on ease of access and usefulness. *European Journal of Cancer Care*, *21*(6), 747-757.

Battles, H. T. (2010). Exploring ethical and methodological issues in internet-based research with adolescents. *International Journal of Qualitative Methods*, *9*(1), 27-39.

Beecham, E., Hudson, B. F., Oostendorp, L., Candy, B., Jones, L., Vickerstaff, V., Lakhanpaul, M., Stone, P., Chambers, L., Hall, D., Hall, K., Ganeshamoorthy, T., Comac, M., & Bluebond-Langner, M. (2016). A call for increased paediatric palliative care research: identifying barriers. *Palliative Medicine*, *30*(10), 979-980.

Beecher, H. K. (1976). Ethics and clinical research. *Biomedical Ethics and the Law*, 193-205.

Bekhet, A. K., & Zauszniewski, J. A. (2012). Methodological triangulation: an approach to understanding data. *Nurse Researcher*, *20*(2), 40-43.

Ben-Ze'ev, A. (2003). Privacy, emotional closeness, and openness in cyberspace. *Computers in Human Behavior*, *19*(4), 451-467.

Bender, J. L., Jimenez-Marroquin, M. C., & Jadad, A. R. (2011). Seeking support on Facebook: a content analysis of breast cancer groups. *Journal of Medical Internet Research*, *13*(1), e16.

Bender, J. L., Yue, R. Y. K., To, M. J., Deacken, L., & Jadad, A. R. (2013). A lot of action, but not in the right direction: systematic review and content analysis of smartphone applications for the prevention, detection, and management of cancer. *Journal of Medical Internet Research*, *15*(12), e287.

Bessell, T. L., McDonald, S., Silagy, C. A., Anderson, J. N., Hiller, J. E., & Sansom, L. N. (2002). Do internet interventions for consumers cause more harm than good? A systematic review. *Health Expectations*, *5*(1), 28-37.

Blank, G. 2013. OxIS 2013 top-line findings: Internet use continues to grow; big increases in low-income households [Online]. Oxford: Oxford Internet Surveys. Accessed February 3rd 2015. Available fromhttp://oxis.oii.ox.ac.uk/blog/oxis-2013-top-line-findings-internet-use-continues-grow-big-increases-low-income-households/.

Bluebond-Langner, M., & Korbin, J. E. (2007). Challenges and opportunities in the anthropology of childhoods: An introduction to "Children, Childhoods, and Childhood Studies". *American Anthropologist*, *109*(2), 241-246.

Bobicev, V., Sokolova, M., El Emam, K., Jafer, Y., Dewar, B., Jonker, E. and Matwin, S. (2013). Can anonymous posters on medical forums be reidentified?. *Journal of Medical Internet Research, 15*(10), e215.

Borghi, M., Ferretti, F., & Karapapa, S. (2013). Online data processing consent under EU law: a theoretical framework and empirical evidence from the UK. *International Journal of Law and Information Technology*, *21*(2), 109-153.

Bouvier, G. (2012). How Facebook users select identity categories for self-presentation. *Journal of Multicultural Discourses*, *7*(1), 37-57.

Braun, V., & Clarke, V. (2006). Using thematic analysis in psychology. *Qualitative Research in Psychology*, *3*(2), 77-101.

Brier, M. J., Schwartz, L. A., & Kazak, A. E. (2015). Psychosocial, health-promotion, and neurocognitive interventions for survivors of childhood cancer: a systematic review. *Health Psychology*, *34*(2), 130.

Brownlow, C., & O'Dell, L. (2002). Ethical issues for qualitative research in on-line communities. *Disability & Society*, *17*(6), 685-694.

Bruckman, A. (2002) Ethical guidelines for research online. Accessed on February 3rd 2015. Available from http://www- static.cc.gatech.edu/~asb/ethics/.

Buchanan, E. A., & Hvizdak, E. E. (2009). Online survey tools: Ethical and methodological concerns of human research ethics committees. *Journal of Empirical Research on Human Research Ethics*, *4*(2), 37-48.

Burgess, M. M. (2007). Proposing modesty for informed consent. *Social Science & Medicine*, *65*(11), 2284-2295.

Burris, S. (2008). Regulatory innovation in the governance of human subjects' research: a cautionary tale and some modest proposals. *Regulation & Governance*, *2*(1), 65-84.

Caldwell, J. G., Price, E. V., Schroeter, A. L., & Fletcher, G. F. (1973). Aortic regurgitation in the Tuskegee study of untreated syphilis. *Journal of Chronic Diseases*, *26*(3), 187-190.

Critical Appraisal Skills Programme. (2016). CASP Checklist. [online] Accessed on March 5th 2015. Accessed from http://www.casp-uk.net.

Castellino, S. M., Ullrich, N. J., Whelen, M. J., & Lange, B. J. (2014). Developing interventions for cancer-related cognitive dysfunction in childhood cancer survivors. *Journal of the National Cancer Institute*, *106*(8), dju186.

Chambers, E. (2000). Applied ethnography. *Handbook of Qualitative Research*, *2*, 851-869.

Chen, D., Zhao, H. (2012). Data security and privacy protection issues in cloud computing. Presented at the International Conference on Computer Science and Electronics Engineering at 23-25 March 2012 in Washington, DC, USA.

Childress, C. A., & Asamen, J. K. (1998). The emerging relationship of psychology and the internet: proposed guidelines for conducting Internet intervention research. *Ethics & Behavior*, *8*(1), 19-35.

Cohen, D. J., & Crabtree, B. F. (2008). Evaluative criteria for qualitative research in health care: controversies and recommendations. *The Annals of Family Medicine*, *6*(4), 331-339.

Cohen, L., Manion, L., & Morrison, K. (2013). *Research Methods in Education*. Abingdon: Routledge.

Collier, D., & Mahoney, J. (1996). Insights and pitfalls: selection bias in qualitative research. *World Politics*, *49*(01), 56-91.

Cook, C., & Sheets, C. (2011). Clinical equipoise and personal equipoise: two necessary ingredients for reducing bias in manual therapy trials. *Journal of Manual & Manipulative Therapy*, *19*(1), 55-57.

Coons, S. (2012). Informed consent forms growing too complex. *Research Practitioner, 13*, 175-187.

Coulson, N. S., & Greenwood, N. (2012). Families affected by childhood cancer: an analysis of the provision of social support within online support groups. *Child: Care, Health and Development*, *38*(6), 870-877.

Crocker, J. C., Beecham, E. C., Kelly, P., Dinsdale, A. D., Hemsley, J., Jones, L., & Bluebond-Langner, M. (2014). Recruiting parents to paediatric palliative care research: impact of low invitation rates on sample bias. *BMJ Supportive & Palliative Care*, *4*(1), 110-110.

Davey, K. G. (2009). Reflections on my experience in human research ethics. *Journal of Academic Ethics*, *7*(1-2), 27.

Davis, M., Bolding, G., Hart, G., Sherr, L., & Elford, J. (2004). Reflecting on the experience of interviewing online: perspectives from the Internet and HIV study in London. *AIDS Care*, *16*(8), 944-952.

de Montjoye, Y. A., Radaelli, L., & Singh, V. K. (2015). Unique in the shopping mall: on the re-identifiability of credit card metadata. *Science*, *347*(6221), 536-539.

de Terwangne, C. (2014). The work of revision of the Council of Europe Convention 108 for the protection of individuals as regards the automatic processing of personal data. *International Review of Law, Computers & Technology*, *28*(2), 118-130.

Dekker, N., Hermens, R. P. M. G., Mensenkamp, A. R., Zelst-Stams, W. A. G., & Hoogerbrugge, N. (2014). Easy-to-use online referral test detects most patients with a high familial risk of colorectal cancer. *Colorectal Disease*, *16*(1), 26-34.

DerSimonian, R., & Laird, N. (1986). Meta-analysis in clinical trials. *Controlled Clinical Trials*, *7*(3), 177-188.

Dias, K. (2013). The ana sanctuary: women's pro-anorexia narratives in cyberspace. *Journal of International Women's Studies*, *4*(2), 31-45.

Dixon-Woods, M., & Angell, E. L. (2009). Research involving adults who lack capacity: how have research ethics committees interpreted the requirements?. *Journal of Medical Ethics*, *35*(6), 377-381.

Dixon-Woods, M., Angell, E., Ashcroft, R. E., & Bryman, A. (2007). Written work: the social functions of research ethics committee letters. *Social Science & Medicine*, *65*(4), 792-802.

Dobransky, K., & Hargittai, E. (2016). Unrealized potential: exploring the digital disability divide. *Poetics*, *58*, 18-28.

Donovan, E. E., LeFebvre, L., Tardif, S., Brown, L. E., & Love, B. (2014). Patterns of social support communicated in response to expressions of uncertainty in an online community of young adults with cancer. *Journal of Applied Communication Research*, *42*(4), 432-455.

Downe-Wamboldt, B. (1992). Content analysis: method, applications, and issues. *Health Care for Women International*, *13*(3), 313-321.

Dutton, W.H., Blank, G., & Groselj, D. (2013) Cultures of the Internet: the internet in Britain. Oxford Internet Survey 2013. Oxford Internet Institute, University of Oxford.

Eaton, D. K., Brener, N. D., Kann, L., Denniston, M. M., McManus, T., Kyle, T. M., Roberts, A. M., Flint, K. H. & Ross, J. G. (2010). Comparison of paper-and-pencil versus Web administration of the Youth Risk Behavior Survey (YRBS): Risk behavior prevalence estimates. *Evaluation Review*, *34*(2), 137-153.

Edwards, S. J., Stone, T., & Swift, T. (2007). Differences between research ethics committees. *International Journal of Technology Assessment in Health Care*, *23*(01), 17-23.

Egan, R., Stockley, D., Lam, C. Y., Kinderman, L., & Youmans, A. S. (2016). Research ethics board (REB) members' preparation for, and perceived knowledge of research ethics. *Journal of Academic Ethics*, *14*(3), 191-197.

Elwell, L., Grogan, S., & Coulson, N. (2010). Adolescents living with cancer: the role of computer-mediated support groups. *Journal of Health Psychology*, *16*(2), 236-248.

Ess, C. (2002). Ethical decision-making and Internet research: recommendations from the aoir ethics working committee. *Readings in Virtual Research Ethics: Issues and Controversies*, 27-44.

Ewing, L. J., Long, K., Rotondi, A., Howe, C., Bill, L., & Marsland, A. L. (2009). Brief report: A pilot study of a web-based resource for families of children with cancer. *Journal of Pediatric Psychology*, *34*(5), 523-529.

Eysenbach, G., & Till, J. E. (2001). Ethical issues in qualitative research on internet communities. *BMJ*, *323*(7321), 1103-1105.

Fasciano, K. M., Souza, P. M., Braun, I., & Trevino, K. (2015). An innovative website in the United States for meeting the emotional and supportive care needs of young adults with cancer. *Journal of Adolescent and Young Adult Oncology*, *4*(1), 44-49.

Fazil, Q., Aujla, N., Catherine Hale, R. N., & Kai, J. (2015). Unequal treatment: health care experiences and needs of patients with cancer from minority ethnic communities. *Diversity & Equality in Health and Care, 12*(3), 95-103.

Feldman, M. S., Sköldberg, K., Brown, R. N., & Horner, D. (2004). Making sense of stories: a rhetorical approach to narrative analysis. *Journal of Public Administration Research and Theory*, *14*(2), 147-170.

Fernandez, C. V., & Barr, R. D. (2006). Adolescents and young adults with cancer: an orphaned population. *Paediatrics & Child Health*, *11*(2), 103-106.

Flick, U. (2017). Mantras and myths the disenchantment of mixed-methods research and revisiting triangulation as a perspective. *Qualitative Inquiry*, *23*(1), 46-57.

Fisher, C. B. (1993). Integrating science and ethics in research with high-risk children and youth. *Social Policy Report, 7*(4), 1-27.

Fox, F. E., Morris, M., & Rumsey, N. (2007). Doing synchronous online focus groups with young people methodological reflections. *Qualitative Health Research*, *17*(4), 539-547.

Fouka, G & Mantzorou**,** M. (2011). What are the major ethical issues in conducting research? Is there a conflict between the research ethics and the nature of nursing?. *Health Science Journal*, *5*(1), 3-14.

Frankel, M. S., & Siang, S. (1999). Ethical and legal aspects of human subjects research on the Internet: A Report of a Workshop June 10-11, 1999. Workshop organised by the American Association for the Advancement of Science.

Fraser, L. K., Miller, M., Aldridge, J., McKinney, P. A., Parslow, R. D., & Hain, R. (2011). *Life limiting and life threatening conditions in children and young people in the United Kingdom; national and regional prevalence in relation to socioeconomic status and ethnicity. Final report for Children's Hospice UK*. Leeds: Division of Epidemiology, University of Leeds.

Freer, Y., McIntosh, N., Teunisse, S., Anand, K. J., & Boyle, E. M. (2009). More information, less understanding: a randomized study on consent issues in neonatal research. *Pediatrics*, *123*(5), 1301-1305.

Galman, S. C. (2016). *The good, the bad, and the data: Shane the lone ethnographer's basic guide to qualitative data analysis*. Abingdon: Routledge.

General Medical Council. (2008). *Seeking patients' consent: the ethical considerations*. London: General Medical Council.

Gibson, S., Benson, O., & Brand, S. L. (2013). Talking about suicide: confidentiality and anonymity in qualitative research. *Nursing Ethics*, *20*(1), 18-29.

Gittens, D. (2004). The historical construction of childhood. In M. J. Kehily (Ed.), *An Introduction to Childhood Studies* (pp. 25-38). London: Open University Press.

Gosling, S. D., & Mason, W. (2015). Internet research in psychology. *Annual Review of Psychology*, *66*, 877-902.

Guadagno, R. E., Muscanell, N. L., & Pollio, D. E. (2013). The homeless use Facebook?! Similarities of social network use between college students and homeless young adults. *Computers in Human Behavior*, *29*(1), 86-89.

Guillemin, M., Gillam, L., Rosenthal, D., & Bolitho, A. (2012). Human research ethics committees: examining their roles and practices. *Journal of Empirical Research on Human Research Ethics*, *7*(3), 38-49.

Guillemin, M., Gillam, L., Rosenthal, D., & Bolitho, A. (2010). Resources employed by health researchers to ensure ethical research practice. *Journal of Empirical Research on Human Research Ethics*, *5*(2), 21-34.

Guta, A., Nixon, S. A., & Wilson, M. G. (2013). Resisting the seduction of "ethics creep": Using Foucault to surface complexity and contradiction in research ethics review. *Social Science & Medicine*, *98*, 301-310.

Gysels, M., Evans, C. J., Lewis, P., Speck, P., Benalia, H., Preston, N. J. & Higginson, I. J. (2013). MORECare research methods guidance development: recommendations for ethical issues in palliative and end-of-life care research. *Palliative Medicine*, *27*(10), 908-917.

Hartling, L., Hamm, M. P., Milne, A., Vandermeer, B., Santaguida, P. L., Ansari, M., & Dryden, D. M. (2013). Testing the risk of bias tool showed low reliability between individual reviewers and across consensus assessments of reviewer pairs. *Journal of Clinical Epidemiology*, *66*(9), 973-981.

Hain, R., Devins, M., Hastings, R., & Noyes, J. (2013). Paediatric palliative care: development and pilot study of a 'Directory' of life-limiting conditions. *BMC Palliative Care*, *12*(1), 43.

Hair, N., & Clark, M. (2007). The ethical dilemmas and challenges of ethnographic research in electronic communities. *International Journal of Market Research*, *49*(6), 781-800.

Hammersley, M., & Atkinson, P. (2007). *Ethnography: principles in practice*. Abingdon: Routledge.

Hammersley, M. (2009). Against the ethicists: on the evils of ethical regulation. *International Journal of Social Research Methodology*, *12*(3), 211-225.

Han, J. Y., Hou, J., Kim, E., & Gustafson, D. H. (2014). Lurking as an active participation process: a longitudinal investigation of engagement with an online cancer support group. *Health Communication*, *29*(9), 911-923.

Hanna, P. (2012). Using internet technologies (such as Skype) as a research medium: a research note. *Qualitative Research*, *12*(2), 239-242.

Hannes, K., Lockwood, C., & Pearson, A. (2010). A comparative analysis of three online appraisal instruments' ability to assess validity in qualitative research. *Qualitative Health Research*, *20*(12), 1736-1743.

Health Research Authority. Research Ethics Committees (RECs). Accessed on August 3rd 2016. Accessed from http://www.hra.nhs.uk/about-the-hra/our-committees/research-ethics-committees-recs/

Hedgecoe, A. (2009). "A form of practical machinery": the origins of research ethics committees in the UK, 1967–1972. *Medical History*, *53*(03), 331-350.

Henderson, E. M., Law, E. F., Palermo, T. M., & Eccleston, C. (2012). Case study: Ethical guidance for pediatric e-health research using examples from pain research with adolescents. *Journal of Pediatric Psychology*, *37*(10), 1116-1126.

Henderson, E. M., Rosser, B. A., Keogh, E., & Eccleston, C. (2012). Internet sites offering adolescents help with headache, abdominal pain, and dysmenorrhoea: a description of content, quality, and peer interactions. *Journal of Pediatric Psychology*, *37*(3), 262-271.

Henderson, M., Johnson, N. F., & Auld, G. (2013). Silences of ethical practice: dilemmas for researchers using social media. *Educational Research and Evaluation*, *19*(6), 546-560.

Hewson, C., & Buchanan, T. (2013). *Ethics guidelines for internet-mediated research*. London: The British Psychological Society.

Hinds, P. S., Burghen, E. A., & Pritchard, M. (2007). Conducting end-of-life studies in pediatric oncology. *Western Journal of Nursing Research*, *29*(4), 448-465.

Higgins, J. P., Altman, D. G., Gøtzsche, P. C., Jüni, P., Moher, D., Oxman, A. D., & Sterne, J. A. (2011). The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ*, *343*, 5928.

Horrigan, J. B., & Smith, A. (2008). Home Broadband Adoption 2008. PewResearch Center.

Huang, J. S., Dillon, L., Terrones, L., Schubert, L., Roberts, W., Finklestein, J., Swartz, M. C., Norman, G. J. & Patrick, K. (2014). Fit4Life: a weight loss intervention for children who have survived childhood leukemia. *Pediatric Blood & Cancer*, *61*(5), 894-900.

Hudson, J. M., & Bruckman, A. (2004). "Go away": participant objections to being studied and the ethics of chatroom research. *The Information Society*, *20*(2), 127-139.

Humphreys, L. (1970). Tearoom trade. *Trans-action*, *7*(3), 10-25.

Hunter, D. (2014). Can significant differences in regulating medical and non-medical research be justified?. *Monash Bioethics Review*, *32*(3), 254-267.

Hunter, D. (2011). The irrationality of research ethics regulation in the UK: is medical research really the only risky research?. Accessed on March 14th 2016. Available at http://dx.doi.org/10.2139/ssrn.1926152

Hunter, D., & Pierscionek, B. K. (2007). Children, Gillick competency and consent for involvement in research. *Journal of Medical Ethics*, *33*(11), 659-662.

Im, E. O., & Chee, W. (2006). An online forum as a qualitative research method: practical issues. *Nursing Research*, *55*(4), 267.

International Telecommunication Union. (2014). The World in 2014 - ICT Facts and Figures. Geneva, Switzerland: International Telecommunication Union.

Ivanov, L., and Oden, T. L. (2013). Public health nursing, ethics and human rights. *Public Health Nursing*, *30*(3), 231-8.

Jääskeläinen, J., Haltia, M., & Servo, A. (1986). Atypical and anaplastic meningiomas: radiology, surgery, radiotherapy, and outcome. *Surgical Neurology*, 25(3), 233-42

Jackson, M. K., Burns, K. K., & Richter, M. S. (2014). Confidentiality and treatment decisions of minor clients: a health professional's dilemma & policy makers challenge. *SpringerPlus*, *3*(1), 320.

James, A., Jenks, C., & Prout, A. (1998). *Theorizing Childhood*. New York: Teachers College Press.

James, N., & Busher, H. (2009). *Online interviewing*. London: Sage Publications.

Jamieson, L., & Milne, S. (2012). Children and young people's relationships, relational processes and social change: reading across worlds. *Children's Geographies*, *10*(3), 265-278.

Jennings, S. L. (2010). Two models of social science research ethics review. *Research Ethics Review*, *6*(3), 86-90.

Jibb, L. A., Stevens, B. J., Nathan, P. C., Seto, E., Cafazzo, J. A., & Stinson, J. N. (2014). A smartphone-based pain management app for adolescents with cancer: establishing system requirements and a pain care algorithm based on literature review, interviews, and consensus. *JMIR research protocols*, *3*(1), e15.

Joinson, A. N. (2001). Self-disclosure in computer-mediated communication: the role of self-awareness and visual anonymity. *European Journal of Social Psychology*, *31*(2), 177-192.

Joinson, A. (2007). *Oxford Handbook of Internet Psychology*. Oxford: Oxford University Press.

Jones, S. (Ed.). (1998). *Doing Internet research: Critical issues and Methods for Examining the Net*. Thousands Oaks, Californa: Sage Publications.

Juritzen, T. I., Grimen, H., & Heggen, K. (2011). Protecting vulnerable research participants: a Foucault-inspired analysis of ethics committees. *Nursing Ethics*, *18*(5), 640-650.

Katikireddi, S. V., Egan, M., & Petticrew, M. (2015). How do systematic reviews incorporate risk of bias assessments into the synthesis of evidence? A methodological study. *Journal of Epidemiology and Community Health*, *69*(2), 189-195.

Keim-Malpass, J., & Steeves, R. H. (2012). Talking with death at a diner: young women's online narratives of cancer. *Oncology Nursing Forum-Oncology Nursing Society*, *39*(4), 373-378.

Keipi, T., & Oksanen, A. (2014). Self-exploration, anonymity and risks in the online setting: Analysis of narratives by 14–18-year olds. *Journal of Youth Studies*, *17*(8), 1097-1113.

Kelly, D. (2008). *The physical and emotional impact of cancer in adolescents and young adults* (pp. 23-43). Oxford: Blackwell Publishing Ltd.

Kennedy, E. T. (2008). Implementing ethically-sound research on online health-related support groups. *Internet Journal of Allied Health Sciences and Practice*, *6*(4), 9.

King, S. A. (1996). Researching Internet communities: proposed ethical guidelines for the reporting of results. *The Information Society*, *12*(2), 119-128.

Kirk, S. (2007). Methodological and ethical issues in conducting qualitative research with children and young people: a literature review. *International Journal of Nursing Studies*, *44*(7), 1250-1260.

Klitzman, R. (2012). From anonymity to "open doors": IRB responses to tensions with researchers. *BMC Research Notes*, *5*(1), 347.

Kondracki, N. L., Wellman, N. S., & Amundson, D. R. (2002). Content analysis: review of methods and their applications in nutrition education. *Journal of Nutrition Education and Behavior*, *34*(4), 224-230.

Kosinski, M., Stillwell, D., & Graepel, T. (2013). Private traits and attributes are predictable from digital records of human behavior. *Proceedings of the National Academy of Sciences*, *110*(15), 5802-5805.

Kreicbergs, U., Valdimarsdóttir, U., Onelöv, E., Henter, J. I., & Steineck, G. (2004). Talking about death with children who have severe malignant disease. *New England Journal of Medicine*, *351*(12), 1175-1186.

Krugman, S., & Shapiro, S. (1971). Experiments at the Willowbrook State School. *The Lancet*, *297*(7706), 966-967.

Kuhlau, F., Eriksson, S., Evers, K., & Höglund, A. T. (2008). Taking due care: moral obligations in dual use research. *Bioethics*, *22*(9), 477-487.

Lana, A., Faya-Ornia, G., & López, M. L. (2014). Impact of a web-based intervention supplemented with text messages to improve cancer prevention behaviors among adolescents: Results from a randomized controlled trial. *Preventive Medicine*, *59*, 54-59.

Lasagna, L. O. U. I. S. (1968). Some ethical problems in clinical investigation. *South African Medical Journal*, *42*(1), 2-5.

Leask, J., Booy, R., & McIntyre, P. B. (2010). MMR, Wakefield and the Lancet: what can we learn. *Medical Journal of Australia*, *193*, 5-7.

Levine, D., Madsen, A., Wright, E., Barar, R. E., Santelli, J., & Bull, S. (2011). Formative research on MySpace: online methods to engage hard-to-reach populations. *Journal of Health Communication*, *16*(4), 448-454.

Lewis, D., Gundwardena, S., & El Saadawi, G. (2005). Caring connection: developing an Internet resource for family caregivers of children with cancer. *Computers, Informatics, Nursing*, *23*(5), 265-274.

Lewis, K., Kaufman, J., Gonzalez, M., Wimmer, A., & Christakis, N. (2008). Tastes, ties, and time: a new social network dataset using Facebook. com. *Social networks*, *30*(4), 330-342.

Lidz, C. W., & Garverich, S. (2013). What the ANPRM missed: additional needs for IRB reform. *The Journal of Law, Medicine & Ethics*, *41*(2), 390-396.

Lindsay, D. F., Monotti, A., Paterson, M., & Chin, A. (2007). Legal issues in e-research: dataset acquisition, accessibility and annotation e-research technologies project (Dart). Accessed January 20th 2016. Available at http://dx.doi.org/10.2139/ssrn.1160126

Lomborg, S. (2012). Researching communicative practice: web archiving in qualitative social media research. *Journal of Technology in Human Services*, *30*(3-4), 219-231.

Lucey, B. P., Nelson-Rees, W. A., & Hutchins, G. M. (2009). Henrietta Lacks, HeLa cells, and cell culture contamination. *Archives of Pathology & Laboratory Medicine*, *133*(9), 1463-1467.

Lyratzopoulos, G., Elliott, M., Barbiere, J. M., Henderson, A., Staetsky, L., Paddison, C., & Roland, M. (2012). Understanding ethnic and other socio-demographic differences in patient experience of primary care: evidence from the English General Practice Patient Survey. *BMJ Quality & Safety*, *21*(1), 21-29.

Macpherson, C. F., Linder, L. A., Ameringer, S., Erickson, J., Stegenga, K., & Woods, N. F. (2014). Feasibility and acceptability of an iPad application to explore symptom clusters in adolescents and young adults with cancer. *Pediatric Blood & Cancer*, *61*(11), 1996-2003.

Madge, C. (2007). Developing a geographers' agenda for online research ethics. *Progress in Human Geography*, *31*(5), 654-674.

Madhavan, S., Sanders, A. E., Chou, W. Y. S., Shuster, A., Boone, K. W., Dente, M. A., & Hesse, B. W. (2011). Pediatric palliative care and eHealth: opportunities for patient-centered care. *American Journal of Preventive Medicine*, *40*(5), S208-S216.

Majeed-Ariss, R., Hall, A. G., McDonagh, J., Fallon, D., & Swallow, V. (2015). Mobile phone and tablet apps to support young people's management of their physical long-term conditions: a systematic review protocol. *JMIR Research Protocols*, *4*(2), e40.

Malik, S., & Coulson, N. S. (2011). The therapeutic potential of the internet: exploring self-help processes in an internet forum for young people with inflammatory bowel disease. *Gastroenterology Nursing*, *34*(6), 439-448.

Markham, A., & Buchanan, E. (2012). Ethical decision-making and Internet research: Version 2.0. Recommendations from the AoIR Ethics Working Committee. Accessed on January 20th 2015. Available from www.aoir. org/reports/ethics2. pdf.

McGuire, B., Henderson, E., & McGrath, P. (2016). Translating e-pain research into patient care. *Pain*, 158(2), 190-193.

McLaughlin, M., Nam, Y., Gould, J., Pade, C., Meeske, K. A., Ruccione, K. S., & Fulk, J. (2012). A videosharing social networking intervention for young adult cancer survivors. *Computers in Human Behavior*, *28*(2), 631-641.

McNamara, P. M. (2013). Giving voice to children and young people in research: Applying rights-based frameworks to meet ethical challenges. *Developing Practice: The Child, Youth and Family Work Journal*, *37,* 55-57.

Luppicini, R. (Ed.). (2008). *Handbook of research on technoethics*. New York: IGI Global.

Milgram, S. (1978). Obedience to authority. Chicago: Ziff-Davis Publishing Company.

Mo, P. K., Malik, S. H., & Coulson, N. S. (2009). Gender differences in computer-mediated communication: a systematic literature review of online health-related support groups. *Patient Education and Counseling*, *75*(1), 16-24.

Modi, N., Vohra, J., Preston, J., Elliott, C., Van't Hoff, W., Coad, J., Gibson, F., Partridge, L., Brierley, J., Larcher, V., Greenough, A., & Working Party of the Royal College of Paediatrics and Child Health. (2014). Guidance on clinical research involving infants, children and young people: an update for researchers and research ethics committees. *Archives of Disease in Childhood*, *99*(10), 887-91.

Mohrmann, C., Henry, J., Hauff, M., & Hayashi, R. J. (2015). Neurocognitive outcomes and school performance in solid tumor cancer survivors lacking therapy to the central nervous system. *Journal of Personalized Medicine*, *5*(2), 83-90.

Mokkink, L. B., Van der Lee, J. H., Grootenhuis, M. A., Offringa, M., & Heymans, H. S. (2008). Defining chronic diseases and health conditions in childhood (0–18 years of age): National consensus in the Netherlands. *European Journal of Pediatrics*, *167*(12), 1441-1447.

Moody, L., Turner, A., Osmond, J., Hooker, L., Kosmala-Anderson, J., & Batehup, L. (2015). Web-based self-management for young cancer survivors: consideration of user requirements and barriers to implementation. *Journal of Cancer Survivorship*, *9*(2), 188-200.

Department of Health. (2013). The Handbook to the NHS Constitution. London: Department of Health.

Nicholls, S. G., Hayes, T., Brehaut, J. C., Carroll, K., McDonald, M., Weijer, C., & Fergusson, D. (2014). Watching the watchers: a scoping review of empirical studies evaluating research ethics review. Paper presented at 35th Meeting of the Society of Clinical Trials, Philadelphia, PA. Accessed on February 13th 2016. Accessed from: https://www.researchgate.net/publication/262379596_Watching_the_watchers_a_scoping_review_of_empirical_studies_evaluating_research_ethics_review

Nilsson, J., Jervaeus, A., Lampic, C., Eriksson, L. E., Widmark, C., Armuand, G. M., & Wettergren, L. (2014). 'Will I be able to have a baby?' Results from online focus group discussions with childhood cancer survivors in Sweden. *Human Reproduction*, 29(12), 2704-2711.

Nissenbaum, H. (2009). *Privacy in Context: technology, policy, and the integrity of social life*. Stanford, California: Stanford University Press.

Nosek, B. A., Banaji, M. R., & Greenwald, A. G. (2002). E-research: ethics, security, design and control in psychological research on the Internet. *Journal of Social Issues*, *58*(1), 161-176.

Nwosu, A. C., Debattista, M., Rooney, C., & Mason, S. (2014). Social media and palliative medicine: a retrospective 2-year analysis of global Twitter data to evaluate the use of technology to communicate about issues at the end of life. *BMJ Supportive & Palliative care*, *5*(2):207-12.

O'Conner-Von, S. (2009). Coping with cancer: a web-based educational program for early and middle adolescents. *Journal of Pediatric Oncology Nursing*, *26*(4), 230-241.

O'Reilly, M., Dixon-Woods, M., Angell, E., Ashcroft, R., & Bryman, A. (2009). Doing accountability: a discourse analysis of research ethics committee letters. *Sociology of Health & Illness*, *31*(2), 246-261.

Ocholla, D. (2011). Is African information ethics unique?. Paper presented at the 6th Biennial ProLISSA Conference, Milwauke*,* 9th -11th March 2011. Milwauke, University of Wisconsin.

Office for National Statistics. (2016). Social Capital. London: Office for National Statistics.

Office for National Statistics. (2008). Internet Access - Households and Individuals, 2008. London: Office for National Statistics.

Orgad, Shani. (2009). How can researchers make sense of the issues involved in collecting and interpreting online and offline data? In: Markham, A. and Baym, N., (eds.) *Internet inquiry: conversations about method*. SAGE, Thousand Oaks, CA, 33-53.

Picot, A., & Wernick, C. (2007). The role of government in broadband access. *Telecommunications Policy*, *31*(10), 660-674.

Popay, J., Roberts, H., Sowden, A., Petticrew, M., Arai, L., Rodgers, M. & Duffy, S. (2006). Guidance on the conduct of narrative synthesis in systematic reviews. A product from the ESRC methods programme. Lancaster: Institute of Health Research.

Punch, S. (2002). Research with children: the same or different from research with adults?. *Childhood*, *9*(3), 321-341.

Purcell, K. 2011. Trends in teen communication and social media use [Online]. Accessed on November 20th 2014. Accessed from http://www.pewinternet.org/2011/02/09/trends-in-teen-communication-and-social-media-use/

Qvortrup, J. (2009). Are children human beings or human becomings? A critical assessment of outcome thinking. *Rivista Internazionale di Scienze Sociali*, 631-653.

Rajadhyaksha, V. (2010). Conducting feasibilities in clinical trials: an investment to ensure a good study. *Perspectives in Clinical Research*, *1*(3), 106-109.

Resnik, D. B. (2014). Scientific misconduct and research integrity. In *Handbook of global bioethics* (pp. 799-810). Springer: Netherlands.

Ritterband, L. M., & Palermo, T. M. (2009). Introduction to the special issue: eHealth in pediatric psychology. *Journal of Pediatric Psychology*, *34* (5): 453-456.

Robinson, J. K., Gaber, R., Hultgren, B., Eilers, S., Blatt, H., Stapleton, J., & Martini, M. (2014). Skin self-examination education for early detection of melanoma: a randomized controlled trial of Internet, workbook, and in-person interventions. *Journal of Medical Internet Research*, *16*(1), e7.

Rodham, K., & Gavin, J. (2006). The ethics of using the internet to collect qualitative research data. *Research Ethics Review*, *2*(3), 92-97.

Rolfe, G. (2006). Validity, trustworthiness and rigour: quality and the idea of qualitative research. *Journal of Advanced Nursing*, *53*(3), 304-310.

Rourke, L., Anderson, T., Garrison, D. R., & Archer, W. (2001). Methodological issues in the content analysis of computer conference transcripts. *International Journal of Artificial Intelligence in Education*, *12*, 8-22.

Rowbotham, M. C., Astin, J., Greene, K., & Cummings, S. R. (2013). Interactive informed consent: randomized comparison with paper consents. *PLoS One*, *8*(3), e58603.

Ruland, C. M., Borosund, E., & Varsi, C. (2009). User requirements for a practice-integrated nurse-administered online communication service for cancer patients. *Nursing Informatics*, *145*, 221-225.

Saginur, M. (2014). From Research "Involving" Humans to Research "Affecting" Humans: A Proposal for a Principled Expansion of Research Ethics' Jurisdiction to Create Traction for a Philosophy of Technology. *Laws*, *3*(3), 509-528.

Sandelowski, M. (2010). What's in a name? Qualitative description revisited. *Research in Nursing & Health*, *33*(1), 77-84.

Sansom-Daly, U. M., Wakefield, C. E., Bryant, R. A., Butow, P., Sawyer, S., Patterson, P., & Cohn, R. J. (2012). Online group-based cognitive-behavioural therapy for adolescents and young adults after cancer treatment: a multicenter randomised controlled trial of Recapture Life-AYA. *BMC cancer*, *12*(1), 339.

Saunders, C. L., Abel, G. A., & Lyratzopoulos, G. (2015). Inequalities in reported cancer patient experience by socio-demographic characteristic and cancer site: evidence from respondents to the English Cancer Patient Experience Survey. *European Journal of Cancer Care*, *24*(1), 85-98.

Schaap, G., Konig, R., Renckstorf, K., & Wester, F. (2009). Conceptualizing television news interpretation by its viewers: the concept of interpretive complexity. *Interpreting Television News*, *7*, 61.

Scherer, D. G., Annett, R. D., & Brody, J. L. (2007). Ethical issues in adolescent and parent informed consent for pediatric asthma research participation. *Journal of Asthma*, *44*(7), 489-496.

Schneider, S. J., Kerwin, J., Frechtling, J., & Vivari, B. A. (2002). Characteristics of the discussion in online and face-to-face focus groups. *Social Science Computer Review*, *20*(1), 31-42.

Schuman, S. H., Olansky, S., Rivers, E., Smith, C. A., & Rambo, D. S. (1955). Untreated syphilis in the male negro: background and current status of patients in the Tuskegee study. *Journal of Chronic Diseases*, *2*(5), 543-558.

Scott, J. T., Harmsen, M., Prictor, M. J., Sowden, A. J., & Watt, I. (2003). Interventions for improving communication with children and adolescents about their cancer. *The Cochrane Database of Systematic Reviews, 3.*

Shah, N. (2011). Ethical issues in biomedical research and publication. *Journal of Conservative Dentistry*, *14*(3), 205.

Shah, S., Whittle, A., Wilfond, B., Gensler, G., & Wendler, D. (2004). How do institutional review boards apply the federal risk and benefit standards for pediatric research?. *The Journal of the American Medical Association, 291*(4), 476-482.

Shapiro, R. B., & Ossorio, P. N. (2013). Regulation of online social network studies. *Science*, *339*(6116), 144-145.

Silverman, D. (Ed.). (2016). *Qualitative research*. London: Sage.

Silverman, H. I. (2011). Qualitative analysis in financial studies: Employing ethnographic content analysis. *Journal of Business & Economics Research*, *7*(5), 133-136.

Sin, C. H. (2005). Seeking informed consent: reflections on research practice. *Sociology*, *39*(2), 277-294.

Spriggs, M. (2010). *Understanding consent in research involving children: the ethical issues*. *A handbook for human research ethics committees and researchers.* Children's Bioethics Centre, The Royal Children's Hospital, Melbourne.

Sparkes, A. C. (2001). Myth 94: qualitative health researchers will agree about validity. *Qualitative Health Research*, *11*(4), 538-552.

Stevens, M. M., Lord, B. A., Proctor, M. T., Nagy, S., & O'Riordan, E. (2010). Research with vulnerable families caring for children with life-limiting conditions. *Qualitative Health Research*, *20*(4), 496-505.

Stinson, J. N., Jibb, L. A., Nguyen, C., Nathan, P. C., Maloney, A. M., Dupuis, L. L., & Portwine, C. (2013). Development and testing of a multidimensional iPhone pain assessment application for adolescents with cancer. *Journal of Medical Internet Research*, *15*(3), e51.

Swift, C. L. (2016). Conflating rules, norms, and ethics in intercollegiate forensics. *Speaker & Gavel*, *43*(1), 5.

Tates, K., Zwaanswijk, M., Otten, R., van Dulmen, S., Hoogerbrugge, P. M., Kamps, W. A., & Bensing, J. M. (2009). Online focus groups as a tool to collect data in hard-to-include populations: examples from paediatric oncology. *BMC Medical Research Methodology*, *9*(1), 15.

Taylor, L. (2013). The scramble for Africa's data. Accessed on February 20th, 2015. Available at http://blogs.oii.ox.ac.uk/policy/the-scramble-for-africas-data/ 2015.

Taylor, R. M., Gibson, F., & Franck, L. S. (2008). The experience of living with a chronic illness during adolescence: a critical review of the literature. *Journal of Clinical Nursing*, *17*(23), 3083-3091.

Thomas, S. B., & Quinn, S. C. (1991). The Tuskegee syphilis study, 1932 to 1972: implications for HIV education and AIDS risk education programs in the black community. *American Journal of Public Health*, *81*(11), 1498-1505.

Tilley, S. A. (2008). A troubled dance: doing the work of research ethics review. *Journal of Academic Ethics*, *6*(2), 91-104.

Tisdall, E. K. M., & Punch, S. (2012). Not so 'new'? Looking critically at childhood studies. *Children's Geographies*, *10*(3), 249-264.

Tisdall, E. K. M. (2012). The challenge and challenging of childhood studies? Learning from disability studies and research with disabled children. *Children & Society*, *26*(3), 181-191.

Torres, L., Ojeda, J., Monguet, J., & Gonzalez, H. (2012). PLEs from virtual ethnography to social web. *Digital Education Review*, (20), 37-49.

Vaismoradi, M., Turunen, H., & Bondas, T. (2013). Content analysis and thematic analysis: Implications for conducting a qualitative descriptive study. *Nursing & Health Sciences*, *15*(3), 398-405.

Valsecchi, M. G., Silvestri, D., Covezzoli, A., & De Lorenzo, P. (2008). Web-based international studies in limited populations of pediatric leukemia. *Pediatric Blood & Cancer*, *50*(2), 270-273.

van Cleave, J., Gortmaker, S. L., & Perrin, J. M. (2010). Dynamics of obesity and chronic health conditions among children and youth. *The Journal of the American Medical Association, 303*(7), 623-630.

Vayena, E., Mastroianni, A., & Kahn, J. (2013). Caught in the web: informed consent for online health research. *Science Translational Medicine, 5*(173), 173-176.

Vig, E., Irwin, S., & Casarett, D. (2010). Can my patient make that decision? Assessing capacity to make decisions about clinical care and research participation (516). *Journal of Pain and Symptom Management*, *39*(2), 413.

Wagener, D. K., Sporer, A. K., Simmerling, M., Flome, J. L., An, C., & Curry, S. J. (2004). Human participants challenges in youth-focused research: perspectives and practices of IRB administrators. *Ethics & Behavior*, *14*(4), 335-349.

Ward, E., Jemal, A., Cokkinides, V., Singh, G. K., Cardinez, C., Ghafoor, A., & Thun, M. (2004). Cancer disparities by race/ethnicity and socioeconomic status. *CA: A Cancer Journal for Clinicians*, *54*(2), 78-93.

Watson, J. B., & Rayner, R. (1920). Conditioned emotional reactions. *Journal of Experimental Psychology*, *3*(1), 1.

Whelan, J., & Fern, L. (2008). Cancer in adolescence: incidence and policy issues. *Cancer Care for Adolescents and Young Adults,* 7-22.

White, M. D., & Marsh, E. E. (2006). Content analysis: a flexible methodology. *Library Trends*, *55*(1), 22-45.

Whitmore, A., Agarwal, A., & Da Xu, L. (2015). The Internet of Things—a survey of topics and trends. *Information Systems Frontiers*, *17*(2), 261-274.

Wiles, R., Bengry-Howell, A., Crow, G., & Nind, M. (2013). But is it innovation?: The development of novel methodological approaches in qualitative research. *Methodological Innovations Online*, *8*(1), 18-33.

Wilson, D. (2011). Creating the 'ethics industry': Mary Warnock, in vitro fertilization and the history of bioethics in Britain. *BioSocieties*, *6*(2), 121-141.

Woodgate, R. (2008). Getting on with life during treatment. *Cancer Care for Adolescents and Young Adults*, 130-145.

Wu, W. W., Johnson, R., Schepp, K. G., & Berry, D. L. (2011). Electronic self-report symptom and quality of life for adolescent patients with cancer: a feasibility study. *Cancer Nursing*, *34*(6), 479-486.

Zahedi, M., Mashal, H., & Salehi, S. M. (2011). An online community for the deaf. *Procedia Computer Science*, *3*, 1089-1093.

Zebrack, B., Bleyer, A., Albritton, K., Medearis, S., & Tang, J. (2006). Assessing the health care needs of adolescent and young adult cancer patients and survivors. *Cancer*, *107*(12), 2915-2923.

Zimmer, M. (2010). “But the data is already public”: on the ethics of research in Facebook. *Ethics and Information Technology*, *12*(4), 313-325.

Zwaanswijk, M., Tates, K., van Dulmen, S., Hoogerbrugge, P. M., Kamps, W. A., & Bensing, J. M. (2007). Young patients', parents', and survivors' communication preferences in paediatric oncology: Results of online focus groups. *BMC Pediatrics*, *7*(1), 35.

Search terms for the systematic review per database

Pubmed search terms

(("internet"[MeSH Terms] OR "internet"[All Fields]) OR
web[All Fields] OR online[All Fields] OR
(mobile[All Fields] AND
("technology"[MeSH Terms] OR
"technologies"[All Fields])) OR
("text messaging"[MeSH Terms] OR
("text"[All Fields] AND "messaging"[All Fields]) OR
"text messaging"[All Fields]) OR
("telemedicine"[MeSH Terms] OR
"telemedicine"[All Fields]) OR "ehealth"[All Fields]) OR
e-health[All Fields] AND (ipad[All Fields] OR
ipads[All Fields] OR
iphone[All Fields] OR
("cell phones"[MeSH Terms] OR
"phones"[All Fields] OR
("smart"[All Fields] AND
"phone"[All Fields]) OR
"smart phone"[All Fields]) OR
"android"[All Fields]) OR
androids[All Fields] OR
(online[All Fields] AND
game[All Fields]) OR
(online[All Fields] AND
games[All Fields]) OR
("computers"[MeSH Terms] OR
"computers"[All Fields] OR
"computer"[All Fields]) OR
("computers"[MeSH Terms] OR

"computers"[All Fields]) OR
laptop[All Fields] OR
laptops[All Fields] OR
"apps"[All Fields] OR
(online[All Fields] AND applications[All Fields]) AND
("neoplasms"[MeSH Terms] OR
"neoplasms"[All Fields] OR
"cancer"[All Fields]) AND
("infant"[MeSH Terms] OR
"child"[MeSH Terms] OR
"adolescent"[MeSH Terms])
AND ("2007/01/01"[PDAT] : "2016/12/31"[PDAT])

Embase search terms

(cancer.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] OR exp neoplasm/) AND

((ipad or ipads or anroid or androids or online game or computer or computers or laptop or laptop or mobile applications or mobile apps or mobile app).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] AND

(internet/ OR computer program/ or mobile application/ OR mobile phone/ OR computer/ or personal digital assistant/ OR text messaging/ OR exp telemedicine/ OR telehealth/) AND (yr="2007 -Current" and child <unspecified age>)

PsychINFO search terms

(cancer.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
OR exp neoplasm/) AND

((ipad or ipads or anroid or androids or online game or computer or computers or laptop or laptop or mobile applications or mobile apps or mobile app).mp. [mp=title, abstract,

heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] AND

(internet/ OR computer program/ or mobile application/ OR mobile phone/ OR computer/ or personal digital assistant/ OR
text messaging/ OR exp telemedicine/ OR telehealth/)
AND limit 23 to (adolescence <13 to 17 years> or adulthood <18+ years>)

Web of Science search terms

TOPIC: (internet) *OR*
TOPIC: (web) *OR*
TOPIC: (online) *OR*
TOPIC: (mobile technology) *OR*
TOPIC: (mobile technologies) *OR*
TOPIC: (text messaging) *OR*
TOPIC: (telemedicine) *OR*
TOPIC: (ehealth) *OR*
TOPIC: (e-health) AND
TOPIC: (ipad) *OR*
TOPIC: (ipads) *OR*
TOPIC: (iphone) *OR*
TOPIC: (iphones) *OR*
TOPIC: (smartphone*) *OR*
TOPIC: (android) *OR*
TOPIC: (androids) *OR*
TOPIC: (computer) *OR*
TOPIC: (computers) *OR*
TOPIC: (laptop) *OR*
TOPIC: (laptops) *OR*
TOPIC: (app) *OR*
TOPIC: (apps) *OR*
TOPIC: (mobile application) AND

TOPIC: (cancer) AND

TOPIC: (child*) *OR*

TOPIC: (teenage*) *OR*

TOPIC: (adolecen*) *OR*

TOPIC: (13 to 25) *OR*

TOPIC: (young person) *OR*

TOPIC: (young people)

Refined by: PUBLICATION YEARS: (2011 OR 2013 OR 2014 OR 2009 OR 2012 OR 2003 OR 2010 OR 2008 OR 2015 OR 2007)

Standardised data extraction form for the systematic review.

The extraction sheet has been adapted from Social Care Institute for Excellence (SCIE). 2005. Guidelines for preparing a research review: Appendix 2. Accessed on 24/8/2015 from http://www.scie.org.uk/opportunities/ commissions/files/appendix2.pdf.

Drafted on August 24th 2015 by Johanna Kempe and is project specific. This extraction sheet relates to a review titled "Internet-mediated research with young people with cancer: a systematic review of research methodologies and intervention efficacy."

The review is part of a project titled "Online Research: An Exploration of Guidance, Policies and Regulations Governing Research with Young People with Cancer", and will contribute towards an MPhil to PhD upgrade at the Institute of Child Health, UCL in March 2016.

Please remember to use the authors own words and not your interpretation.

Part I	**Administrative notes**
Date of review	
Reviewer initials	1. JK 2. EH
Decision following extraction	1. Remain included 2. Excluded (please specify reasons for exclusion)
Part II	**General information**
Full reference (in APA format)	
Document type	1. Article 2. Book 3. Book chapter 4. Other (please specify)

Has the document been peer reviewed?	1. Yes 2. No 3. Unsure
Short summary of article (250 words max)	
Part III	**Setting**
Area	1. Primary care setting 2. Secondary care setting 3. Tertiary care setting 4. Outpatient setting 5. Upper secondary school setting 6. University/college setting 7. Other (please specify)
Rationale given for setting (if not described please mark "not described")	
Other details of setting, if described (e.g. ICT class in a secondary school, outpatients ward in a tertiary care hospital)	
Part IV	**Sample**
Study sample inclusion/exclusion	1. Described (please list) 2. Not described

criteria (e.g. a certain age group, cancer type, stage of illness (remission, diagnosed within the past 6 months etc)	
Sampling method used	1. Random sampling 2. Snowballing 3. Theoretical sampling 4. Stratified sampling 5. Cluster sampling 6. Convenience sampling 7. Quota sampling 8. Panel sampling 9. Other (please specify)
Group	1. Patients (please describe) 2. Survivors (please describe) 3. Other (please describe)
Sample age group	
Sample size	N =
Gender distribution	
Ethnicity distribution	
Other sample distribution features	
Part V.	**Ethics**

REC committee approached for approval	1. Higher Education REC 2. NHS REC 3. No ethical approval needed 4. Other (please specify)
Please describe:	
i) Internet related ethical issues mentioned in the text	
ii) General ethical issues mentioned in the text	
Part VI. Data collection and Result	
Data collection environment (please list all that apply)	1. Online environment 2. Offline environment 3. Mobile environment (please specify the operating system) 4. Mix (please specify) 5. Other (please specify)
Data collection method (please list all that apply)	1. Focus group 2. Unstructured/semi-structured/ structured Interviews - offline (please specify) 3. Unstructured/semi-structured/ structured Interviews - online (please specify) 4. Social media - observational study of pre-existing social media, (please describe) 5. Social media - observational study of social media created for research purposes (please describe) 6. Observational study (other – please describe) 7. Online questionnaire 8. Offline questionnaire 9. Information from a database/Big data

	10. Online games 11. Mobile game 12. Mobile app 13. Online intervention (website based) 14. Mobile app intervention 15. Symptom checkers 16. Other (please specify)
Research type	1. Clinical trial- non-psychological(please specify) 2. Clinical trial-psychological (please specify) 3. Observational study 4. Other (please specify)
Mode of access	1. Computer 2. Laptop 3. Mobile device (e.g. phone, tablet) 4. Mix (please describe)
Result (please copy and paste)	
Conclusion	
Part VII. Stakeholder involvement	
Who create the Internet technology?	
Who was consulted prior to the study commencing?	
Other information regarding stakeholder involvement	
Part VIII. Implications	

Please list any implications for:	
Healthcare policy	•
Clinical practice	•
Research policy	•
Research practice	•

Outline of the nodes, analytical codes and attributes for the document analysis

This document is the fifth version (draft 13) of a code book for a document analysis titled "Ethical issues in Internet-mediated research with children and young people (aged 0 to 25 years) with life-limiting illnesses or life-threatening conditions: A document analysis of research ethics committee documentation". The document contains the definitions associated with the nodes, A-codes and the attributes. The codebook was drafted by JK with input from other members of the research team at the Louis Dundas Centre for Children's Palliative Care. It should not be used for other projects without the written approval of the original author.

Table 1: Nodes and definitions

Scientific evaluation		
Node	**Definition**	**Source(s)**
N-1	Recruitment: Portions of text relating to the way participants are recruited into the study. This includes, but is not limited to, discussion of recruitment through databases, health care professionals, flyers and other types of advertisement.	Angell and Dixon-Woods, (2009) Angell et al., (2008)
N-2	Sampling: Portions of text relating to the way participants are sampled. This includes, but is not limited to, eligibility and numbers to be recruited to the sample.	
N-3	Research question: Portions of text relating to the study hypotheses, aims and objectives.	
N-4	Procedure: Portions of text relating to the study methodology.	The node was added following discussion by EH and JK on 2016-05-25
N-5	Measurements: Portions of text relating to how outcomes are determined, the data is collected, particularly	

	questionnaire data, biological data and symptom data.	
N-6	Bias: Portions of text associated with systematic errors (e.g. in study design or data measurements).	
N-7	Feasibility: The likelihood of a study being delivered successfully and as planned.	
N-8	Data analysis: Portions of text relating to how the data is processed and analyzed	
N-9	Equipoise: Portions of text associated to the genuine uncertainty of the merits and/or benefits of the whole and/or part of study.	Cook and Sheets (2011) Note. The definition was revised following discussion by EH and JK on 2016-05-25
N-10	Other issues related to scientific evaluation: Portions of text related to scientific evaluations that are not captured by the other codes.	
Process errors		
Node	**Definition**	**Source(s)**
N-11	Procedural violation: Failures of the applicant to follow correct procedures in their application to the REC (e.g. submitting the wrong form).	Angell and Dixon-Woods, (2009) Angell et al., (2008)
N-12	Missing information: Information absent in the original application, or in the associated documents sent to the REC.	
N-13	Slip-ups: Minor spelling and/or grammatical errors and/or issues in the translation of research documents in the application to the REC or any of the associated documents.	The definition was revised following discussion by EH and JK on 2016-05-25
N-14	Discrepancies: Inconsistencies within the application or the associated documents given to the REC.	

N-15	Other related to process errors: Portions of text related to process errors in the REC applications or associated documents that are not captured by the other codes.	
Research involving young people		
Node	**Definition**	**Source(s)**
N-16	Responsibility for consent: Portions of text relating to the process of obtaining affirmation of participation from potential participants. This includes discussion of the consent or assent forms that researcher should use and the procedure for seeking consent.	Angell and Dixon-Woods, (2009) Angell et al., (2010)
N-17	Responsibility for assent: Portions of text relating to the process of obtaining affirmation of participation from potential participants. This includes discussion of the consent or assent forms that researcher should use and the procedure for seeking consent.	
N-18	Language and adjustments: Portions of text related to revisions to study documents which the REC cites as being requested due to the participant's age or developmental stage. It includes edits to consent or information sheets, revisions to the methodology or study protocols and procedures including changing the sample participants' age, allowances for perceived capacity and/or being a child (e.g. prevention of interference with school).	
N-19	Other issues related to research involving young people: Portions of text relating to research involving young people that are not captured by the other codes.	
Ethical principles		
Node	**Definition**	**Source(s)**

N-20	Privacy: Portions of text related to the collection, use, retention, disclosure and/or destruction of personally identifiable information. Specifically, this code relates to the steps taken to protect individuals. NB: data access and data sharing is covered by N-21 Confidentiality.	Chen and Zhao (2012)
N-21	Confidentiality: Portions of text related to who has access to it during the course of the study and how data is shared between a) the researcher and the participant, b) the participants, c) participants and their healthcare professional, and/or d) research team and healthcare professionals.	Zimmer (2010) The definition was revised following discussion by EH and JK on 2016-05-25
N-22	Anonymity: Portions of text related to the steps taken to protect information and the degree of control an individual has over what it is known about his or hers private information.	(Gibson et al., (2013)
N-23	Harm: Portions of text related to **negative effects** of participation including but not limited to detrimental physical and psychological.	The node was added following discussion by EH and JK on 2016-05-25 Note: The definition was revised following discussion by EH and JK on 2016-06-02.
N-24	Voluntariness: Portions of text related to the young person's and/or parent's autonomous choice as to whether he or she wishes to participate in the research process. It includes how participants are recruited in a way which respects their ability to retain their research participation as separate to the care they may be receiving by the research and/or clinical team supporting it. In addition this code applies to portions of the text relating to the right to refuse/withdraw participation in whole and/or parts of the study.	McNamara (2013) Vayena et al., (2013) The definition was revised following discussion by EH and JK on 2016-05-25

N-25	Consent process: Portions of text relating to who should be approached during the consent seeking process and the documents used during the consenting process (e.g. information sheets). **NB.** This code covers portions of text not covered by the code "Responsibility for consent and/or assent".	Vayena et al., (2013) Note. The definition was revised following discussion by EH and JK on 2016-05-25
N-26	Assent seeking: Portions of text relating to who should be approached during the consent seeking process. **NB.** This code covers portions of text not covered by the code "Responsibility for consent and/or assent".	Vayena et al., (2013)
N-27	Other ethical principles: Portions of text relating to ethical principles that are not captured by the other codes. **NB**. This code not apply to portions of the text relating to harm.	
The presence of an illness		
Node	**Definition**	**Source(s)**
N-28	Interference with clinical care: Portions of text describing issues arising from the extent to which research participation interferes with a young person's clinical care. This can also be applied to repeated measures that are part of clinical care.	Note. The definition was revised following discussion by EH and JK on 2016-05-25 Note. The definition was revised following discussion by EH and JK on 2016-06-02.
N-29	Importance of participation: Portions of text relating to why patients with an illness are recruited.	Dixon-Woods and Angell (2009)
N-30	Capacity: Portions of text relating to capacity for participation (this code includes intellectual and/or physical capacity). **NB**. This code should not be applied to capacity to consent.	Dixon-Woods and Angell (2009) Note. The definition was revised following discussion by EH and JK on 2016-05-25

N-31	Burden of participation: Portions of text relating to the actual or perceived burden of participation, including time taken to participate, costs associated with participation.	
N-32	Other issues related to the presence of an illness: Portions of text relating to the presence of an illness that are not captured by the other codes.	
The REC		
Node	**Definition**	**Source(s)**
N-33	Collaborative nature of decision: The emphasis on shared authorship of the decision and the REC as a collective unit and the shared authorship between the REC and the applicant(s).	O'Reilly et al., (2009) Definition revised after discussion between JK and EH on 2016-05-25
N-34	Holding applicants accountable: Instances where the REC appeals to the ethical, legal and/or scientific deficiencies of the applications or the research team.	Definition revised after discussion between JK and EH on 2016-06-02.
N-35	The individual nature of decision: Portion of the text relating to the individual nature of the decision and/or opinion (e.g. an individual REC member making a decision or expresses an opinion).	Added after discussion between JK and EH on 2016-05-25
N-36	Referring to specialist expertise: Instances where the REC appeals to specialist expertise (e.g. a statistician other institutions and/or a specialist patient groups including PPI, and/or regulative bodies giving advice and materials) to reinforce their requests, suggestions or directives for amendments. **NB**: this code excludes sub-committees.	Note. The definition was revised following discussion by EH and JK on 2016-05-25
N-37	Rituals: Portion of the text relating to processes and/or activities associated with meetings including (but not limited) to who takes the meeting minutes and how the REC are meeting (e.g. in private).	Added after discussion between JK and EH on 2016-06-02.

N-38	Administration: Portion of the text relating to study or REC-specific processes and/or activates that the applicant or REC members are expected to follow. This code should also be applied to portion of the text relating to standardised texts provided by the REC to the applicant.	Added after discussion between MBL, EH and JK on 2016-05-19 Note. Edited after discussion between JK and EH on 2016-05-25 as "Clerical information" and "Administration" significantly overlapped.
N-39	Further approvals: Portion of the text relating to any further approvals that the researcher may be required to obtain (e.g. registration with other organisations).	Added after discussion between JK and EH on 2016-05-25
N-40	Other issues related to the REC: Portions of text relating to the REC that are not captured by the other codes.	
Administration of the study		
Node	**Definition**	**Source(s)**
N-41	Start and end date: Portion of the text relating to when a study will start and/or end. In addition this node should be applied to portions of the text relating to study duration.	
N-42	Funding: Portion of the text relating to the funders and/or funding.	
N-43	Suitability of research staff: Portions of text relating to the appropriateness of research staff including who the person is, credentials, qualifications and training opportunities (e.g. accessing professional development course on statistics) and support systems in place to support the staff (e.g. psychological support).	Added after discussion between JK and EH on 2016-05-25 Definition revised after discussion between JK and EH on 2016-06-02.

N-44	Equipment: Portion of the text relating to the devices used during the study.	
N-45	Sponsor: Portions of text relating to study sponsorship.	Added after discussion between JK and EH on 2016-05-25
Outline of Opinion		
Node	**Definition**	**Source(s)**
N-46	Favourable with conditions: Portions of text relating to issues around further revisions/amendments and/or other changes requested by the REC following a favourable opinion and how the section was written.	Added after discussion between JK and EH on 2016-05-25
N-47	Favourable without conditions: Portions of the text relating to the outline of opinions where the REC does not require further revisions/amendments and/or other changes. Includes how the section was written.	Added after discussion between JK and EH on 2016-05-25
N-48	Other issues related to the outline of opinion not covered by other codes: Portions of the text relating to the REC opinion that are not captured by the other codes.	Added after discussion between JK and EH on 2016-05-25
Other		
Node	**Definition**	**Source(s)**

N-49	Revisions: Portions of text related to changes/adjustments to study documents which the REC request. It includes edits to consent or information sheets, revisions to the methodology or study protocols and procedures. **NB.** This code covers portions of text not covered by the code N-18 "Language and adjustments".	Added after discussion between JK and EH on 2016-05-25

Table 2: A-codes and definitions.

Number	A-code and description
A-1	The process behind the decision: The emphasis in the letters and minutes on the process leading up to the REC decision.
A-2	Clarity of the RECs recommendations: The difference between a mandatory and a suggested amendment.
A-3	Relationship between applicant and REC: The relationship between the REC and the applicant (e.g. the level of formality in the language used, the difference in implied power).
A-4	Conflicts: Instances where there is a disagreement between the applicant and the REC, between applicants or between individual REC members.

Table 3: Attributes with descriptions

Number	Name and description	Notes
Att-1: Decision: The REC opinion that is given to the	Favourable (without conditions): Approval of the application for a research study by the ethics committee without the need to make revisions.	Added after discussion between JK and EH on 2016-05-25

applicant after the REC meet.	Favourable (with conditions): Approval of the application for a research study by the ethics committee **with** the need to make revisions before the study can go ahead.	Added after discussion between JK and EH on 2016-05-25
	Provisional: The REC has identified some ethical issues within the application. The ethical issues will need to be addressed before the REC can provide a final opinion and the study can begin.	
	Unfavourable: A rejection of the application for a research study by the ethics committee.	
	Outside remit: Certain types of research (e.g. service evaluations) do not require a REC review, and these are not given an opinion. The REC in this instance reserves the right to defer the application to another body for approval (e.g. an audit committee).	
Att-2: Methodology This attribute applies to the research methodology used in the study.	Online discussion forum: An online discussion forum is a virtual space where individuals can connect and exchange information and support (Bender et al., 2011). It is usually text based, but posters can also post videos, pictures and other media.	
	Online focus group: A text-based group discussion conducted for the purpose of research on an Internet-based platform where participants are geographically disperse (Tates et al., 2009). Usually these groups are mediated by a researcher who poses questions to the group as in an offline focus group. Groups can be synchronous or asynchronous and can employ a variety of technologies to connect participants and researchers.	

	Internet-mediated clinical feasibility study: A study evaluating the capability of using Internet-mediated platforms to collect data prior to conducting a clinical trial (Rajadhyaksha, 2010). Examples include: - Smartphone applications - Symptom checkers - Pilot studies of online surveys - Pilot studies of outcomes for larger studies	
	Internet-mediated intervention: An intervention which aims to deliver a positive behavioural change where a majority of the content delivered via Internet-based platforms (Barak et al., 2009).	
	Other/Internet: Methodologies that are not captured by the other categories but which use internet mediated platforms.	
	Other/offline methodologies: Methodologies that does not include Internet platforms	.
Att-4 Document type: decision letter versus meeting minutes	Decision letter: A letter that is circulated to the applicants following a meeting with the REC. The letters contain details of the REC opinion, revisions and/or suggestions. The letter is written by staff attached to the REC.	Added after discussion between JK and EH on 2016-06-02
	Meeting minutes: A formal record of what happened during the meeting.	Added after discussion between JK and EH on 2016-06-02
Att-5 Participant age: This attribute applies to the participant's age and should be used when there is a	0-10 years old: Apply this code when the age range 0-10 years is explicitly mentioned.	**NB.** Select all codes that apply (e.g. if the age range of the study is 8-13 years, then use
	10-16 years old: Apply this code when the age range 10-16 years is mentioned.	

reference to the age of the participant expressed either as a number (e.g. 10-16 year olds) or expressed as a developmental/transitional stage (e.g. young people, child).	16-18 years old: Apply this code when the age range 16-18 years is mentioned.	code “0-10” and code “10-16).
	18-25 years old: Apply this code when the age range 18-25 years is mentioned.	
	Upper limit exceeded: Apply this code when the age range of the participants exceeds 25 years.	
	Age not defined but in range: Apply this code when a developmental stage (e.g. child, teenager) is mentioned but there is no explicit mention of an age range.	
Att-6 Participant diagnosis: This attribute relates to the type of illness. All diagnoses must be listed in the Hain Directory.	Malignant: A life-limiting or life-threatening cancer (e.g. leukaemia).	
	Non-malignant: A life-limiting or life-threatening condition that excludes cancer diagnosis (e.g. cystic fibrosis, SMA 1, SMA 2).	
Att-7 Malignant illness trajectory: The illness stages of a malignant condition.	Diagnosis: The stage between the time of receiving the diagnosis up until the first recurrence of the disease.	
	First recurrence: The stage between the first recurrence until the second recurrence (if there was one) or death or end of study (whichever comes first).	
	Second recurrence: The stage between the second recurrence until the third recurrence or death or end of studies (whichever comes first).	
	Third recurrence: The stage between the third recurrence until the fourth recurrence or death or end of studies (whichever comes first).	

	Fourth recurrence: The stage between the fourth recurrence up until death or end of study (whichever comes first).
	Post-death (malignant): Up to 40 days after the death of the child including information on storing the child's body, post-mortem and collection of other tissue after death.
Att-8 Non-malignant illness trajectory: This attribute relates to the stages of non-malignant condition.	Diagnosis: The stage between the time of receiving the diagnosis and the first examination.
	First examination: The stage between the time of the first examination and the first exacerbation.
	First exacerbation: The stage between the first exacerbation and recovery.
	Recovery: The stage between recovery and a period of increased hospitalisation.
	Increased hospitalisation: The stage between the period of increased hospitalisation and an increasing number of complications.
	Complications: The stage between an increasing number of complications and further deterioration.
	Deterioration: The stage between increasing deterioration and the terminal phase of the illness.
	Terminal phase: The stage between the terminal phase and death.

	Post-death (non-malignant): Up to 40 days after the death of the child including information on storing the child's body, post-mortem and collection of other tissue after death.	