Reporting of Ethical Requirements in Published Physiotherapy Research

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Declaration

I, Denise Frank, declare this dissertation embodies my original work, except where acknowledgement indicates otherwise and that no part of it has been or is being submitted for a degree at any other university.

Signed:

Date:

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Abstract

Background

Efforts to make physiotherapy practice more evidence-based and patient-focused have led to the expansion of research using a combination of quantitative and qualitative methodologies. In order to protect participants in research, contemporary research standards require approval of a study by a research ethics committee (REC), subjects' informed consent, confidentiality assurances, and disclosure of sponsorship and conflicts of interest. This study examined how often articles in physiotherapy (PT) journals report these basic ethical requirements.

Design

A retrospective audit of human subject research published in 6 leading PT journals between 1996 and 2001 and a physiotherapy evidence database (PEDro) between 1990 and 2002.

Main Outcome Measures

Editorial policies in PT journals regarding documentation of REC approval, informed consent, confidentiality, authorship, sponsorship and conflicts of interest; documentation rates in published articles of these ethical requirements, and rates of documentation of REC approval, informed consent and confidentiality according to study design and study population.

Results

Of the instructions to authors surveyed in the 6 PT journals, 5 required written permission for publication of confidential information, 4 required written confirmation of REC approval, and 3 required confirmation of informed consent; 4 requested information on funding, 2 requested information on authorship, and 2 required statements on conflicts of interest. Of the articles published in PT journals, 54% documented REC approval, 65% documented informed consent and 48% properly documented both REC approval and informed consent. Articles reporting clinical interventions and paediatric randomised clinical trials (RCTs) had the highest reported rates of REC approval and informed consent: 64% and 61% respectively. Articles reporting qualitative methods, chart reviews and case reports had the lowest documented rates of both REC approval and informed consent: 30%, 17% and 11% respectively. Documentation rates in PT journals of both REC approval and informed consent in research involving vulnerable populations were 55% for children, 48% for students and 33% for employees. Twenty six percent of articles in PT journals reported confidentiality protections. Case reports were most likely and chart reviews least likely to mention confidentiality: 88% and 8% respectively. Twenty two percent of articles in PT journals specified authors' contributions, 65% made no mention of sponsorship and <1% documented a conflict of interest.

Conclusion

There is no standard editorial policy among PT journals for reporting basic ethical requirements. Consequently rates of documentation of ethical safeguards vary among PT journals and according to study design and research population. Editors of PT journals should standardise and make explicit their ethical requirements for publication, both as protection for research subjects, to educate researchers and to maintain public trust in the research process. Journal editors should make compliance with these ethical safeguards a requirement for publication.

Abbreviations

APTA	American Physical Therapy Association
AJPT	Australian Journal of Physiotherapy
BMJ	British Medical Journal
CJPT	Canadian Journal of Physiotherapy
CIOMS	Council for International Organizations of Medical Sciences
COPE	Committee on Publication Ethics
FDA	Food and Drug Administration
HIPAA	Health Insurance Portability and Accountability Act
ICMJE	International Committee of Medical Journal Editors
IRB	Institutional Review Board
JAMA	Journal of the American Medical Association
PEDro	Physiotherapy Evidence Database
PT	Physiotherapy
PTI	Physiotherapy Research International
NEJM	New England Journal of Medicine
RCT	Randomised controlled trial
REC	Research Ethics Committee
SAJPT	South African Journal of Physiotherapy
UK	United Kingdom
UKJPT	Physiotherapy (journal)
USA	United States of America
USAJPT	Physical Therapy (journal)

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Chapter 1 Introduction, Aims and Methodology

1.1 Introduction

The pursuit of knowledge is a highly valued human endeavour, and research through systematic, empirical investigation is an essential means to attain this end. Medical research, now a vast academic and commercial activity, has contributed to major advances in the treatment and prevention of disease. Although the rewards for society are enormous, in some cases research can seriously harm participants as illustrated, among others, by the Nazi atrocities committed on prisoners of war in the name of science[1] and a series of well-publicised scandals in the United States. These included the Tuskegee Syphilis Study involving 399 black men who without their knowledge were denied treatment for their condition, and experimentation on institutionalised mentally retarded children who were intentionally infected with hepatitis to determine the effects of a vaccine.[2] Indeed, over the past century, children have proved especially vulnerable in the face of human experimentation.[3] More recent examples include the death of an 18 year-old patient in a gene therapy trial and the death of a 24 year-old healthy volunteer in an asthma study.[4] Nor, in the future, must the research community forget these lessons from the past. It must not, for example, allow threats of global bioterrorism to be used to justify dubious experimental practices under the guise of either national security or the public interest.[5]

Since research with human subjects inevitably involves putting some at risk or inconvenience in the hope of benefiting others, protecting participants is a fundamental tenet of ethical research. Consequently, human experimentation is regulated by international and national codes requiring that the rights and welfare of research subjects be elevated above scientific and societal goals. International guidelines for research ethics are located in the Nuremberg Code (1947),[6] the World Medical Association Declaration of Helsinki (1964, revised in 1975, 1983, 1989, 1996 and 2000),[7] and the International Ethical Guidelines for Biomedical Research Involving Human Subjects (1993, revised 2002).[8] Industrialised countries including Japan, the European Union and the United States (US), also expect clinical researchers to comply with the Good Clinical Practice (GCP) guidelines, an international quality standard, when conducting trials that include human subjects.[9] Additionally, the US has enacted federal regulations to protect human subjects in federally-funded research.[10] These codes and regulations are evidence of a societal commitment to advance knowledge according to ethically sound principles and practices, which stipulate that a study must show potential social and scientific value, scientific validity, fair subject selection, a favourable risk/benefit ratio, respect for enrolled subjects as well as meet procedural requirements for informed consent and research ethics committee (REC) or institutional review board (IRB) approval.[11,12]

Advances in medicine and related disciplines depend not only on the generation of information through research but also on its dissemination,[13] and whilst the protection of human subjects rests mainly with investigators and their institutions, journals and their editors have a responsibility to ensure the research they publish meets current ethical standards.[14,15] According to principle 27 in the Declaration of Helsinki (2000) 'Both authors and publishers have ethical obligations... Reports of experimentation not in accordance with the principles laid down in this Declaration should not be accepted for publication'.[7] Because journal articles carry so much weight in career advancement, appointments and sponsorship, researchers feel great pressure to publish. In turn, as a major mechanism for publication, journals' publication requirements exert a strong influence on researchers' behaviour since failure to abide by the requirements translates into failure to get published. In this sense, peer-reviewed journals play an important gatekeeping and oversight role in promoting patient safety.[14,15]

In order to meet their obligations to publish ethical research, biomedical and science editors are moving towards greater consensus regarding the basic ethical safeguards needed for publication of research. Drafted by the International Committee of Medical Journal Editors (ICMJE)[16] and the Committee on Publication Ethics (COPE),[17] ethical standards for peer-reviewed journals include documentation of the ethical protections employed in studies such as REC approval, informed consent, measures to ensure confidentiality, incentives offered to subjects, conflicts of interest and sources of sponsorship. The World Association of Medical Editors (WAME) is a web-based platform where editors can share ethical problems that arise in the publication process.[18] In addition, it includes a syllabus for newly appointed editors which addresses issues relating to publication of ethical research. The Forum for African Medical Editors is another important mechanism for local editors to network and share experiences.[19] The forum has published its own guidelines for African editors.

The latest development is the publication for comment of a draft code of conduct for medical editors who are members of COPE.[20] The code offers both aspirational and concrete guidance. It extends well beyond the standard requirement that editors ensure that there is ethical approval of the material they publish to holding them responsible for publishing unethical research even if previously approved by RECs.

Much effort has also gone into developing a uniform standard for conducting and reporting randomized control trials (RCTs). The CONSORT (Consolidated Standards of Reporting Trials) checklist consists of items that must be included in a manuscript submitted for publication of clinical trials.[21] A similar standard modeled on the CONSORT Statement is recommended for the ethical conduct and evaluation of clinical trials. Furthermore, compliance with the ASSERT (A Standard for the Scientific and Ethical Review of Trials) Statement would imply investigators and sponsors are, at a minimum, aware of their ethical responsibilities during and after trials.[22] In similar vein, Bernstein and Upshur[23] propose an ethical framework which editors and readers can use to assess whether published trials have met accepted ethical requirements. This framework goes beyond Emaunuel *et al's*[11] widely cited criteria for ethical research to include a commitment to trial registration, the dissemination of findings, a declaration of all conflicts of interest as well as accurate and honest reflection of authorship.

Miller and Rosenstein[24] recommend even broader reporting requirements especially where research includes features many might consider morally dubious, but not necessarily unethical. They suggest that in the methods and materials section of a manuscript, authors provide their ethical justification for using a morally controversial study design such as placebo controls, symptom provocation or deception. Authors could also describe added safeguards used to minimise potential harms. For example, if research is conducted in less developed countries, they recommend that authors indicate the potential relevance of trial results to the subjects' community and the extent of access to treatment should a study drug prove to be effective. Just as readers judge a study's scientific validity and reliability from information gleaned in the methods section, they could assess a study's ethical adequacy through authors' elaboration on pertinent ethical issues. In much the same way as structured abstracts have helped improve the quality of scientific reporting, structured reporting of ethical safeguards would further the protection of human subjects. If journals face space constraints, authors could provide a brief statement about key ethical issues in a published article and place a more detailed account on a journal's website.[24] At the very least, editors could ask authors to complete a checklist of compliance with standard ethical practices bearing on their specific areas of research.[25]

Despite widely acknowledged international obligations and uniform publication requirements, evidence suggests major shortcomings in the quality of both the requirements for[26-29] and reports[30-45] of ethical protections in journal articles. These studies examine how frequently published articles report whether or not researchers obtained research ethics committee (REC) approval and oral or written informed consent. This research which included vulnerable or captive populations such as children,[30-34] medical students,[35] the aged[36] and nursing home residents,[37] patients needing cardiopulmonary resuscitation,[38] and in areas such as critical care,[39] emergency services[40] and human movement science,[41] reveals the magnitude of the gap between manuscript requirements and the actual manuscript content. In a review of two widely read psychopathology journals, Sigmon and colleagues found low reported rates of ethical practices important in psychopathology research, such as debriefing, confidentiality assurances and limitations, and treatment referrals for participants in psychological distress.[25] The rate of documented REC approval and informed consent in published studies using human tissue was equally low.[42] In comparison, reports of ethical safeguards in clinical trials were slightly higher.[43-45]

Shapiro and co-workers[46] also show that rates of reporting depend on the type of publication. Whereas investigators mentioned ethical and legal safeguards in 83% of original protocols ('methods papers'), this information was included in only 52% and 14% respectively of journal articles and clinical alerts. These combined findings show that authors and editors alike fail to comply with explicit publication instructions that manuscripts document REC approval and informed consent or why these requirements have been waived.

Even though attention to ethical detail in published reports cannot guarantee the ethical conduct of a study and will not eliminate unethical research,[47] the requirement to include ethical issues as a condition of publication can serve to remind researchers of ethical standards they must observe.[24] Consistent disclosure of ethical safeguards would add another level of assurance to patients, editors and readers and help maintain trust in medical and related research. Indeed, as the face of biomedical research, publication of research involving human subjects must not only be ethical, it must be seen to be ethical.[48]

Significantly, COPE[49] has published a preliminary taxonomy of research misconduct ranging from the most serious offences such as fabrication, falsification, plagiarism, through offences such as failing to obtain REC approval and informed consent, to more minor examples of misconduct such as not attempting to publish completed research or failing to do an adequate literature search of existing findings before undertaking new research. Since many, if not most, authors would likely be guilty of some or other form of research misconduct according to this classification, it is rightly argued that more emphasis must be placed on describing best practice. Thus in addition to the general guidelines provided by the ICJME,[16] many journals such as the Journal of the American Medical Association,[50] the New England Journal of Medicine,[51,52] the American Respiratory and Critical Care Medicine Journal,[53] the Archives of Child and Adolescent Medicine,[54] Biological Psychiatry,[55] the Annals of Emergency Medicine[56] and Palliative Medicine[57] have their own publication requirements governing specific ethical issues. Furthermore, a growing body of scholarly articles[58-60] and empirical research[61-64] on topics such as multiple authorship and conflicts of interest illustrates the ongoing debate surrounding these largely unresolved ethical issues in the publication arena.

Yet, despite these good intentions, Frank Davidoff, a past editor of the Annals of Internal Medicine (1995-2001) in a recent address was moved to comment '... if you want to keep a secret, put it in your "information to authors" no-one ever reads that stuff.' He did, however, add '... it's also where lurk the heavy-duty ethical issues... that tend to bite you on the leg if ignored'.[65] (p. 235) Finally, not everyone agrees that journals are the gatekeepers of ethical research. A long time campaigner against fraudulent medical research, Peter Wilmshurst, believes journals are more concerned about libel suits than dubious research.[66] He feels editors are too trusting of investigators' findings. Just as there are spot checks to detect drug abuse in sport, he proposes routine checks of raw data during research and after its submission for publication. An investigator's failure to produce raw data should lead to a ban on future research for a specified period or a review of previously published research.[66]

In summary, although the ethical review of research mostly takes place in advance of its performance, ethical issues can arise at any point throughout a study's conception, conduct and dissemination of its findings. Although editors do not get involved until well after a study's completion, they nonetheless carry responsibility to maintain public trust in published research.

Pressure is growing for physiotherapy to become more evidence-based and less reliant on expert opinion to guide clinical practice.[67] In a recent survey, 84% of physical therapist members of the American Physical Therapy Association acknowledged that they must use more evidence in their daily practice.[68] Evidence about the effectiveness of interventions and diagnostic tools depends on accelerating the output of clinically relevant physiotherapy research. In turn, this has increased the demand for human subjects in physiotherapy research with concomitant concerns for the methodological quality [69,70] of empirical studies and the protection of participants' welfare.[71-73] Significantly, a literature review spanning 30 years (1970-2000) of advances in ethics knowledge in physiotherapy identified only nine articles in research ethics, eight of which were published in the seventies and eighties.[74] In light of reports indicating neglect of ethical safeguards in published medical articles and the need for more clinically relevant physiotherapy research, the present study examined the quality of reported ethical information in published physiotherapy research.

1.2 Aims

Efforts to make physiotherapy practice more evidence-based have led to the expansion of empirical research. This can increase pressures to subordinate the interests of research subjects to those of science and society. Protecting human subjects in research is based on a chain of judgments made against a background of international and national ethical principles and regulations. As gatekeepers of published research, journals and their editors are a crucial final link in this chain of protections. This study aimed to identify gaps in reporting ethical safeguards in physiotherapy and physiotherapy-related publications in order to establish if more explicit policies concerning ethical issues were needed in physiotherapy journals.

1.2.1 Objectives

More specifically the study aimed to:

1. Determine the frequency of documented ethical safeguards in published reports of physiotherapy research.
2. Examine documented ethical safeguards in relation to study design and study population.
3. Identify the extent of documented authorship, sponsorship and conflicts of interest.

4. Identify the ethical requirements for human subjects research reported in the 'instructions to authors' section in physiotherapy journals.

1.3 Methodology

1.3.1 Design

The study was a descriptive audit of documented ethical requirements and safeguards in published research in physiotherapy journals and in randomised control trials (RCTs) of interventions relevant to physiotherapy practice.

1.3.2 Methods and Materials

Structured data collection and coding sheets were used to review the content of six physiotherapy journals and paediatric RCTs (Appendices 1 and 2) indexed in the Physiotherapy Evidence Database (PEDro).[75] Structured data collection and coding sheets (Appendices 3 and 4) were used to collect data on publication requirements in the 'instructions to authors' section of the six physiotherapy journals.

1.3.2.1 Physiotherapy Journals

The physiotherapy journals were (in alphabetical order) the Australian Journal of Physiotherapy, Physical Therapy, Physiotherapy, Physiotherapy Canada, Physiotherapy Research International and the South African Journal of Physiotherapy. These journals were chosen because they include the publications of professional physiotherapy societies with large circulations. For example, the publications from Australia, Canada, the United Kingdom (UK) and the US delineate a group of well-established journals for physiotherapists and are distributed to over 125000 association members worldwide.[76] Furthermore, based on the quality of published clinical trials, the Australian Journal of Physiotherapy, Physical Therapy, Physiotherapy and Physiotherapy Canada are among the highest ranked exclusively physiotherapy journals[77]; and according to a citation analysis, they are considered core physiotherapy journals.[78] Additionally, the Australian Journal of Physiotherapy and Physical Therapy are indexed in the prestigious MEDLINE database. All the journals are peer-reviewed and listed in the Cumulative Index to Nursing and Allied Health Professions (CINAHL). Physiotherapy Research International was selected because of its empirical and international focus.

All research articles published between 1996 and 2001 were reviewed. Letters to the editor, editorials, abstracts, presidential addresses, meta-analyses, systematic reviews and technical and managerial articles were excluded from review.

1.3.2.2 Physiotherapy Evidence Database (PEDro)

Although physiotherapy journals contain high quality evidence, it is recommended that physiotherapists also refer to journals with a larger multidisciplinary readership.[76] Ideally, evidence-based practitioners need to access a combination of health care journals which goes beyond their own professional discipline. Accordingly, articles were drawn from PEDro which is a free internet-based resource comprising information on systematic reviews and RCTs related to physiotherapy.[75] Well-designed randomised trials provide the strongest evidence of the effectiveness of health care interventions.[79] To this end, trained PEDro staff and volunteer physiotherapists rate the methodological quality of all RCTs included in this database. RCTs with a rating of 5 or more are of moderate to high quality. Inclusion of research from this comprehensive database should extend the generalisability of findings beyond predominantly physiotherapy journals.

All RCTs indexed in PEDro that met the following criteria were examined:

- Published between 1990 and 2001 with a methodological quality rating of 5 or more on the PEDro scale.
- Classified under the sub-discipline of paediatrics. This included trials where the age of the study sample was 16 or under, and trials on conditions that commonly affected children (for example, cystic fibrosis).[75]

Clinical trials were included because their use of interventions makes reporting of ethical safeguards particularly important.[79] Children were selected because they are a vulnerable population needing special protection.[80] Although they deserve the same access to safe and effective therapies as adults, any presumption in favour of children's participation in research must be accompanied by heightened concern for their protection and safety.[81,82]

The following information was extracted from each article:

- Journal title, year of publication, volume, range of pages
- Authorship (university affiliation, country of origin)
- Authors' contributions
- Sponsorship (industry, non-industry, both, none)
- Setting (hospital, other)
- Gender (male, female, both, other)
- Vulnerable groups (children, students, pregnant women, critical care, decisionally impaired, employees, other)
- Design (clinical, behavioural, chart review)
- Case report
- Qualitative methods
- Informed consent
- Assent
- REC/IRB approval
- Confidentiality

Standardised definitions of variables such as study design, case reports and qualitative methods are provided in the coding sheet (Appendix 2). Case reports were included because they raise contentious ethical issues relating to informed consent and confidentiality.[83-85]

1.3.2.3 'Instructions to Authors'

A structured data collection and coding sheet (Appendices 3 and 4) were used to extract information on 'instructions to authors' in the six physiotherapy journals. Specific information related to journals' requirements for informed consent, REC approval, and disclosure of sponsorship and conflicts of interest, confidentiality and individual authors' contributions.

'Instructions to authors' were not examined in articles drawn from PEDro as they comprised a wide base of journals, with a correspondingly wide range of individual journal requirements not amenable to meaningful analysis.

1.3.3 Reliability

The author (DF) and a second reviewer Lesley Henley (LH) extracted data respectively from the six physiotherapy journals and PEDro respectively. DF and LH independently reviewed the first twenty completed forms from each other's data sets. Any discrepancies in the interpretation of the coding rules were settled by consensus. Interrater agreement was not statistically determined.

In several articles informed consent was implied. For example, it was reported that 'parents agreed to take part', 'parents had an opportunity to decline' or 'there were no refusals'. Where informed consent was implicit, informed consent was coded as being present. Where informed consent had been waived, informed consent was coded as being present. Similarly, confidentiality was not always directly documented. Frequently photographs of participants had only the eyes covered. Although this protection did not strictly meet the definition of confidentiality, nonetheless confidentiality was reported as being present. During data capture, these interpretations were consistently applied.

1.4 Data Analysis

Data were analysed on a personal computer using Epi Info Version 6. Data analysis was limited to the use of descriptive statistics and chi square analyses to examine associations between variables. A value of < 0.05 was considered significant. Percentages were rounded to the nearest whole number.

1.5 Ethical Approval

Since the study did not involve human subjects and the data were in the public domain REC approval was not needed (Appendix 5).

1.6 Overview

In the following chapter, theoretical and empirical literature pertinent to the present study is reviewed. Analysis and discussion of this study's findings are presented in Chapters 3 and 4. Finally in Chapter 5, recommendations are offered to improve documentation of ethical safeguards in physiotherapy research.

Chapter 2 Literature Review

2.1. Introduction

Along with calls for physiotherapy to become more evidence-based,[67] is the growing demand for clinically-based research. To this end the American Physical Therapy Association (APTA) developed a Clinical Research Agenda[86] to prioritise and maximise research efforts needed to develop a scientific body of evidence to answer the most frequently asked questions in clinical practice. Significantly, empirical examination of research trends in physiotherapy had found only modest gains in the use of experimental designs.[87-89]

The APTA set itself five years to make substantial progress toward completion of the agenda.[86] Implementation of the agenda which focuses on more research in out-patient clinics, hospitals and rehabilitation facilities has direct implications for human subjects research.[69] For example, Fitzgerald and Delitto[69] point out that investigators must be knowledgeable about scientific design and have sufficient resources to complete a study, they must judge whether or not a study is feasible within available constraints, they need to follow established ethical guidelines, they must know how to manage adverse events and they need to recognise if a study ought to be terminated. With similar end points in mind, the UK-based Chartered Society of Physiotherapy, the Royal College of Speech and Language Therapists and the College of Occupational Therapists undertook a survey of registered therapy researchers to determine the extent of scientific capacity and suitably qualified candidates who could act as peer reviewers and REC members.[90] Meanwhile, Shephard published a timely article comprehensively detailing the ethical requirements for research in sports medicine, with clear and direct implications for closely aligned physiotherapy research.[91] Together these reports suggest that the physiotherapy profession has identified evidence-based clinical practice as a research priority and, as importantly, that future research must be conducted in accordance with the highest ethical standards.

Unfortunately, history shows that human subjects research has not always followed basic ethical principles. This literature review will briefly examine some highly publicised examples of abuses in human experimentation, the subsequent evolution of international and national research ethics codes and guidelines, and the synthesis of these principles and guidelines into a coherent framework to facilitate the performance ethical research.

In addition, editors are increasingly being called upon to devote more space in the 'methods' section of articles or on dedicated websites to publication of the actual ethical practices that investigators used during the conduct of their studies. Thus the role of editors and journals in promoting ethical research is also reviewed, along with empirical studies that show poor compliance with publication requirements. These studies provide the context for the present study.

It is important to note that apart from the major ethical codes, such as the Declaration of Helsinki, different countries will have different laws, regulations and guidelines governing human subjects research. For example, the exact requirements for ethical review of a research protocol will vary depending on the jurisdiction and circumstances in which an investigator is working. Given the scope and volume, it is not possible to include all such material in this literature review. Accordingly, much of the review focuses on requirements in the US with an attempt to relate them to internationally accepted ethical standards, and in the recognition that local practices although country-specific are all directed at the same ends: to protect the rights and welfare of research subjects. Likewise, terminology such as IRBs and RECs and subjects and participants will be used interchangeably.

2.1 Historical Overview of Research Ethics

According to the medical historian, Stephen Lock,[92] the earliest statements about research ethics appeared in the 1830s and addressed the need for subjects' informed consent if investigators were not to be held liable for damages for any injuries incurred during experimentation. A prominent exponent of informed consent at this time was Claude Bernard who famously stated that research per se was an ethical necessity for the advancement of medicine. Armauer Hansen, another leading investigator in the late nineteenth century, was dismissed from his hospital post in Bergen, Norway, for inoculating material taken from a leprous nodule into a patient-subject's eye, without consent, in order to establish whether leprosy was infectious.[92]

Early in the twentieth century, in the US, dubious research into inoculation against yellow fever and syphilis was creating adverse comment in the press.[92] Walter Reed had, for example, given American servicemen and Spanish workers one hundred dollars in gold for taking part in his yellow fever experiments, and a further one hundred dollars if they developed the disease. In their defense, researchers at this time argued that admission to public hospitals implied consent to participation in experimentation. Children were also regularly involved in non-therapeutic vaccine research much of which was reported in leading paediatric journals such as the American Journal of Disease of Children.[3] To counter public criticism, in 1914 the American Medical Association formed a Committee on the Protection of Medical Research which urged medical journals to inspect original manuscripts submitted for publication and to remove language that might imply unethical behaviour.[92] Several years later, the Committee condemned the publication of an unethical experiment in the Journal of Experimental Medicine whose editor was the famous Abraham Flexner. Flexner pleaded that he was abroad at the time of the publication.[92] Were it not for the US involvement in the First World War in 1917, Lock believes the US Federal Government would have developed guidelines for ethical research in response to simmering public discontent.[92]

Between the two World Wars there was little debate about research ethics in the US or the UK. Lock feels that political concerns overshadowed ethical concerns during this period. Moreover, Nobel prize-winning and life-saving discoveries such as insulin for the treatment of diabetes underscored the benefits rather than dangers of human experimentation.[92]

In contrast to a general apathy towards research ethics in the US and UK, the rapidly developing pharmaceutical industry in Germany was heavily criticised for using subjects as guinea pigs.[92] A public outcry against the death of one hundred children in a BCG experiment in Lübeck led the German Interior Ministry to issue a set of guidelines (Reich Circular) for ethical research in 1931. The status of these guidelines was fiercely debated during the Nuremberg Trials – did the rules have legal standing or were they merely intimations of ideal practice that should be followed where practicable.[92]

In 1946 at the end of the Second World War, 23 Nazi doctors and co-conspirators were tried for crimes related to cruel experimentation on concentration camp prisoners.[93] These included studies relating to battlefield injuries, freezing, induced infectious diseases, ways to prevent the noxious effects of high altitude flight, sterilisation research undertaken in the service of Nazi ideology and experiments to develop the most efficient methods of killing.[93] In their defense, the accused argued that the experiments were morally justified because the subjects would die anyway and the knowledge gained from their sacrifice would benefit society in general. Furthermore, the defendants' lawyers mounted a strong case that the Allies had also undertaken medical experimentation in the service of the war effort. As the prosecution's attempts to show there were international guidelines governing human experimentation faltered, in their final verdict the four judges created their own 10 point set of rules, which became known as the Nuremberg Code.[6,93] The first line states that 'the voluntary consent of the human subject is absolutely essential'.[93] (p. 348) The Code further stated that the subject should be legally competent to consent, animal experimentation should precede human experimentation, all unnecessary physical and mental suffering and injury should be avoided, the degree of risk to the subjects should never exceed the 'humanitarian importance of the problem' and should be minimised through 'proper preparations' and that subjects could withdraw from the experiments.[93] (p. 350) Although never adopted into law in individual countries, the Nuremberg Code is considered the first statement of professional ethics for medical researchers. It provided authoritative guidelines so that no one could plead ignorance of their ethical obligations. Shuster puts it like this: 'The Nuremberg Code focuses on the human rights of research subjects, the Declaration of Helsinki focuses on the obligations of physician-investigators to research subjects, and the (US) federal regulations emphasize the obligations of research institutions that receive federal funds'.[94] (p. 1440)

As noted by the Nazi lawyers during the Nuremberg Trial, the Allies had also undertaken extensive research during World War II.[92, 95] The research, aimed mainly at medical conditions affecting the troops, was performed on soldiers, prisoners, conscientious objectors, orphaned children and institutionalised mentally retarded persons.[92] Volunteer prisoners were hailed as heroes for their service to the advancement of science and the war effort. Hornblum writes that '... prisoners had become the guinea pigs of choice for scores of inspired researchers... the overriding goal was to win the war in Europe and Asia; everything else was secondary, including research ethics and the issue of consent'.[95] (p. 1439) Even in the post-war period, and despite the formulation of the Nuremberg Code by American judges, highly questionable research continued in the US, particularly among vulnerable prisoners.[95] Clearly, the Nuremberg Code had little effect on ethical discourse or public policy in the US, and the remarkable advances produced by medical research during this period seemed to trump any serious attention to research ethics.[92] Since the Code was formulated in the context of a criminal trial, it is possible that US researchers viewed it as a code for '... barbarians, the Nazis, who were guilty of brutal excesses, not a code for civilized researchers.'[93] (p. 350) Alternatively, researchers may have ignored the code because it effectively ruled out all research with incompetent persons, including children.

In 1964, the World Medical Association adapted the Nuremberg Code to the needs of the biomedical research community, producing the first version of the Declaration of Helsinki.[93] Whereas, the Nuremberg Code was written by lawyers and judges against the background of a criminal trial, the Declaration was written by physicians for physicians.[93] Importantly, the Declaration made provision for surrogate consent in research when informed consent could not be obtained because the subject was a minor or cognitively incapacitated. In 1975, the second version of the Declaration mandated ethical review committees and stated that reports of experimentation in violation of its principles should not be accepted for publication. To date there have been five revisions of the Helsinki Declaration: in 1975 in Tokyo, in 1983 in Venice, in 1989 in Hong Kong, in 1996 in Somerset West in South Africa and in 2000 in Edinburgh, Scotland. Controversially, the fifth revision claimed priority over national laws and regulations. In principle 9, it states that although investigators need to '... be aware of ethical, legal and regulatory requirements for research on human subjects in their own countries... No national ethical, legal or regulatory requirement should be allowed to reduce or eliminate any protections for human subjects set forth in this Declaration'.[7] The authority of this doctrinaire claim is unknown.[96] Attempts in Helsinki, Finland to finalise the sixth revision of the Declaration have ended in deadlock over the wording of clause 30, dealing with access to study interventions after a study is completed.[97]

Subsequently, various international groups have promulgated standards that elaborate on the Declaration of Helsinki. In 1982, the Council for the International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO) formulated the 'International Ethical Guidelines for Biomedical Research Involving Human Subjects'.[8] CIOMS addresses ethical issues pertinent to developing countries, such as culture and socio-economic circumstances, as well as issues relating to medical records and biological specimens not mentioned in the Helsinki Declaration. CIOMS was revised in 2002. In 1997, the International Conference on Harmonization adopted the Good Clinical Practice: Consolidated Guideline as an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve human subjects.[9] Compliance with the standard, compiled by representatives of the European Union, Japan, the US and the pharmaceutical industry, provides public assurance that the rights, safety and well-being of trial subjects are protected in a manner consistent with principles that originate in the Declaration of Helsinki.[9]

Reports in the sixties of unethical research by Henry Beecher in Boston and Maurice Pappworth in London shattered perceptions that unethical research was not happening in the US and the UK.[92] In 1966 Beecher, a Harvard anaesthesiologist, reported 22 cases of unethical research in the prestigious New England Journal of Medicine.[98] Amongst Beecher's revelations was the study undertaken among elderly indigent patients in the Brooklyn Jewish Chronic Disease Hospital. Without their permission, patient-subjects were injected with live cancer cells as part of a study of immunity to cancer. Furthermore, the hospital's research committee had not reviewed the protocol and it had proceeded despite the objections of three physicians consulted in connection with the study. Another notorious example of unethical research was the Willowbrook studies In New York involving institutionalised mentally retarded children.[3] Starting in 1956 and continuing into the early seventies, these studies were designed to gain insight into the natural history of infectious hepatitis, and subsequently, to test the effects of gamma globulin in preventing and ameliorating the condition. The subjects, all children, were deliberately infected with hepatitis. The investigators justified the research on grounds that the children would eventually become infected anyway because of crowded and unsanitary conditions. The issue of parental consent for experimentation was the subject of controversy. During the course of the research, Willowbrook State School closed its doors to new admissions because of overcrowding. However, children could still be admitted to a special study unit if parents consented to their child's inclusion in the study. Thus for some parents gaining admission to Willowbrook was only possible if they agreed to enrol their child in the research study. Critics rightly argued that parental consent was effectively coerced and therefore constituted unethical research. Other criticisms included failure to include adult staff in the investigation.[2,3] Lederer and Grodin assert that '... no one should doubt the impetus that the public controversy over the deliberate infection of mentally retarded children with a serious disease gave to the demand for the protection of the rights of human subjects'.[99] (p. 18)

Arguably, the most notorious example of unethical research in the US was the Tuskegee Syphilis Study.[2] Started in 1932 by the US Public Health Service as a study of the natural history of untreated syphilis, the research involving 399 poor black American men continued until 1970, despite the wide availability of penicillin after 1951. Subjects were enticed into the study with offers of free medical examinations. Subjects thought they were receiving treatment for 'bad blood'. They were not told about the nature of their disease, the risks of ongoing sexual activity or the fact that the research held no therapeutic benefit for them. It is noteworthy that results from the research were published in reputable medical journals over the course of the study. It is estimated that 20% of subjects died prematurely from untreated syphilis. In 1972, the New York Times exposed the study on its front page. In response the Department of Health, Education and Welfare (DHEW) appointed the Tuskegee Ad Hoc Panel to review the Department's policies and procedures for the protection of human subjects. The panel recommended that the Tuskegee study be stopped immediately and that the remaining subjects be given necessary medical care.[2]

Significantly, the legacy of Tuskegee continues to this day, as the African American community remains distrustful of medical research. In an attempt to heal the wounds US President Bill Clinton apologised to the study's eight survivors and the African American community on May 16, 1997 saying 'The United States government did something that was wrong – deeply, profoundly, morally wrong... An apology is the first step, and we take it with a commitment to rebuild broken trust. We can begin by making sure there is never again another episode like this one. We need to do more to ensure that medical research practices are sound and ethical, and that researchers work more closely with communities... Since the study was halted, abuses have been checked by making informed consent and local review mandatory in federally funded and mandated research... We face a challenge in our time. Science and technology are rapidly changing our lives with the promise of making us much healthier... But with these changes we must work harder to see that as we advance we don't leave behind our conscience....'[100]

In 1973, the DHEW published a first set of proposals concerning the protection of human subjects in biomedical and behavioural research. On May 30, 1974, specific legal guidelines for researchers were published (45 CFR 46). In July 1974, the US Congress passed the National Research Act which led to the establishment of a National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research.[93] Meeting between 1975 and 1978, the National Commission made substantive and procedural recommendations for protecting human research subjects.[93] Procedurally, it proposed the introduction of institutional review boards to evaluate and monitor human experimentation, and substantively, it formulated ethical principles and guidelines on which to base regulations. These were published in the Belmont Report in 1979.[101]

The Belmont Report identified three basic ethical principles as being particularly relevant to research: respect for persons, beneficence and justice.[101] Respect for persons incorporates the moral conviction that individuals should be treated as autonomous agents and those with diminished autonomy are entitled to protection. Children and persons with limited capacity must be able to choose to participate to the extent that they are able, and their refusal to take part should generally be respected, unless the research offers therapy that is otherwise unavailable. Thus the principle of respect for persons serves as the moral foundation for the procedural requirements of informed consent, assent and permission.[101] The principle of beneficence requires investigators to promote subjects' well-being through avoiding harm, maximising possible benefits and minimising possible harms. In the research context, beneficence includes proper research design, evaluating the competence of investigators to conduct the research and determining that the research provides a favourable balance of risk and benefit. The National Commission recognised that this assessment must include the assessment of physiological, psychological, social and economic harms and benefits.[101] The principle of justice requires that the benefits and burdens of research be fairly distributed. Potential subjects must be selected for reasons directly related to the problem under investigation and not because of their easy availability such as prisoners.[101] The Report pointed to special instances of injustice that might arise from using vulnerable subjects in research, for example, the very sick, the economically disadvantaged and the institutionalised.[101]

The Belmont Report also examined the distinction between medical practice and research in order to identify which activities needed prior review. The report noted that this distinction was often difficult to make since research might include medical treatment and innovative departures from standard practice that might be considered experimental.[101] Although, the Belmont Report remains the ethical foundation for the practice and regulation of biomedical research in many countries, it has been criticised for not considering the principles '...through the lens of community'.[93] (p. 357) Instead of considering only harms and benefits to individual subjects in research, attention ought also to focus on harms and benefits to communities, for example, the possible harm to a group identified as having particular genes that are considered harmful such as cancer genes.[93] Likewise, justice may require participation by communities in the design and evaluation of research.[93]

In summary, the passage of the National Research Act and the promulgation of DHEW's regulations were important milestones in the development of federal standards for human subjects protection in the US. In 1981, the Federal Drug Administration (FDA) promulgated separate regulations that apply to all studies of investigational drugs, medical devices and biological products. In 1991, federal policy known as the Common Rule consolidated the regulations governing research in fifteen federal agencies.[10] The FDA brought its informed consent and IRB regulations in line with the Common Rule (21 CFR 40 and 21 CFR 56). The Common Rule, formally titled 'Protection of Human Subjects, Part 46 of Title 45 of the Code of Federal Regulations (45 CFR 46), applies to all federally funded research conducted inside and outside the US. The rule directs a research institution to assure the federal government that it will provide and enforce protections for human subjects of research conducted under its auspices. Local research institutions must assess research proposals in terms of their risks and benefits, and they must ensure that the Common Rule's requirements for selecting subjects and obtaining informed consent are met.[10]

The mechanism for ensuring that the rights and well-being of human subjects are protected is the institutional review board, an administrative body of the institution where the research is conducted. IRBs fall under the jurisdiction of the Office of Human Research Protections (OHRP) which has the authority to halt all federally funded research activity at institutions violating IRB regulations.[102] If suspended, no federally-funded research may continue at the institution. [102] This means subjects cannot receive treatments, enrol or be recruited and data cannot be analysed. Self-evidently, suspending research at an institution is likely to severely damage its reputation.[102]

The Common Rule requires that a research institution, as a condition of receiving federal funding, establish and delegate to an IRB the authority to review, approve or disapprove, request changes in, and oversee human subjects protections for research conducted at the institution. The Common Rule identifies categories of human subject research which are exempt from IRB review.[10] Crucially, exemption does not mean that investigators no longer have ethical responsibilities to their subjects, rather it means IRB approval is not needed by federal regulations.[102] Exempt studies do not require ongoing IRB review. The Common Rule also enumerates categories of research that may receive an expedited review.[10] In an expedited review, only one or two experienced reviewers ensure that a protocol meets ethical standards and exercise oversight on behalf of the entire committee. IRBs must have at least five members, reflecting a diverse membership including clinicians, scientists, administrators, and lay or community representatives.[10] Experts from various fields can be co-opted as necessary, depending on the protocols under review. For example, if an institution frequently reviews research involving children, a paediatrician or child psychologist should be included on the IRB committee.[102] By the same token, people with disabilities should be included as active members of IRBs to enlighten members to the needs of the disabled.[102]

Another important feature of the Common Rule is the informed consent requirement.[10] According to the Common Rule, informed consent must include the following elements:

- A statement that the study involves research, an explanation of the purposes of the research, and a description of the procedures to be followed;
- A description of any reasonably foreseeable risks or discomforts to the subject;
- A description of any benefits to the subjects or to others that might reasonably be expected;
- A disclosure of alternative procedures or courses of treatment;
- A statement describing the extent to which confidentiality or records identifying subjects will be maintained;
- For research involving more than minimal risk, an explanation of the availability and nature of any compensation or medical treatment if injury occurs;
- Identification of whom to contact for further information about the research and about subjects' rights, and whom to contact in the event of a research-related injury;
- A statement that participation is voluntary, that refusal to take part will incur no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject can withdraw at any time.[10]

The federal regulations go beyond informed consent for adults. In Subpart D which covers additional protections for children, the Common Rule makes provision for parental permission as well as children's assent to participation in research.[10] Permission refers to the agreement of the parents or guardian to the participation of their child or ward in research. In turn, assent refers to a child's affirmative agreement to take part in research. Significantly, the regulation states that 'a child's mere failure to object should not, in the absence of affirmative agreement, be interpreted as assent'. The requirement for assent can be waived if a child lacks the necessary capacity to be consulted or the research intervention or procedure offers direct benefit and is important for the child's health and well-being and is only available in the research context. Unless, due to limited capacity or potential benefit unavailable outside the research, the dissent of a child to either initial or continued participation in the research must be respected.[10] Put plainly, with few exceptions, children should have veto power to research participation.

Depending on the nature of a research project, an IRB can approve a consent procedure that does not include all the elements of informed consent or it may waive the requirement entirely.[10] Importantly, IRBs must be satisfied with the procedures and consent documents for obtaining informed consent. The IRB must be allowed to observe the process of obtaining informed consent if it is concerned about subjects' welfare.[10]

Whereas research ethics initially focused on the protection of human subjects, on keeping them safe from exploitation and injury, in the eighties the focus shifted to ensuring equal access to participation in research; or put differently, to protecting subjects from being excluded from experiments.[103] Ethical guidelines for this paradigm shift emphasise voluntary, informed consent.[93] This shift resulted mainly from pressure from advocacy groups demanding access to participation in clinical research.[93] AIDS activists argued that the only way for patients to receive treatment for life-threatening conditions was through participation in clinical trials. Similarly, advocates of women's health argued that the exclusion women of child-bearing age from drug trials had resulted in a dearth of scientific data about how certain diseases affect women.[93] Commenting on this shift in focus, Childress reminds us that '... we should not totally abandon the protectionist paradigm. The hard ethical task is to combine what is valuable in both in order to protect subjects' rights and welfare in light of a principle of justice that now rejects exclusion as well as exploitation'.[93] (p. 356)

In the last twenty years, human subjects research has grown globally, as has the number of protocols needing IRB review. In the US, several government-sponsored inquiries raised serious concerns as to whether IRBs can and do adequately protect human subjects in research.[103] Faced with heavy and complex workloads, limited funds and too few staff, the oversight system is in jeopardy.[103] In response, federal policies have emphasised procedural solutions such accreditation and education of investigators, including web-based tutorials on research ethics.[104] But Kahn and Mastroianni take issue with federal policies which focus on increasing investigators' and institutions' compliance with regulatory requirements.[104] They recommend moving from a culture of compliance to 'a culture of conscience' in which researchers take responsibility for human subjects protection.[105] They contend that a focus on compliance with rules misses the point. In their words '... the protection of subjects can quickly be lost in the shuffle of paperwork necessary to satisfy the letter, if not the spirit, of regulations.'[105] (p. 925) In the absence of evidence that investigators and institutions are taking their ethical responsibilities seriously, public support for research will disappear, and without the public's trust research will abate.[105]

The history of research ethics includes a litany of scandals: World War II Nazi experiments, the Willowbrook State School in New York in which children were intentionally exposed to hepatitis, the Tuskegee Syphilis Study, reports of human radiation experiments from the 1940s to the 1970s[93] and, most recently, deaths of healthy volunteers[4] at leading US universities. Each instance involved some ethical lapse. Meslin hopes that these cases do not recede into history; instead they should provide a basis for ongoing learning and continuing ethical vigilance.[106] In similar vein, Childress urges ongoing sensitive, imaginative and rigorous reflection on ethical standards for human subjects research, in keeping with the legacies of Nuremberg, Helsinki, CIOMS and the National Commissions.[93] He argues for a '... continuing societal conversation about the foundations, meaning, weights, and implications of various ethical principles... in light of various changes in research and its context.'[93] (p. 360) He believes this conversation must include professionals and the public, amongst whom he includes the 'socially marginalized'.[93] (p. 360)

2.2 Ethical Requirements for Research

In a seminal article, Emanuel and colleagues offer seven requirements, synthesized from traditional ethical codes, declarations and relevant literature, for determining whether human subjects research is ethically justifiable.[11] Crucially, these requirements are not limited to a specific scandal or tragedy or to any particular country; '... they are meant to be universal, although their application will require adaptation to particular cultures, health conditions, and economic settings.'[11] (p. 2702) Following the authors,[11] these requirements are discussed in chronological order, in other words, from the study's conception through to its implementation. Other commentators offer a similar framework.[12] Moreover, Roberts and her co-authors[12,107] have developed an instrument, the Research Protocol Ethics Assessment Tool, which poses a number of useful questions which researchers and IRBs can ensure are answered in a research proposal. The tool also has a valuable educative component as researchers are reminded of the values and safeguards central to conducting ethical research. Examples of questions from this assessment tool are given at the end of each ethical requirement.

A study must have *social or scientific value.*[11,12,107] It must enhance scientific knowledge and improve the health and well being of the subjects or society. It should make a significant contribution to a discipline or topic. A determination that a research question or topic is relevant requires an assessment of the proposed study in the light of existing knowledge, which in turn depends on a thorough literature review. If for practical or economical reasons an intervention is unlikely to be implemented in a particular setting, a study is unlikely to be valuable. Importantly, a judgement that a research proposal is scientifically or socially valuable presupposes that the research results will be publicly disseminated. Exposing subjects to risk during research can only be justified if society gains valuable and accessible knowledge.

- Is the study scientifically valuable?
- Can this study yield meaningful data?
- Does the investigator have the necessary expertise and institutional support to complete the study?
- Does the protocol provide for dissemination of the findings?

A study must be *scientifically sound.*[11,12,107] Research that is not conducted in line with valid scientific principles cannot produce generalisable results. In other words, there must be a reasonable chance that the study will generate the knowledge being sought. If research on humans is unsound, it is unethical because it exposes subjects to risks or inconvenience to no purpose. However, Emanuel *et al* make the point that not all well-designed research is ethically acceptable; for example, research that addresses previously answered questions or research that involves the questionable use of healthy volunteers or seriously ill populations may be unethical even if the design is scientifically valid.

- Will the hypotheses be tested adequately?
- Does the protocol use accepted scientific methods?

The *selection of subjects should be fair.*[11,12,107] The scientific goals of the study are the primary basis for determining which individuals or groups should be recruited. Fair subject selection requires that as far as possible groups and individuals that bear the risks and burdens of participation should also enjoy its benefits, and that those who benefit should also share some of the burdens. Fairness demands protection and opportunity for inclusion, which raises the problem of how to balance protection and access. Although, the history of human subjects research documents the abuse of special or vulnerable populations, such as prisoners and institutionalised children, these groups ought not to be excluded from research that may confer benefit to them. Vulnerable groups should be included in research when their inclusion is integral to the scientific intent of the study and they will benefit from participation. Currently, researchers and sponsors from affluent nations are turning to developing countries to obtain large and relatively cheap samples of subjects for their studies. Many of these poorer countries have high disease rates and are in a period of epidemiological transition to non-communicable conditions such as diabetes and heart disease. However international codes such as Helsinki and CIOMS contain guidelines insisting that subjects from poorer communities have access to any benefits that may accrue from these multinational studies.

- Does the selection and recruitment process assure that members of vulnerable populations will be included *only* if essential to the study's hypothesis?
- Will benefits derived from the study, if any, be conferred to the specific population under investigation?

The study must have a *favourable risk-benefit ratio.*[11,12,107] Research is only justified if potential risks to individual subjects are minimized, potential benefits to individual subjects are enhanced, and potential benefits to individual subjects and society are proportionate to or outweigh the risks. That risks are reasonable in relation to personal and societal benefits is a precondition to offering people the opportunity to volunteer, since informed consent alone cannot justify enrollment in an unduly high-risk study. If studies include therapeutic and non-therapeutic components, the risks and potential benefits of each should be examined separately lest the possibility of great benefit or monetary inducement in one component causes potential subjects or IRBs to minimise or overlook risk in another. No matter how great a potential benefit to an individual or society, the possibility of benefit from one element of a study should not be used to justify otherwise unacceptable risk. In order to allow an IRB to perform ongoing assessment of the ratio of risks to benefits, the investigator must inform the committee of any changes in a study design, in the tests being done, in known side effects, or in the availability of alternative treatments. If subjects who are harmed as a direct result of participation in a study they should receive compensation.

- Does the design minimize experimental risks to subjects?
- Does the protocol pose excessive risk to individual subjects, the community, and/or society at large?
- What benefits exist for subjects?
- Is the likelihood of benefit accurately described?

Because investigators have inherent and legitimate conflicts of interest (such as career advancement or publication) that might distort their evaluation of a study, *independent review* is necessary for subjects' protection and for public accountability.[11,12,107] Independent review assures potential subjects that if they enroll in research, the study is likely to be scientifically valid and the risk-benefit ratio will be favourable. Impartial review is designed to minimize potential harm to subjects. In the US, the ethical issues an IRB must consider are codified in the Common Rule.[10] The kinds of study designs that require ethical review are examined in the following section.

- Should the protocol undergo additional review, (for example, by community leaders)?
- Does the protocol require on ongoing monitoring by a data safety monitoring board?
- Do the IRB members possess the necessary expertise to review the protocol?

Exposing people to risk in the name of science is justified only with their *voluntary informed consent.*[11,12] Respect for persons implies that they be allowed to choose for themselves whether to take part in research and to take part only when the research is consistent their values, interests and preferences. To provide informed consent, subjects must be informed of their options, the risks and possible benefits of those options, they must be able to reach a decision without undue pressure, and they must know they can withdraw from the study at any point. If subjects' capacity to choose for themselves is compromised, for example, if they are children or unconscious, they must receive additional protections such as parental permission or surrogacy respectively. Importantly, an IRB should focus on the entire process of obtaining informed consent, not just on the readability of written consent documents. Thus informed consent is a continuous process, not simply a document or moment; signed consent forms are necessary but not sufficient. Informed consent forms are typically impenetrable for even well-educated subjects much less disadvantaged participants.[108] Reading levels are often too high,[108] the forms contain medical jargon and potential risks may be under-estimated.[10] Specific problems related to obtaining informed consent such as vulnerability and the therapeutic misconception will be examined in the following section.

- Is the consent form concise, readable, accurate and understandable?
- Is there reasonable assurance of adequate decisional capacity of potential subjects?

The principles or rules of *privacy and confidentiality* set further limits on human subjects research.[11,12,107] In conducting research using identifiable medical records or case histories, social and psychological harms (including stigmatisation) resulting from breaches of confidentiality must receive as much consideration as physical harms. For example, although genetic research may pose no physical risk beyond that of drawing blood, it can pose significant psychological and economic risks if insurers or employers learn that subjects are predisposed to an untreatable condition. Careful attention to confidentiality concerns means that researchers must develop and use data collection and storage practices that safeguard confidentiality internally and externally, and fully communicate confidentiality limitations to subjects prior to their enrollment. Additionally, new information technologies such as computerised medical records increase threats to privacy and raise ethical concerns regarding legitimate access to these electronic databases for purely research purposes.

- Does data collection and analysis adequately protect subjects' confidentiality?
- Will subjects' identities be protected during data presentation and dissemination?

Emanuel and his team[11] do not guarantee that their framework will lead to unanimous agreement among researchers and IRB members on the ethics of a proposal. Still, the framework provides a platform '... to generate traditions of interpretation', to understand and locate disagreement, and to work towards shared solutions. (p. 2711)

Since this study focuses specifically on the documentation of REC approval, informed consent and confidentiality, the literature on these ethical safeguards is examined in more detail in the next sections.

2.2.1 Independent IRB/REC Review

According to the Helsinki Declaration 2000 in Article 13, research proposals '... should be submitted for consideration, comment, guidance, and where appropriate, approval to a specially appointed ethical review committee, which must be independent of the investigator, the sponsor or any other kind of undue influence...'[7]

In the USA most universities, medical schools and large hospitals have a Multiple Project Assurance (MPA) negotiated with the Office for Human Research Protections of the National Institutes of Health.[42] The MPA binds the institution to establish an IRB and comply with federal regulations in the Common Rule.[42] Before engaging in any research involving human subjects, researchers must comply with their institutional policies for submission to and approval of their IRB.[109] Under the Common Rule, research which is presumed to present very little or no risk, is exempt from IRB review and need not be submitted for review.[10] However, most MPA institutions have adopted more thorough ethical guidelines and require the submission of all research protocols involving human subjects for IRB approval.[109] If necessary, the IRB will write a letter to document that the study is exempt from IRB approval.[109]

All human research should have IRB approval as investigators may have inherent conflicts of interest and appraise their study risk as much lower than IRB committees would rate them.[109]

A new set of arrangements for the governance of local and multicentre RECs has recently been published in the UK.[110] These proposals arose in response to increasing criticism from disgruntled investigators that the ethics review process was inconsistent, lacked accountability and led to bureaucratic delays.[110] Indeed, this variation in ethics committee decisions has been confirmed in a study which compared the amendments requested by RECs in an international study conducted concurrently in New Zealand, the UK, Israel, Canada and the USA.[111] The widely differing interpretations of 'minimal risk' by RECs confirm the complex and often subjective nature of these decisions.[111] The authors conclude that RECs must balance the ethical principles enunciated in the Belmont Report in such a way that they promote ethical research rather than prevent unethical research '... which inevitably results in researchers being impeded from doing their work'.[111] (p. 7) Significantly, the authors also admit that 'How the balance is to be achieved requires further consideration'.[111] (p. 7)

Because most research requires ethical approval, an important first question facing investigators and RECs is whether or not an activity constitutes research with human subjects.[109] This is not a silly question as the boundaries between research and practice may be blurred.[101] As a general rule, practice refers to interventions designed to improve individuals' well-being and which have a reasonable chance of success.[101] In comparison, research refers to an activity designed to develop or test an hypothesis or contribute to generalisable knowledge.[109] Furthermore, research usually includes a formal protocol that states an objective and a set of procedures to meet it.[109]

The Common Rule[10] defines research as 'a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge' (45 CFR 46. 102 (d). The South African Medical Research Council has an identical definition of research.[112] At times it may be difficult to determine if any given activity constitutes research.[109] If an investigator interacts with an individual, or collects data about that individual for other than clinical care, that activity may constitute research and should be discussed with an REC.[109] In addition, the evaluation component of a health services program may include research activities that may require REC review.[109] Generally, investigators are advised to consult their local REC if they are in doubt about the status of an intervention.[109]

The Common Rule provides specific criteria that an IRB must use when reviewing and approving research (45 CFR 46.111).[10] For example, regardless of whether an IRB undertakes a full or an expedited review, risks to subjects must be minimised by using procedures which are consistent with sound research design, which do not unnecessarily expose subjects to risk, and by using procedures already being performed for diagnostic or treatment purposes.[10] The IRB is also responsible for conducting continuing review of research appropriate for the degree of risk, but not less than once a year.[10]

IRB review spans a wide spectrum of research designs ranging from RCTs to nonmedical interventions and retrospective audits.[109] For example, quality assurance studies now require IRB review if the investigator intends to publish a study's findings.[109] Not surprisingly, many researchers resent the extra paperwork and regulation. Sometimes researchers may not realise that studies, in particular medical record reviews, need prior ethical review.[109] Most IRBs will reject applications for ethical approval after a study has been completed.[109] Wagner provides a useful analysis of which types of human research require IRB review, including the more ambiguous and problematic designs.[109]

Most studies which include medical interventions require IRB approval.[109] Importantly, phases 1, 2, 3 and 4 of clinical trials require separate ethical approval since an IRB cannot evaluate the risks of later phases until a safe dose range and profile of side effects has been established in the initial stages.[109] In the case of novel interventions, IRB approval must be sought as soon as investigators recognise their intent to generalise the results of novel treatments.[109] IRB approval, including informed consent, is needed if investigators systematically examine interventions that are part of *standard* treatment.[109] Examples of nonmedical interventions requiring IRB approval include physiotherapy, exercise training, psychological therapy and social work counselling.[109] Studies of unproven diagnostic tests and medical devices also need IRB review. This is because patients' treatment is changed and private information may be collected, neither of which may directly benefit individual patients.[109]

If retrospective studies collect private information from medical records, even if only for clinical purposes, then IRB approval is necessary. In the course of such research, patient privacy can be lost as a range of research personnel gain access to patients' personal information, violating their rights and causing them potential harm. If patients later learn that record reviews have been undertaken without their knowledge, they may become suspicious and lose trust in their physicians, the institutions and the research enterprise.[113] Indeed, 55.4% of respondents suffering from a range of conditions did not believe that researchers should have access to their medical records without their permission.[113] Kass and her co-authors believe IRBs can act as a safeguard to ensure patients do not give blanket consent to future access to their records as a substitute for individual informed consent. Blanket consent would likely serve investigators' interests more than those of potential subjects.[113] Kass and her colleagues also recommend that IRBs scrutinise requests for use of private medical information on a case-by-case basis.[113] Kass *et al* contend that '... patients must be partners in the research enterprise, and clearly they are unwilling to be partners when they believe research takes advantage of their personal data, without their knowledge, and for a benefit that may be elusive'.[113] (p. 433)

Patients who exemplify a previously unreported condition or who have distinguishing features of a known disorder often become the subjects of case reports in medical[114] and physiotherapy[115] journals. Case reports describe the medical history of a single patient in a narrative form, and although methodologically weak, they serve a useful purpose and can rapidly provide a great deal of information.[115] Such reports are an accepted method of informing health professionals of new aspects of patient care in order to improve care of similarly affected persons in the future.[114,115] Single case reports are usually not considered research, as they are not systematic investigations.[109,] However, the inclusion in a report of more than about six cases would probably require systematic data collection[115] and would need IRB approval.[109]

The publication of clinical case reports can raise complex ethical issues.[114] The clinical data belong within the confines of a confidential, professional relationship and patients are unaware that they may be contributing to scientific knowledge.[114] Significantly, case reports may contain information that is sufficiently unique to enable identification of particular patients.[114] For example, family histories, physical findings or physical documentation such as photographs and radiographs might lead to inadvertent identification of the individual(s) under discussion.[114] If published, even incognito in medical or physiotherapy journals, single case reports can violate a patient's right to privacy and confidentiality causing distress at the dissemination of private medical information.[109,114] Since anonymity cannot be guaranteed, many authors agree that informed consent for publication should always be obtained.[83-85,114] Ideally, the intent to publish should be discussed with the patient or family prior to publication and a signed consent obtained.[114] To improve the consent process for photograph publication, Murray and Pagon[114] recommend that the individual or the family (in the case of a child) be contacted just prior to publication of the material (not years before) to obtain, or re-obtain, informed consent. A copy of the consent form should be provided to the individual or family.[114] Whether IRB approval is needed for publication of individual case reports remains controversial.[109] Fost and Cohen view the journal editor as the final gatekeeper holding the power of veto if ethical standards are missing from submitted case reports.[83]

The priority accorded to improving health care quality internationally has led to an expanding number of quality improvement (QI) initiatives in a variety of health care settings.[117] Given their inherently managerial nature, there is uncertainty as to which QI activities require IRB review.[109,117] It is useful to distinguish between research and nonresearch interventions so that IRBs do not needlessly focus on activities in which patient safety and protection clearly are not issues.[117] Nerenz *et al* argue that QI activities that do not attempt to investigate '... any generalizable, universal processes or causal relationships' are not research.[117] (p. 169) They contend that these activities are designed to understand *local* processes and relationships. In contrast, IRB approval is needed for QI studies where the intent is to contribute to generalisable knowledge or to publish outside the particular setting.[109] Additionally, if patient care is being changed and the results are systematically measured, this is considered research and requires both IRB approval and patients' informed consent.[109] Wagner holds that IRB approval should be obtained whenever a QI intervention resembles a standard research design, no matter how the results will be used.[109] Exactly when IRB approval is needed for QI initiatives is controversial and remains subject to debate.[109] For instance, investigators wishing to publish interesting findings may seek IRB approval after completion of a QI intervention. Wagner believes IRB approval may be granted if the committee feels the investigator did not initially set out to collect generalisable data.[109] However, he would not support IRB approval if from the outset a researcher intended to contribute to generalisable knowldedge.[109] Likewise, product evaluations are considered managerial activities not requiring IRB approval as long as the results of the evaluations are limited to particular institutions.[109]

In general, most public health activities, such as the routine collection of data on notifiable conditions or the maintenance of disease registries, are not subject to IRB review.[109]

Whilst large medical databases are an important resource for health-related research, use of these databases raises serious ethical concerns about confidentiality. IRB approval is required if identifiable private information will be recorded as, according to the Common Rule, this makes persons research subjects by definition.[109] IRBs must find the right balance between the research needs and privacy.[118] IRBs must be convinced that proposed research on medical databases is of high quality and therefore justifies any risk to subjects.[118] Research which has no personal identifiers may be exempt from IRB review.[109] In the US, use of health information is now further regulated by the Health Insurance Portability and Accountability Act (HIPAA) which erects new barriers to the use and disclosure of identifiable information by imposing complex organisational and procedural requirements on the entities it covers.[119] Significantly, the Privacy Rule defines 'identifiable' information far more precisely and expansively than the Common Rule. There is concern that after de-identification, which now includes birth dates and zip codes, research data may not have enough identifiers to allow linking with other databases to determine relationships between patterns of care and long-term outcomes.[119] IRBs must ensure that protocols comply with both Common Rule and HIPAA requirements.[109]

Surveys, interviews and participant observation, research methods typically found in the social sciences, generally require IRB approval since they often involve the collection of sensitive information.[109] However, the role of predominantly medical IRBs in the evaluation of anthropological and sociological research is currently the subject of much criticism.[120,121] It is contended that because IRBs are unfamiliar with ethnographic and qualitative research methods, they may delay or place unnecessary obstacles in the way of important research. IRBs need thorough training in biomedical and qualitative research methods.[102,120,121]

In sum, despite its cumbersome nature, the process of obtaining IRB approval focuses investigators' minds on the ethical implications of their interactions with human subjects, which include the right to choose whether to participate in a study.[109]

2.2.2 Informed Consent in Research

An unavoidable aspect of human subjects research is individuals' preparedness to put themselves at risk in return for benefits that are likely to accrue to future patients rather than themselves.[105] This distribution of risks and benefits is partly justified by the notion of informed consent which reflects the basic principle of respect for persons.[101] With few exceptions (such as emergency and resuscitation research),[122] informed consent has become an international[6-9] and national[10,112] ethical precondition of including human subjects in research. Ideally informed consent for research participation should be a process of communication between the researcher and the subject.[123] Informed consent is more than merely obtaining a participant's signature on a consent document. Indeed, by itself, the signed form does not guarantee that the potential subject has understood any of the information.[123] In short, informed consent is a process requiring time and effort.[123]

Typically, informed consent contains the following elements: the provision of adequate information enabling subjects to make an informed choice, subjects' capacity to understand what they are being told so that they can make a reasoned choice based on the information, and subjects' voluntariness to make choices without coercion or undue influence.[124] Put simply, informed consent includes the provision of information, the requirement that the information is understood, and a voluntary decision whether or not to take part in a study.

Each component of informed consent raises practical questions: what and how much information should be disclosed, how is a subject's competence to participate accurately determined, and how is a subject's voluntariness gauged, especially when an investigator is also the subject's treating physician.[123] Lidz and Appelbaum make the point that providing information merely initiates the process of obtaining informed consent, following which subjects must then make the information relevant to their particular needs and preferences.[125]

A particular concern in the informed consent process is the voluntariness of subjects' consent.[123,125,126] Nelson and Merz define voluntariness as '... an exercise of free will or choice - an act being done volitionally or with intent and deliberateness, one that is free from coercion and undue influence.'[126] (p. V-69) Threats to voluntariness can arise when individuals with health problems take part in studies investigating those problems.[126] If patients are accustomed to receiving medical care for their disorders, they may assume that enrolling in a study is simply another way to obtain treatment. However, because research carries a different distribution of risks and benefits than clinical care, it is essential that subjects appreciate the distinction between research and therapy.[105] Unfortunately, this distinction is not always clear in the minds of patients who choose to enter a study. Lidz and Appelbaum coined the term 'therapeutic misconception' to describe patients' failure to understand the differences between therapy and research.[126] The therapeutic misconception occurs when subjects consent to participate in clinical research because they believe they will receive the same individually focused treatment that they would normally receive in a non-research clinical context.[126] Subjects fail to grasp that research is designed primarily to produce generalisable knowledge, not to help individual subjects.[123] Furthermore, patient-subjects may fail to understand that the constraints of a scientific protocol may compromise their clinical options.[125] For example, if the study design is a double-blinded clinical trial neither subjects nor physician-investigators is aware of the agent that a given subject is receiving.[126] Although some studies allow a degree of flexibility in the medication dosages subjects may receive, the acceptable range is generally narrower than the corresponding range for patients in a clinical setting.[125] In sum, patients may fail to comprehend that providing the best care to individual patients is not the primary goal of research and that the constraints of the scientific method possibly may affect their clinical options.[127]

The therapeutic misconception may be reinforced through the research process or investigators' behaviour. For example, if researchers are also clinicians caring for patients, they can face a conflict of interest.[105] The obligation to do what is best for the individual patients may conflict with what is best for the outcome of the study.[123] Furthermore, the need to recruit a certain number of patients into a study may influence the way a physician-researcher conducts the informed consent process.[127] They may convey undue optimism or present a study as being another form of alternative treatment which is better than standard care.[127] Researchers who wear white coats and meet potential subjects in medical settings may signal therapeutic intent.[127] Because patients trust their doctors, they may assume that if their doctor offers or suggests participation in a study it is in their best interest to enroll.[123] Likewise, patients trust the health care institutions where they receive their medical care not to take advantage of them.[123] Furthermore, physician-investigators may be unable to acknowledge the uncertainty that makes clinical trials necessary. To do this the investigator must openly admit to a patient that the medical community is unsure about the best treatment approach.[127]

The informed consent forms may inadvertently encourage the therapeutic misconception.[127] For example, informed consent forms may overstate the benefits of participation or they may describe the research intervention as a form of 'treatment' rather than an experiment.[127] Conversely, informed consent forms may understate the risks of participation.[127] Alternatively, informed consent forms may be so complex, that important information is lost among the detail.[127]

According to the principle of respect for persons, human subjects research is only morally permissible if potential subjects make an informed and voluntary choice.[127] Accordingly, the increased emphasis on informed consent in the research setting takes into account the different goals of therapy and research. However, Dresser contends that as long as the therapeutic misconception is a problem, '... it is hypocritical to claim that informed consent supplies moral justification for patients' participation in research'.[127] (p. 294) She offers several strategies to address the therapeutic misconception: using an independent or neutral person to obtain consent, simpler informed consent sheets that highlight the benefits and risks of participation and the differences between how patient-subjects will be treated if they choose research versus ordinary care.[127] In turn, Lidz and Appelbaum recommend that subjects be told not only how treatment and research differ, but also why they differ.[125] For instance, subjects need to know randomisation will take place so that researchers and medical science as a whole can find out what interventions do and do not work.[125] Crucially subjects need to know that randomisation is being used for non-therapeutic reasons.[125] By the same token, subjects need to know about the risks and benefits that accrue from treatment as well as those that result from participation in the study.[125] In short, subjects need to know that clinical care is more individualised and research tends to be standardised.[125]

Another worrying problem is obtaining valid and voluntary informed consent from vulnerable populations. Vulnerable groups include those viewed as more open to harm (for example, children or those with certain mental or developmental disorders), more subject to coercion (for example, institutionalized persons), more complex (for example, women who might fall pregnant and expose their foetuses to harm) or more susceptible to exploitation (for example, persons with incurable diseases or lacking essential social goods).[128]

The Nuremberg Code's insistence on subjects' informed consent effectively ruled out the inclusion of children and the cognitively impaired in biomedical research.[6] Subsequent research scandals such as took place at Willowbrook, the Brooklyn Jewish Chronic Disease Hospital and Tuskegee,[2] further highlighted the plight of certain vulnerable subpopulations in research, namely institutionalized children, hospitalised elderly and impoverished and poorly educated black American men. To address some of the shortcomings of Nuremberg, the 1979 Belmont Report[101] briefly considered children, the institutionalized mentally ill and prisoners, mentioning dependency and compromised capacity for consent as hallmarks of vulnerability. In the US, the more recent federal regulations[10] require IRBs to ensure that additional safeguards have been included in the study to protect the rights and welfare of subjects who are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons or economically or educationally disadvantaged persons. Mandatory additional protections are found in Subparts B to D of the Common Rule.[10] These additional subpart protections raise the bar when research is undertaken among these special groups.

Kipnis argues that this subpopulation focus inescapably ' ... assumes a baseline standard for a default "paradigmatic" research subject... a mature, respectable, moderately well-educated, clear thinking, literate, non-pregnant, self-supporting, United States citizen in good standing'.[128] (p. 107) Clearly, many potential subjects fall outside this paradigm research subject. Thus, in contrast to a subpopulation approach, Kipnis offers an analytical or conceptual approach which identifies characteristics that can be used as criteria for vulnerability.[128,129] Because these criteria may adversely affect informed consent or the permissibility of certain research, supplementary measures should be considered if persons with these characteristics are to serve as research subjects. The distinct vulnerabilities and relevant related literature as summarized below offer a useful framework for examining specific problems and solutions for obtaining informed consent in these populations.[128,129]

Cognitive vulnerability is concerned with a potential subject's capacity to deliberate about and decide whether or not to participate in a study. Circumstances that suggest the presence of this type of vulnerability would include immaturity, dementia, certain types of mental illness, mental retardation, and educational deficits.[128,129]

Children may be inappropriate subjects in some research owing to their lack of decisional capacity or maturity.[127] Children fall along a spectrum of decisional capacity: from the newborn who is totally helpless to the mature adolescent who may possess full decision making capacity, if not the legal authority to consent to participation in research.[127] To protect immature children, ethical[112] and regulatory guidelines[10] restrict the types and levels of harm and risk that investigators may impose or that parents may allow. Under this framework, research that provides a prospect of benefit to the child or poses minimal risk to subjects is allowed.[10] For research that does not offer the prospect of direct benefit, the allowable risk exposure is restricted to minimal risk for healthy children or a minor increase over minimal risk for children with a condition that is the focus of the research.[10]

The Common Rule defines 'minimal risk' as the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.[10] Of note, in the SA guidelines, negligible risk (the smallest possible risk) must be 'equal to the probability and magnitude of physical or psychological harm encountered in the daily lives of people in a stable society or in the routine performance of physical or psychological examination or test'.[112] (p. 41) In the US, if researchers want to conduct studies with children that involve more than a minor increase over minimal risk, a federal oversight body must review the study, the public must be offered the opportunity to comment, and the US Secretary of Health and Human Services must give his or her approval.[10]

Although vulnerable individuals need additional protections, they ought not to be arbitrarily excluded from research. Progress in diagnosing, treating and preventing medical conditions that impair decision making depends on research involving individuals who may either be unable to or have diminished ability to give consent. Diminished decision making capacity is found in many medical conditions, for example cerebrovascular disease, HIV/AIDS, ischaemic heart disease, neuropsychiatric disorders and victims of motor vehicle accidents.[130]

Blackmer draws attention to specific problems that can arise when obtaining informed consent for research in the field of rehabilitation medicine, which is likely to include physiotherapy studies.[131] He examines difficulties associated with determining decision making capacity among stroke patients. Whereas some stroke patients may have no cognitive deficits, others may have such significant damage to parts of the brain involved in judgment and reasoning, that they cannot make a truly informed decision to enter a study. Other populations, often included in research, who might suffer some cognitive deficits are patients with Parkinson's disease and multiple sclerosis. He cautions researchers to be hyper vigilant and where there is doubt to obtain capacity assessments to ensure that patients' participation is truly informed and voluntary.[131] Similarly, he gives examples of patients with aphasia who may require thorough assessments to establish if they have adequate communication skills to participate in the consent process.[131] He advises researchers to be sensitive to the timing of subject recruitment. For instance, some patients with life-threatening injuries, such as severe trauma to the spinal cord, may need to readjust to their new circumstances. Researchers need to take this into account whenever they enroll such patients in a study. Blackmer warns against the overuse of certain captive populations such as residents in rehabilitation centres.[131] Even though these groups may benefit from findings about their condition, they must not bear a disproportionate share of the burdens of such research.[131] In similar vein, because of relatively small patient numbers, some diagnostic categories (such as spinal cord injuries) in rehabilitation medicine may be unduly inconvenienced by research.[131] Over time, by virtue of their dependency, some patients will develop close emotional bonds with their health care providers. Clinician-researchers must take great care that patients do not agree to research participation from a sense of gratitude and appreciation.[131]

When patients are judged incompetent to make treatment decisions, surrogate decision makers must be engaged.[130] Two legal and ethical standards govern surrogate decision making. If the prior preferences of the patient are known then the surrogate should make a substituted judgment that (s)he believes the patient would have made if able; if not known, then the surrogate and physician should choose an option believed to promote the patient's best interests.[130] Exceptions include emergencies or when surrogate decision makers are not available, in which case physicians or other officially designated individuals make treatment decisions for the patient.[130] If no surrogate is designated in advance, next-of-kin are generally considered appropriate decision makers. They are presumed to know the patient's preferences and values which should determine or inform treatment decisions.[130] Although this conceptual and ethical framework is largely applicable to the research context, it must be evaluated in light of ethically significant differences between clinical practice and clinical research.[130]

As a consequence of these differences, Chen and colleagues raise four issues needing attention before incompetent adults can be enrolled in research.[130] First, assessments of competence must ensure that patient-subjects appreciate the differences between clinical practice and clinical research. Second, levels of risk normally justified in clinical practice may not be acceptable in clinical research. Chen *et al* believe the federal framework of protections for children offers guidance for the determination of acceptable levels of risk.[130] Third, IRBs must be certain that all research involving decisionally incapacitated subjects has a formal plan to assess capacity prior to enrollment. Moreover, capacity assessments should be made by professionals with appropriate experience such as a psychiatrist or neurologist.[130] Documentation of the capacity assessment should remain in the subject's research record and needs to be ongoing throughout the duration of the study.[130] Fourth, surrogate decision makers also need to recognize differences between treatment and research.[130] Importantly, there may be scant evidence to support a substituted judgment standard since potential subjects may never have expressed a preference for participation in research.[130] Likewise, the best interest standard may be difficult to interpret in the context of non-beneficial research.[130] Additionally, there is disagreement regarding the extent of discretion that ought to be given to surrogate decision makers regarding participation of incompetent adults in clinical research.[130] Chen *et al* recommend more empirical research in the field of surrogate decision making for incompetent adults.[130]

Juridic vulnerability focuses on the formal authority relationships that exemplify many social structures.[129] For example, in prisons and the military wardens and officers have legal authority over inmates and enlistees, children are under the authority of parents, students are subordinated to teachers and professors, and, in some societies, women are subject to their husband's authority.[129] In these examples, researchers must try to ensure that subjects' consent does not merely reflect the wishes of those in authority.[129] Roberts *et al* note that students are particularly vulnerable because they are readily available in settings which often actively promote educational, clinical and scientific research.[35] Students may feel pressured to participate, fearing reprisals (such as low grades) if they should refuse.[35]

Jago and Bailey highlight potential problems in obtaining informed consent in the sports sciences which also includes a significant element of physiotherapy research.[132] Much sport and exercise-based research is undertaken among students who may feel compelled to take part in a study if the investigator is their teacher or sports coach.[132] As a possible solution, the authors suggest researchers should ask for volunteers from courses or classes for which they are not directly responsible. This would reduce problems of undue influence.[132]

Rose and Pietri refer to 'paycheck vulnerability' which may occur when research is undertaken in the workplace.[133] (p. 802) Workers may feel pressured either to take part or not to take part to satisfy the wishes of management or their unions. Rose and Pietri would like to see IRB review of most research undertaken in the workplace, notwithstanding the ambiguous definition of research in these settings.[133] They also recommend worker representation on the IRB. Privacy and confidentiality, in particular, must be safeguarded to prevent the inappropriate release if identifiable health and personal information.[133]

When obtaining assent from children, researchers need to be aware of parental pressures which may constrain a child from voicing a dissenting opinion.[128] To address potential power differentials researchers may need to interview children separately from their parents.[128]

Deferential vulnerability refers to potential participants' subjective responses to certain others, exemplified by a desire to please.[129] Consent procedures need to take account of powerful social and cultural pressures.[129]

Social vulnerability draws attention to 'entrenched prejudice and stereotypical thinking' that may compromise the consent process.[128] (p. 114) For example, in the 1970s and 1980s women were systematically excluded from participating in clinical trials through fear that unrecognized pregnancy might place the foetus at risk or because a uniform all-male sample would simplify data analysis.[134] Additionally there was fear that inclusion of pregnant women in clinical trials would increase investigators' liability.[134] It is only in the past decade that policy shifts have taken place in order to obtain valid information about the health and disease in this population.[134] The presumption now favours inclusion of women in all clinical studies except for those addressing health issues only relevant to men.[134] In similar vein, Kipnis feels children should have a louder voice and receive more recognition in research development and review.[128]

Medical vulnerability is present if a potential subject suffers from a serious health-related condition for which there is no known effective intervention.[129] Examples include metastatic cancers, end-stage AIDS and Alzheimer's disease.[129] Lacking treatment options, medically vulnerable patients may enter studies with unrealistic expectations that they may benefit from access to new interventions.[129] In other words, these patients experience the therapeutic misconception. Kipnis recommends that investigators try to ensure a fairer distribution of benefits and burdens, such as post-trial access to the experimental interventions if the drugs turn out to be safe.[129] In addition, consent forms must stress differences between treatment and research as well as the low probability of benefit, especially in phase 1 clinical trials.[129]

Allocational vulnerability occurs when individuals lack important social goods such as money, housing, medical insurance and the like.[129] Economically disadvantaged persons may decide to take part in research in order to access health care or other monetary benefits offered as rewards in exchange for participation.[135] Stone believes the Common Rule should extend its special protections to the economically and educationally disadvantaged.[135] For example, research on these groups might be limited to minimal risk interventions and IRBs would need to ensure that rewards for participation are not of such a magnitude that individuals' ability to weigh the risks and benefits is impaired.[135]

Because some subjects may show several types of vulnerability, Kipnis contends that this classification is superior to a subpopulation approach to understanding vulnerability.[129] He recommends the eventual development of a 'master matrix, the columns of which would be subpopulations and the rows of which would be the pertinent vulnerabilities, each cell detailing the compensating measures that might address them.'[129] (p. G12-G13)

In summary, the rights and welfare of those who volunteer to take part in research are fundamental tenets of ethical research. Following scandals in the 1960s and 1970s which involved dubious research among the sick, illiterate and institutionalised, much progress has been made in the ethical conduct of research.[93] Importantly, these groups should not be arbitrarily excluded from research solely on grounds of their vulnerability. Ethical research does not avoid complexity, rather it acknowledges and tries to address the full range of realities of the human condition.[129] Informed consent remains one of the strongest protections for research subjects.[123] However, obtaining informed consent is not always straight forward because of significant obstacles in communication, understanding, linguistic barriers, distinctive social realities and different understandings of what constitutes reasonable ethical practice.[123] Conducting research among vulnerable groups requires special safeguards, particularly in relation to consent. Special efforts are needed to ensure subjects or their surrogates are clear about the differences between research and treatment.[125] And as risk and complexity increase, IRB review and monitoring should intensify.[93]

2.2.3 Privacy and Confidentiality in Research

The expansion of biomedical, social and behavioural research to include diverse populations (for example, hospital patients, scholars, sex workers, gang members, asylum seekers), contexts (for example, schools, workplaces, prisons, shopping centres, private clinics) and sensitive topics (for example, sexuality, addiction, impotence, incontinence, HIV status) raises complex ethical issues of privacy and confidentiality.[136] In addition, the meaning of privacy and confidentiality is likely to depend on the culture and particular circumstances of the individual subject, the nature and context of the research, and the social and political environment in which the research and use of the data will occur.[136]

For Sieber, privacy ' ... is an aspect of respect for persons that can be difficult to translate into respectful behavior in cultures and contexts in which one does not understand the relevant norms and beliefs'.[136] (p.N-6) Without a useful definition of privacy, researchers and IRBs must rely ' ... on their own culture-bound notions of what people consider as private'.[136] (p. N-6) This can lead to arbitrary and subjective standards of protection. Moreover, different research methods will bring their own specific privacy and confidentiality-related concerns. Alternatively, the same method used in different contexts will raise different ethical problems, for instance, survey research conducted in face-to-face interviews, or via mail, telephone or the internet.[136] Thus, investigators and IRBs need to be aware of the distinctive ethical implications for privacy and confidentiality of the various research methods and their impact in different contexts.[136]

Drawing on published examples, Sieber says 'privacy refers to persons and to their interest in controlling the access of others to themselves'.[136] (p. N-7) With its emphasis on control and autonomy, this definition recognizes the crucial role of informed consent in allowing subjects choice or control over whether researchers can gain access to their attitudes, beliefs, opinions, behaviour or medical information.[136] Furthermore, if research is going to be longitudinal or ethnographic, Sieber believes informed consent should be an ongoing process of communication in which the reasons for data collection are repeatedly clarified.[136]

In short, to respect privacy is to let subjects control who has access to them and to provide adequate opportunity for people to decline to participate. To breach privacy is to violate people's space, for instance deceptive research which encourages subjects to react in ways they would not normally wish to be observed or to conduct a study among employees to which management (not the workers) has consented.[136] Subjects' own concepts of privacy are likely to vary according to age, ethnicity, socioeconomic status, gender and location.[136] Notions of privacy are unlikely to be universal across cultural and demographic groups.[136]

Sieber views confidentiality as an extension of the concept of privacy. It refers to data (which may be identifiable) and to the agreements about how data will be managed in keeping with a subject's interest in controlling the access of others to themselves.[136] Confidentiality arrangements acknowledge subjects' right to privacy (that is, their valid claims against unauthorized access[124]) and indicate how this will be achieved.[136] If researchers cannot guarantee confidentiality (for example, in cases of child abuse), this must be disclosed in the informed consent.[136] If researchers intend to archive data or share findings with other scientists, this must also be disclosed.[136]

Recently, data collection and storage practices have undergone dramatic change, due mainly to the digital revolution. Worldwide, new laws to protect privacy are being developed and evaluated.[119,137] A key theme of this legislation is to make individuals aware of how information about them will be used.[137] Still, disagreement remains about how to balance societal and individual interests, in other words, how to protect medical records and at the same time make them accessible for research.[118,137] Drawing on values such solidarity, altruism, medical gift relationships (such as blood donation) and unselfishness,[124] some argue that 'The right to medical care should ... generally continue to include the responsibility to allow the information gained in its course to be used for the benefit of others who develop a similar disease, or are at risk of developing it. Confidential sharing of information about patients between doctors and bona fide medical researchers (with exceptions only in particular cases) has done no harm and has achieved much good. Why destroy it?'.[138] (p. 730) However, privacy and medical research need not be antithetical since privacy is itself a societal interest, and advancing health via research is an interest held by most individuals.[136]

In the US, researchers who anticipate obtaining certain kinds of highly sensitive information (for example, about illicit drug behaviour) may obtain a Certificate of Confidentiality from the Department of Health and Human Services in order to provide additional protection from legal subpoena.[136] A Certificate of Confidentiality must be requested in advance of each research undertaking.[136]

In order to facilitate important research AND protect patients' privacy interests, Appelbaum makes several suggestions.[139] If, at the time medical information is being collected, researchers clearly intend to use the data for research purposes, they should obtain patients' informed consent. If researchers seek access to existing databases of information not collected for research purposes, they should seek IRB review to ensure that the criteria for waiving informed consent are ethically justifiable. Contractual mechanisms could be developed limiting investigators to stipulated use of medical information; and investigators should face stringent penalties for misuse of research data.

In summary, researchers and institutions need to cultivate respect for the privacy of those whose health or social experience is under investigation. There is also a need to compare how different countries deal with consent and its alternatives, anonymisation, societal versus individual interest and IRB review in order to develop internationally consistent practices.

2.3 Reporting Ethical Practices in Journal Articles

2.3.1 Publication Guidelines for Journal Articles

Whereas human subjects protection was first codified in 1946 and subsequently embodied in the Declaration of Helsinki in 1964, the need to document compliance with these guidelines in published research is quite recent.

In 1978, a small group of general medical editors, now the International Committee of Medical Journal Editors (ICMJE) met informally in Vancouver and established a uniform set of requirements for manuscript submission. These guidelines have been revised four times.[16] In the 1981 version, the ICMJE required authors to show that research had research ethics committee approval; and in 1991, they insisted that the procurement of informed consent should be clearly stated in the article. The entire Uniform Requirements document was revised in 1997, and most recently in 2001 when issues pertaining to sponsorship, authorship and accountability were highlighted. Over 500 journals subscribe to the uniform requirements..[16]

Other bodies concerned with publication ethics include the Committee on Publication Ethics (COPE)[17] and the web-based World Association of Medical Editors (WAME).[18] Founded in 1997 as an informal, self-help group of editors, COPE now has a membership of 178 international journals and many UK publishers. According to COPE's Guidelines on Good Publication Practice, research submitted for publication must have documentation of ethical approval of all research involving humans, medical records and anonymised human tissues, fully informed consent, and when subjects are unable to give fully informed consent, research must have followed international guidelines such as those of CIOMS.[17] Recently, COPE produced a draft code of conduct for medical editors.[20] According to the code, prepared by the current editor of the BMJ, editors must '... ensure that research material they publish has been approved by an ethics committee' and furthermore they '... can be held responsible for publishing "unethical" research even if it has been approved by an ethics committee'.[20] (p. 1010) Editors are also expected to ensure subjects' confidentiality, generally by means of written informed consent.[20] The guidelines give no indication as to how an editor might reach such a determination. In similar vein, members of WAME must ensure evidence of IRB review and informed consent in their publications involving human subjects.[18] WAME provides editors some leeway to publish studies not approved by an IRB if they are satisfied that the subjects were adequately protected.[18] Conversely, editors may decline to publish studies they feel are unethical even if approved by an IRB. Again, the guidelines fail to indicate on what objective basis editors might make such assessments.

In 1997, a landmark study by Amdur and Biddle found that many editors failed to communicate these basic ethical requirements to potential investigators and authors.[26] Their review of journals' instructions to authors regarding documentation of IRB approval and informed consent showed less than half (48/102) specified IRB approval as a prerequisite for publication and about one quarter did not provide or refer authors to any information related to research ethics.[26] Fifteen percent of journals referred authors to the Uniform Requirements and 3% to the Declaration of Helsinki. However, Amdur and Biddle make the point that it was unclear from the instructions whether compliance with the Uniform Requirements or the Declaration was a condition of publication.[26] Alarmed by the variability of the requirements relating to the ethical standards in biomedical journals, Amdur and Biddle recommended that journal editors standardise their requirements for publication and that the instructions to authors sections contain a clear and detailed description of the ethical standards needed for publication of human subjects research.[18] Further, authors must be left in no doubt that documentation of IRB review was a condition of publication and where a study was exempt from review, reasons for exemption must be stated.[18] Recently, several journals have published guidelines addressing selected ethical issues in human research.[51-57,60]

2.3.2 Rates of Compliance with Ethical Protections in Journal Articles

Major ethical codes[6-8] and regulations[10] along with international publication requirements,[16-18] determine how human subjects research ought to be conducted. Contemporary ethical standards mandate IRB approval, informed consent and stringent privacy and confidentiality safeguards. Despite widespread consensus on these basic protections, articles in major journals still reflect variable rates of IRB approval and informed consent in research undertaken among at risk groups such as children, the elderly, the critically ill, medical students and patients about to undergo anaesthesia and surgery. In addition, research shows that rates of compliance vary according to study design.

Because clinical trials include interventions which can increase physical risk to subjects, reporting ethical safeguards such as IRB approval and informed consent is especially important. Ruiz-Canela *et al* examined both the methodological and ethical aspects of trials published in the British Medical Journal (BMJ), the Journal of the American Medical Association (JAMA), the Lancet and the New England Journal of Medicine (NEJM) between 1993 and 1995.[43,44] There was evidence of IRB approval and informed consent in 71% and 80% of articles respectively. Approximately two thirds (64%) of articles reported both requirements. Moreover, rates of publication of ethical requirements were positively associated with trials of higher methodological quality.[44] The authors postulated that 'The association between methodological quality and reporting of ethical requirements probably reflects the respect shown for patients during the whole research process'.[44] (p. 175)

Using data from a similar set of journals (Annals of Internal Medicine, BMJ, JAMA, Lancet and NEJM), Yank and Rennie found improved rates of documentation of ethical protections when a random sample of trials 18 months before and after 1997 was compared.[45] Documentation of IRB approval and informed consent rose from 69% to 82% and from 74% and 82% respectively. Although only 9% of articles reported neither ethical protection post 1997, Yank and Rennie are adamant that rates of compliance should be complete.[45] According to these authors, '... there is a moral imperative to assure participants in trials that meticulous attention is being paid to their safety'.[45] (p. 2838)

In the US, Subpart D of the federal regulations stipulates additional protections for children involved in research; for example, parents' permission and children's assent must be obtained.[10] Variable degrees of compliance with these requirements are reported in leading journals in child psychology, general paediatrics, paediatric surgery and general medicine.

Based on articles extracted from predominantly child psychology journals (Child Development, Journal of Consulting and Clinical Psychology, Journal of Pediatric Psychology and the Journal of Clinical Child Psychology), Range and Cotton found that about one third (31.5%)

documented children's assent and 57% reported parental permission.[30] Not surprisingly, assent was noted significantly more frequently in research among older children (mean age 11 years versus 7 years).[30]

Using a similar range of child psychology journals (Child Development, Journal of Clinical Child Psychology, Journal of Pediatric Psychology and the Journal of Abnormal Child Psychology) , Sifers *et al* found even lower documented rates of assent and parental permission (19% and 41.5% respectively).[34] That the rates of reporting had dropped is unexpected given recent efforts to promote research ethics. Furthermore, the instructions to authors in two of these journals (Journal of Clinical Child Psychology and Journal of Pediatric Psychology) require inclusion of these ethical procedures.[34] To its credit, the Journal of Pediatric Psychology had the highest documented rate of parental permission (59%).[34] The authors interpreted their findings cautiously in the knowledge that failure to report assent permission does not necessarily imply the research was unethical. However, they make the point that reporting safeguards '... explicitly models ethical practices in research for fellow scientists and symbolizes adherence to ethical practices in research'.[34] (p. 23)

Even though the research involved children and was reported in journals whose instructions to authors stipulated documentation of IRB approval and informed consent, Bauchner and Sharfstein found relatively low rates of compliance in leading American journals: NEJM (66%), JAMA (53%), Pediatrics (66%), Journal of Pediatrics (60%) and the Archives of Pediatrics and Adolescent Medicine (56%).[31] In total, 61% of all articles had ethical approval. Of note, these authors counted either IRB approval or informed consent as evidence of ethical approval. Predictably, RCTs and prospective studies reported higher compliance rates (97% and 70% respectively) compared to studies which used existing data sets (9%) where the need for ethical approval remains controversial.[31] Whilst these authors acknowledge that failure to report ethical approval does not imply that it was not obtained, they note that it is inconsistent with the journals' publication requirements.[31] To this end, they believe journals should play a greater role in protecting subjects by ensuring that every article contains a statement about participants' protection.[31]

In a review of prospective studies involving children, Roggin, Chwals and Tracy found significantly lower rates of IRB approval in surgical (American Journal of Surgery, Annals of Surgery, Archives of Surgery and the Journal of Pediatric Surgery) compared to medical journals (Journal of Pediatrics and Pediatrics) , with the overall reported rate of IRB approval as low as 27 percent.[32] Counterintuitively, intervention studies which investigated new treatments, medications and surgical techniques or diagnostic procedures were less likely to report IRB approval. The authors speculate that the low rates of IRB approval in studies of new and unproven invasive techniques may reflect the confusion surrounding the distinction between innovative treatment and research.[101,141]

Weil and colleagues also report relatively low rates of documented IRB approval (52%) and parental permission (43%) in three major paediatric journals (Pediatrics, Journal of Pediatrics and the Archives of Pediatrics and Adolescent Medicine) published during 2000.[33] However, a follow-up survey of authors of articles which failed to document any ethical safeguards, confirmed far higher rates of compliance in actual practice (86.5% and 88% for IRB approval and parental permission respectively). Moreover Weil *et al* indicate that most research that did not undergo ethical review would have been exempt under the Common Rule.[33] In keeping with Bauchner and Sharfstein,[31] Weil and co-workers found higher rates of compliance in clinical studies (including RCTs) compared to research which examined pre-existing datasets (such as chart reviews or human tissue collections).[33]

The elderly also require special protections because of their higher prevalence of cognitive, hearing, vision and speech impairment.[130] Additionally, elderly subjects drawn from institutions such as nursing homes may feel unduly pressured to take part.[126] If unable to consent, elderly patients may need to be excluded or consent obtained by proxy. Additionally, informed consent forms must be geared to elderly participants' level of comprehension.[36] Hence, IRB approval of such studies is essential. Yet a review of leading geriatric journals (Journal of the American Geriatrics Society, Journal of Gerontology, Mechanisms of Aging and Development and Age and Aging) established that respectively about one fifth (21%) and less than one third (29%) of journals reported IRB approval or informed consent.[36] In line with other research,[33] rates of IRB approval and informed consent were higher in clinical trials (49% and 62% respectively) compared to prospective studies (26% and 38% respectively).[36] Although none of the instructions to authors of these four journals explicitly specified the need for IRB approval or informed consent, three of the journals referred authors to the Uniform Requirements. Only 2 out of 586 articles described the assessment of decision-making capacity in detail.[36] Olde Rikkert *et al* concluded that documentation of ethical approval, informed consent and assessment of capacity to assent were '... absolute preconditions for publication'.[36] (p. 1117)

Even though a review of 45 articles of research among nursing home residents showed that all offered adequate justification for use of institutionalised subjects, that most reported some information on informed consent (80%) and two fifths documented IRB approval, the authors were dissatisfied with the quality of reported information, especially regarding disclosure of decisional capacity and proxy consent.[37] Because the voluntariness of research participation may be in question in captive populations like the elderly,[129] Karlawish *et al* underscore the need for consistent and detailed reporting requirements regarding competence to consent and its measurement.[37]

Subjects with psychiatric illness may also have impaired decision-making capacity and require additional protections in research.[130] Sigmon and co-researchers examined original research published in the Journal of Abnormal Psychology and the Journal of Clinical and Consulting Psychology between 1996 and 1997.[25] Subjects in these studies, which included some children, typically suffered from depression, anxiety and substance abuse. Investigators generally used questionnaires (84%) and interviews (58%) to collect their data. Informed consent was reported in 39% of articles, confidentiality in 7% and IRB approval in a mere 3 percent.[25] Interestingly, these authors checked for documentation of other ethical practices which might arise amongst this population group. Only 2% of investigators indicated how they responded to patients who became distressed during the course of the study and a further 2% reported debriefing patients at the end of stressful interviews.[25] A survey of investigators regarding their actual practices found that over 80% obtained informed consent and IRB approval and 70% indicated that they would deal with subjects' distress if the need arose.[25] The most frequently cited reasons for not documenting ethical practices included '... a need for brevity, lack of relevance for the study, as well as the belief that these procedures were common practice'.[25] (p. 271) Discouragingly, when asked what information should be reported in articles, most of the information rated as 'very important' or 'extremely important' referred to demographic detail (for example, race, age and gender) and information on study validity. This confirms findings from other psychology journals.[34] In turn, information ranked as 'not at all important' or 'somewhat important' related to the welfare of participants (for example, debriefing and informing subjects that their responses are confidential).[25] Given clear differences between what researchers say they do in actual practice and what they document in journals, Sigmon *et al* recommend that journals ask investigators to complete a checklist of compliance with standard ethical procedures.[25] Although this cannot guarantee ethical implementation of research, the authors feel it will, at a minimum, standardize requirements for article submission.[25]

Students are considered to be a potentially vulnerable research population,[129] the more so if sensitive information (such as academic performance, health data, debt burden or substance abuse) is collected by faculty. In order to establish the extent of ethical safeguards in educational research, Roberts and co-investigators examined 424 empirical articles from two major medical education journals (Academic Medicine and Medical Education) published between 1988-1989 and 1998-1999.[35] Each article was examined for documentation of six ethically important safeguards and features: IRB review, informed consent, confidentiality, education committee approval, use of incentives and funding source. Almost half (47%) of the articles made no mention of any ethical safeguards at all and no article mentioned all six.[35] Approximately one fifth of reports mentioned informed consent (23%) and confidentiality (21.5%). Only 3% of studies mentioned IRB approval. Source of funding was the most commonly reported ethical feature (27%). Notably, despite an increased awareness in research ethics, the rates did increase significantly between the ten year time frame.[35]

Self-evidently, research subjects requiring emergency medical services, cardiopulmonary resuscitation or critical care are particularly vulnerable.[122] They may be either unconscious or cognitively impaired. They may be rendered more vulnerable by pain and fear. Moreover, the time-limited nature of interventions may hinder provision of informed consent.[122] Nevertheless, research is necessary in order to provide treatment in accordance with the best available evidence. A review of surgical research articles published in the Annals of Emergency Medicine and Prehospital and Disaster Medicine between 1991 and 1992 revealed that 45% documented IRB approval (excluding exempt studies) and less than one quarter (23%) mentioned informed consent.[40] Similarly low rates of IRB approval and informed consent were noted in a review of studies involving subjects in cardiac arrest who required cardiopulmonary resuscitation (51% and 26% respectively).[38] More positively, Olson and Jobe found higher reported rates of IRB approval, consent or both when journals specified that IRB approval be documented.[38]

Matot, Pizov and Sprung examined ethical protections in original critical care research published in seven leading journals (American Journal of Respiratory and Critical Care Medicine, Chest, Critical Care Medicine, Intensive Care Medicine, JAMA, the Lancet and the NEJM) in 1994.[39] All journals required that submitted manuscripts document IRB approval and informed consent. The studies involved patients treated in intensive care units, trauma units and in the prehospital emergency services. Twenty four percent of studies provided no evidence of IRB approval or informed consent.[39] Rates of compliance with ethical requirements ranged from 72% (NEJM) to 23% (JAMA). In keeping with other studies,[33,36] IRB approval and informed consent were more common in interventional studies involving medications, fluids and different modes of ventilation compared to retrospective audits or studies involving standard treatment. The authors note that irrespective of the nature of the intervention both ethical safeguards are necessary.[39] In light of strict FDA regulations regarding drug registration,[9] it was not surprising that all studies supported by the pharmaceutical industry received IRB approval and reported informed consent.[39] Indeed, 50% of these drug studies documented a written informed consent.[39]

Research in anesthesia raises distinctive ethical issues, for instance it may be non-therapeutic and when performed during general anesthesia, subjects cannot withdraw their consent once the procedure is underway. Thus anesthetists have special responsibilities to ensure that their research meets the highest ethical standards. Asai and Shingu examined instructions to authors in eleven anesthesia journals published in the January 1995 issues as well as rates of IRB approval and informed documentation in 673 original research articles which appeared in these journals (July-December 1996).[28] Ten of the eleven journals required IRB approval for human subjects research. Eight journals instructed authors to obtain informed consent. Almost all studies documented ethics committee approval (96%) and informed consent (90%).[28] Following findings in other studies,[33,36,39] IRB approval and informed consent were reported most often in interventional studies (98% and 95% respectively) and least often in observational studies (71% and 46% respectively).[28] Asai and Shingu recommend investigators obtain advice from ethics committee chairpersons as to whether or not an observational study (such as the analysis of routine measurements during anesthesia) needs IRB approval and that this should be stated in the article.

In contrast to Asai and Shingu, Myles and Tan examined all human research published in six leading anesthesia journals for the year 2001 (Acta Anaesthesiologica Scandinavica, Anesthesia and Intensive Care, Anesthesiology and the British Journal of Anesthesia).[142] In particular, they included case reports and physician surveys. Of the 1189 articles reviewed, 71% and 66% documented IRB approval and informed consent respectively. Confirming previous findings, [33,36,39,28] almost all RCTs reported both protections. Follow-up contact with authors of RCTs not reporting IRB approval or consent indicated that with one exception both procedures was followed.[29] Only 2% of case reports or case series documented ethics committee approval and informed consent.[29] Because informed consent may be impossible to obtain in emergency situations, the authors recommend that investigators obtain retrospective consent for publication of case reports which may violate subjects' privacy and confidentiality.[142]

Controversy surrounds the kind of ethical safeguards needed for human tissue research.[109] Merz and Leonard explored the degree to which published studies using human tissue documented IRB approval and informed consent.[42] The authors reviewed nine journals in the fields of pathology (American Journal of Pathology and the American Journal of Clinical Pathology), genetics (American Journal of Human Genetics, Nature Genetics, Molecular Diagnosis, Human Molecular Genetics and the Journal of Medical Genetics) and general science (Nature and Science). Rates of documented IRB approval and informed consent were low (30% and 23% respectively).[42] Merz and Leonard note that all family linkage studies received IRB approval. A follow-up survey of investigators led the authors to conclude that ignorance rather deliberate evasion was the most likely explanation for failure to obtain IRB review.[42] They recommend stronger efforts to educate the research community about ethical and practical issues regarding the use of identifiable tissue and the requirements and the desirability of IRB review.[42] Even if investigators think their studies are exempt, Merz and Leonard feel they should submit their protocols for expert review.[42] In addition, pathologists should insist on proof of IRB approval before release of human tissue specimens.[42]

Confusion also surrounds the ethical requirements relating to the publication of pedigrees. Botkin *et al* note that the familial nature of genetic information and the large number of subjects involved pose problems for the protection of subjects' privacy and confidentiality.[141] In light of the psychosocial risks attached to breaches of privacy and confidentiality in genetics research, Botkin and co-workers reviewed documentation of informed consent for publication of pedigrees in prominent genetics journals (American Journal of Medical Genetics, American Journal of Human Genetics, Nature Genetics and Psychiatric Genetics).[141] In addition, they reviewed twenty journals that publish human genetics research to evaluate their information to authors and they surveyed investigators actively involved in human genetics research on their attitudes, experiences and practices regarding privacy and confidentiality issues in the publication of family pedigrees.[141]

The authors report that 18% of journal articles mentioned informed consent for research participation but none of the articles had explicit documentation of consent for the publication of pedigrees.[141] The instructions in 12 of the 20 journals (60%) included some information about the publication of potentially identifying information and two addressed pedigrees specifically. For example, JAMA's information for authors states: 'Include a signed statement of informed consent to publish patient descriptions, photographs, and pedigrees from all persons (parents or legal guardians for minors) who can be identified in such written descriptions, photographs, or pedigrees. Such persons should be shown the manuscript before submission'.[141] (p. 1810) Seventy eight percent (177/226) of investigators responded to the survey, almost half of whom indicated 'little or no concern' over subject confidentiality in the publication. Two fifths of respondents knew family members had read articles published with their pedigrees. These were usually obtained from the researchers. Approximately one quarter of investigators felt family members benefited from reading their pedigrees.[113] A minority (6%) believed some families experienced harm Over half (52%) of investigator, over three quarters (78%) did not obtain written informed consent for pedigree publication, about one quarter (28%) obtained consent from all family members, while many (72%) sought consent from selected family members. Significantly, the proportion of investigators who would not include family members in an article without their permission was slightly higher than those who would include them (44% versus 41%).[141] The finding that almost equal proportions of researchers (42%) felt that confidentiality was or was not a problem suggests considerable uncertainty and lack of professional consensus concerning publication of pedigrees among researchers experienced in medical genetics. This is an important study with implications for publication of case reports and personal information in general. Unfortunately, as yet no equivalent study has determined subjects' perceptions of probable risks and benefits attached to publication of family pedigrees.

In summary, rates of compliance with ethical requirements to obtain IRB approval and informed consent range from 100% in many RCTs and pharmaceutical research to 2% and 3% for case reports. Follow-up surveys of investigators, who failed to document ethical safeguards in their articles, generally resulted in far higher rates of compliance in actual practice. There is agreement that journals should set criteria for publication, communicate these clearly in their instructions and uphold these standards in peer and editorial review. Articles that fail to comply with ethical requirements should not be published. Although important, IRB approval and informed consent are not sufficient to guarantee ethical research. Weil et al comment that 'Much work needs to be done ... to educate researchers regarding the responsible conduct of research, including the purpose of IRB review and IC ... institutions should also have a mechanism for continued education of IRB members regarding current research ethics standards ....'[33] (p. 369)

Efforts to make physiotherapy more evidence-based have increased. Correspondingly, investigators must ensure that physiotherapy research involving human subjects meets the highest ethical standards. The present study examined documentation of basic ethical safeguards in articles published in physiotherapy journals and located in a physiotherapy database. The main results of this study are reported in the next chapter.

Chapter 3 Results

Between 1996 and 2001, 806 articles which met the inclusion criteria were extracted from six peer-reviewed physiotherapy (PT) journals (Table 1). Approximately one third and one quarter of the articles were drawn from Physical Therapy and Physiotherapy respectively. Both these journals publish 12 issues per year. Library access to Physiotherapy Research International was only possible from 1999. Accordingly, this journal accounted for the least proportion of articles (7%).

TABLE 1
Frequency of Articles According to Physiotherapy Journal, 1996-2001[1]

	No.of issues per volume	N	%
Physical Therapy[2]	12	279	**35**
Physiotherapy[3]	12	183	**23**
Australian Journal of Physiotherapy	4	105	**13**
Canadian Journal of Physiotherapy	4	102	**13**
South African Journal of Physiotherapy	4	75	**9**
Physiotherapy Research International[4]	4	62	**7**

[1] N=806
[2] Missing: 2001; 18: Issue 1
[3] Missing: 2000; 85: Issue 11
[4] Years: 1999-2001

Eighty six articles reporting physiotherapy-related RCTs among children were extracted from the Physiotherapy Evidence database (PEDro) (Table 2). Twenty eight percent of RCTs were reported in three leading paediatric journals (Developmental Medicine and Child Neurology, Journal of Pediatrics and the Archives of Diseases of Childhood). Only three journals, containing six articles, were dedicated to physiotherapy (Table 2).

The proportion of articles extracted from PT journals increased unevenly between 1996 and 2001, from 14% to 19 percent (Table 3). Two thirds (65%) of paediatric RCTs reported in PEDro took place between 1996 and 2002 (Table 3). There was no linear increase in RCTs between 1996 and 2002.

TABLE 3
Frequency of Articles According to Year of Publication

	PT Journals (N=806)		PEDro (N=86)	
	N	%	N	%
1990 -1995			30	**35**
1996	116	**14**	13	**15**
1997	130	**16**	9	**11**
1998	122	**15**	9	**11**
1999	144	**18**	7	**8**
2000	138	**17**	5	**5**
2001	156	**19**	11	**13**
2002			2	**2**

TABLE 2
Frequency of Paediatric RCTs According to Journals in PEDro (N=86)

Developmental Medicine and Child Neurology	9
Journal of Pediatrics	8
Archives of Diseases of Childhood	7
Pediatric Pulmonology	4
Chest	3
Lancet	3
Pediatrics	3
American Journal of Occupational Therapy	2
Acta Paediatrica	2
British Medical Journal	2
International Journal of Rehabilitation Research	2
Occupational Therapy Journal of Research	2
Pediatric Physical Therapy[1]	2
Physical Therapy[1]	2
Research in Nursing and Health	2
American Journal of Clinical Nutrition	1
American Journal of Physical Medicine and Rehabilitation	1
American Journal of Public Health	1
Anaesthesia and Intensive Care	1
Archives of Medical Research	1
Archives of Pediatrics and Adolescent Medicine	1
Australian Journal of Physiotherapy[1]	1
Birth	1
Child: Care, Health and Development	1
Clinical Rehabilitation	1
Critical Care Medicine	1
Developmental and Behavioral Pediatrics	1
Early Human Development	1
European Journal of Neurology	1
European Journal of Pediatric Surgery	1
European Respiratory Journal	1
International Journal of Rehabilitation Research	1
Journal of Allergy and Clinical Immunology	1
Journal of Obstetric, Gynecologic and Neonatal Nursing	1
Journal of Pediatrics and Child Health	1
Journal of Pediatric Orthopedics	1
Journal of Pediatric Psychology	1
Journal of Pediatrics	1
Journal of Urology	1
Lung	1
Medicine and Science in Sports and Exercise	1
New England Journal of Medicine	1
Neuromuscular Disorders	1
Pain	1
Pediatric Nursing	1
Physical and Occupational Therapy in Pediatrics[1]	1
Thorax	1

[1] Dedicated Physiotherapy Journals

The demographic characteristics of participants in the articles are presented in Table 4. Study participants were mainly adults (60%), with the elderly and children accounting for only 10% and 8% respectively. Approximately one fifth of participants could not be classified in a specific age category. Where gender was specified, male and female participants were equally represented. One third (270/806) of participants in PT journals was classified as vulnerable, most of whom were children (37%), employees (33%) and students (23%). Only 4% of participants were either decisionally impaired or critically ill. Most research reported in PT journals took place in a hospital or university setting (72% and 14% respectively). Similarly, most (90%) RCTs were performed in a hospital setting.

TABLE 4
Demographic Characteristics of Research Participants in Journal Articles

	PT Journals (N=806)		PEDro (N=86)	
	N	%	N	%
Ages				
Children	61	**8**	86	**100**
Adults	487	**60**		
Elderly	84	**10**		
Age Combinations[1]	138	**17**		
Not specified	36	**5**		
Gender				
Male	84	**10**	5	**6**
Female	80	**10**	3	**4**
Both	473	**59**	58	**67**
Not specified	169	**21**	20	**23**
Vulnerable Groups[2]				
Children	101	**37**	86	**100**
Employees	91	**33**		
Students	63	**23**		
Decisional Impairment	5	**2**		
Critical Care	4	**2**		
Pregnant Women	2	**1**		
Other[3]	4	**2**		
Setting				
Hospital	577	**72**	78	**90**
University[4]	115	**14**		
Private Practice	26	**3**		
Ambulatory Services	22	**3**	4	**5**
Rehabilitation Centres	19	**2**	4	**5**
Residential Care	9	**1**		
Schools	9	**1**		
Other[5]	29	**4**		

[1] Samples include children, adults and elderly
[2] PT Journals (N = 270), PEDro (N=86)
[3] Other: sexual abuse survivors = 2, army recruits = 1, sedated in-patents = 1
[4] Includes Schools of Physiotherapy
[5] See TABLE 5

Less than 2% (15/806) of studies took place in participants' homes or in research institutes (Table 5).

TABLE 5
Frequency of Settings Classified as 'Other' (N=29)

	N
Participants' Homes	8
Research Institutes	7
Major sports events	4
General Practice	2
Australian Army Training Battalion	1
Australian Gymnastics Association	1
Australian Physiotherapy Association	1
Australian Territorial Health Services	1
Chartered Society of Physiotherapists	1
Industry	1
Motor Accident Authority	1
Physiotherapy Conference	1

Characteristics of authors of articles extracted from PT journals and PEDro are shown in Table 6. Most authors in PT journals and Pedro articles were university-affiliated (91% and 97% respectively). A high proportion of authors in PT journals came from North America (42%) and Europe (27%). Likewise, most articles in PEDro were written by authors from Europe (31%), the USA (29%) and Canada (20%). In total, about one in ten (102/892) authors was from a developing country (for example, South Africa, the rest of Africa, Asia, the Middle East and Mexico).

TABLE 6
Frequency of Authorship Characteristics In Extracted Articles

	PT Journals[1] (N=806)		PEDro Articles[2] (N=86)	
	N	%	N	%
University Affiliation[3]				
Yes	737	**91**	83	**97**
Country of Origin[3]				
Australia/ NZ	150	**19**	9	**10**
Canada	126	**15**	17	**20**
South Africa	62	**8**		
UK/ Europe	220	**27**	27	**31**
USA	216	**27**	25	**29**
Other[4]	32	**4**	8	**9**

[1] Physiotherapy Journals
[2] Physiotherapy Evidence Database
[3] First author
[4] Other: Asia = 18, Middle East = 13, Rest of Africa = 8, Mexico = 1

Rates of documentation of consent and REC approval in articles extracted from PT journals and paediatric RCTs in PEDro are shown in Table 7. Rates are reported in relation to source and year of publication, study design, participants' age and membership of a vulnerable group.

TABLE 7

Reported Ethical Protections (Consent and REC Approval) in Journal Articles According to Source and Year of Publication, Study Design, Age and Vulnerability

		Consent		REC Approval	
	Total	N	%	N	%
Source of Publication					
PT Journals	806	524	**65**	431	**54**
AJPT	105	76	**72**	63	**60**
CJPT	102	64	**63**	43	**42**
PTI	61	41	**67**	33	**54**
SAJPT	75	42	**56**	20	**27**
UKJPT	183	85	**46**	44	**24**
USAJPT	279	215	**77**	228	**82**
PEDro	86	68	**79**	58	**67**
Year[1]					
1996	116	78	**67**	53	**46**
1997	130	80	**62**	63	**49**
1998	122	89	**73**	68	**56**
1999	144	90	**63**	74	**51**
2000	138	82	**59**	73	**53**
2001	156	105	**67**	100	**64**
Study Design					
Clinical	382	297	**78**	265	**69**
Behavioural	238	163	**68**	105	**44**
Combined Methods[2]	76	50	**66**	43	**57**
Chart Review	36	5	**14**	11	**31**
Case Report	75	13	**17**	10	**13**
Qualitative Methods	40	30	**75**	13	**32**
RCTs	86	68	**79**	58	**67**
Age					
Children[3]	61	42	**69**	37	**61**
Adults	487	312	**64**	247	**51**
Elderly	83	52	**63**	46	**55**
Age Combinations	139	97	**70**	87	**63**
Not Specified	36	21	**58**	14	**39**
Vulnerable Groups					
Children	101	66	**65**	61	**60**
Children[4]	86	68	**79**	58	**67**
Employees	91	61	**67**	33	**36**
Students	63	43	**68**	32	**51**

[1] PT journals only

[2] Clinical and behavioural methods

[3] Excludes children included in 'age combinations' (children, adults and elderly) category

[4] PEDro

In total, two thirds (65%) of PT articles had evidence of informed consent, and slightly over half (54%) reported REC approval. Overall, PT journals were significantly more likely to report informed consent than REC approval (65% versus 54%, $x^2 = 21.75$, $p=0.0000$). In contrast to the other PT journals, articles in Physical Therapy, were slightly more likely to report REC approval than consent (82% and 77% respectively). The South African Journal of Physiotherapy and Physiotherapy had the lowest rates of consent and REC approval. About three quarters of articles in these journals did not report REC approval. Over three quarters (79%) and two thirds (67%) of RCTs in PEDro had evidence of consent and REC approval. This finding was not statistically significant ($x^2 = 2.95$, $p=0.1210$). Both these rates were higher than the overall rates in the PT journals.

Whereas the rates of reporting consent remained relatively constant in PT journals between 1996 and 2001 (ranging between 59% and 73%), a trend analysis of the documentation of REC approval showed a statistically significant improvement over the six year period: 46% in 1996 to 64% in 2001 ($x^2 = 11.74$, $p=0.034$).

Clinical studies in PT journals and RCTs in Pedro reported high rates of consent (78% and 79% respectively) with lower rates for REC approval (69% and 67% respectively). Approximately two thirds of behavioural studies reported consent with only about two fifths (44%) indicating REC approval. A minority of chart reviews and case reports obtained consent (14% and 17% respectively); and rates of REC approval were correspondingly low (31% and 13%% respectively). Three quarters (75%) of studies using qualitative methods reported consent. This was more than double the reported rate (32%) of REC approval for these studies. No studies met the criteria for classification as quality assurance.

Rates of documentation of consent remained within a narrow range according to subjects' age (69%, 64% and 63% for adults, children and the elderly respectively). Reported rates for REC approval according to age group also fell in a narrow range (61%, 55% and 51% for children, the elderly and adults respectively).

In terms of vulnerability, studies using children in RCTs had the highest rates of consent and REC approval (79% and 67% respectively). In similar vein, investigations which included children in the PT journals had higher rates of REC approval than research involving students and employees (61%, 51% and 36% respectively). Consent was reported in about two thirds of studies including vulnerable groups (68%, 67% and 65% for students, employees and children respectively).

Table 8 shows which combinations of ethical protections (consent and REC approval) were reported in PT journals and PEDro. It also indicates the extent of non-reporting of these requirements according to source and year of publication, study design and subjects' vulnerability. Overall, PEDro publications were twice more likely than PT articles to have no documentation of consent and REC approval as (29% versus 13%). Physiotherapy and the South African Journal of Physiotherapy had the highest rates of non-reporting of any ethical requirements (52% and 43% respectively). Conversely these journals had the lowest rates of documentation of both consent and REC approval (21% and 25% respectively). Physical Therapy had the highest rate of documentation of both consent and REC approval and the lowest rate of non-reporting (73% and 14% respectively). Over half the articles in the Australian Journal of Physiotherapy reported both ethical protections (54%). Overall, less than 10% of articles in PT journals and PEDro reported only REC approval.

TABLE 8

Quality of Documentation of Consent and REC Approval in PT Journals and PEDro According to Source and Year of Publication, Study Design and Vulnerability

Journal	Total	IC only		REC only		IC & REC		Neither[1]	
	N	N	%	N	%	N	%	N	%
PT Journals[2]	806	140	**17**	43	**5**	386	**48**	237	**29**
AJPT	105	20	**19**	6	**6**	57	**54**	22	**21**
CJPT	102	26	**26**	4	**4**	39	**38**	33	**32**
PTI	61	14	**23**	4	**7**	28	**46**	15	**24**
SAJPT	75	23	**31**	1	**1**	19	**25**	32	**43**
UKJPT	183	45	**25**	4	**2**	39	**21**	95	**52**
USAJPT	279	11	**4**	24	**9**	204	**73**	40	**14**
PEDro[3]	86	17	**20**	6	**7**	52	**61**	11	**13**
Year of Publication[4]									
1996	116	28	**24**	4	**3**	49	**42**	35	**30**
1997	130	24	**19**	7	**5**	56	**43**	43	**33**
1998	122	28	**23**	7	**6**	61	**50**	26	**21**
1999	144	24	**17**	7	**5**	67	**46**	46	**32**
2000	138	19	**14**	7	**5**	65	**47**	47	**34**
2001	156	17	**11**	11	**7**	88	**56**	40	**26**
Study Design									
Clinical	382	54	**14**	21	**6**	244	**64**	63	**17**
Behavioural	238	59	**25**	11	**5**	93	**39**	75	**31**
Combined methods	75	12	**16**	4	**5**	38	**50**	22	**29**
Chart Review	36	-	-	5	**14**	6	**17**	25	**69**
Case Reports	75	5	**7**	2	**3**	8	**11**	60	**80**
Qualitative methods	40	18	**45**	1	**2**	12	**30**	9	**22**
RCTS[5]	86	17	**20**	6	**7**	52	**61**	11	**13**
Vulnerable Groups									
Children	101	11	**11**	6	**6**	55	**55**	29	**29**
Children[5]	86	17	**20**	6	**7**	52	**61**	11	**13**
Employees	91	31	**34**	3	**3**	30	**33**	27	**30**
Students	63	13	**21**	2	**3**	30	**48**	18	**29**
Other[6]	15	2	**13**	-	-	10	**67**	3	**20**

[1] Neither informed consent nor research ethics committee approval

[2] Physiotherapy Journals

[3] Physiotherapy Evidence Database

[4] Excludes Physiotherapy Evidence Database

[5] Randomised clinical trails in Physiotherapy Evidence Database

[6] Decisional impairment = 5, critical care = 4, pregnant women = 2, survivors of sexual abuse = 2, army recruits = 1, sedated in-patients = 1

Rates of non-reporting of ethical protections remained steady, in a narrow band (21% to 34%) over the six year period (Table 8). In turn, there was a steady, albeit small, increase in documentation of both consent and REC approval between 1996 and 2001 (42% to 56%).

Clinical studies in PT journals and RCTs in PEDro were most likely to have evidence of both consent and REC approval (63% and 61% respectively); and chart reviews and case reports were the least likely to note both protections (17% and 11% respectively). Most case reports and over two thirds of chart reviews had no documented reports of consent and REC approval (89% and 69% respectively). Articles using qualitative methods were more likely to report only obtaining informed consent than both consent and REC approval (45% and 30% respectively). About one fifth of qualitative studies had neither consent not REC approval.

Studies involving children in RCTs and subjects with, among others, decisional impairment, were the least likely not to report any ethical protections (13% and 20% respectively). About one third of studies in PT journals involving employees, students and children failed to document consent or REC approval (30%, 29% and 29% respectively).

Of the articles that reported informed consent, at least two thirds provided further information on the type of consent obtained (Table 9).

TABLE 9
Format of Informed Consent in PT Journals and PEDro (Percentage Distribution)

	Written %	Oral %	Not Specified %
PT Journals	54	16	30
Journal			
AJPT	57	23	20
CJPT	54	5	41
PTI	49	17	34
SAJPT	43	26	31
UKJPT	58	16	26
USAJPT	61	7	32
***Design*[1]**			
Clinical	56	10	34
Behavioural	59	18	23
Combined Methods[2]	50	10	15
Qualitative Methods	47	20	30
RCTs[3]	43	4	53
Vulnerable Groups			
Children	59	7	33
Children[3]	43	4	53
Employees	59	24	16
Students	39	28	33

[1] Excludes chart reviews and case reports
[2] Clinical and behavioural methods
[3] Physiotherapy Evidence Database

Overall, when specified written consent was far more common than oral consent in both PT journals and PEDro trials. Likewise, written rather than oral consent was obtained more often irrespective of the study design. Behavioural studies and research employing qualitative methods reported the highest rates of oral consent (18% and 20% respectively). Studies involving vulnerable subjects reported obtaining written consent more often than oral consent, although oral consent was used in about one quarter of the research involving employees and students (24% and 28% respectively).

One tenth and about one quarter (26%) of children provided assent to participation in research published in PT journals and PEDro respectively (Table 10). However, where children who were too young to provide assent were excluded (i.e. assent was not applicable), the rates of assent rose to 13% and 46% for PT journals and RCTs respectively (Table 10).

TABLE 10
Documentation of Assent in Articles Published in PT Journals and PEDro (Frequency and Percentage Distribution)

	PT Journals[1] (N=101)		PEDro[2] (N=86)	
	N	%	N	%
Assent				
Yes	10	**10**	22	**26**
No	67	**66**	26	**30**
Not applicable	24	**24**	38	**44**

[1] Physiotherapy Journals
[2] Physiotherapy Evidence Database

In articles that documented REC approval, most reported using only one committee (Table 11).

TABLE 11
Characteristics of Research Ethics Committees Reported in PT Journals and PEDro

	PT Journals[1] (N=431)		PEDro[2] (N=58)	
	N	%	N	%
Number per study				
1	349	**81**	44	**76**
2	73	**17**	9	**16**
≥3	9	**2**	5	**8**
Name				
Yes	402	**93**	43	**74**
Location in article				
Methods section	210	**49**	56	**96**
Title page	10	**2**	1	**2**
Second page	206	**48**	1	**2**
Other	5	**1**		

[1] Physiotherapy
[2] Physiotherapy Evidence Database

The majority of articles in PT journals and three quarters of the articles in PEDro named the ethics committee (93% and 73% respectively) (Table 11). Information on REC approval mostly appeared in the 'Methods' section of PEDro trials compared to only 49% of articles in PT journals. About half the PT journals published this information separately, in free standing format on the second page.

Approximately, one quarter (26%) of articles in PT journals documented evidence of confidentiality (Table 12).

TABLE 12
Documentation of Confidentiality in PT Journals According to Source, Study Design and Vulnerability[1]

	Total	N	%
Total	806	213	**26**
Journal			
AJPT	105	29	**28**
CJPT	102	27	**27**
PTI	61	12	**20**
SAJPT	75	14	**19**
UKJPT	183	56	**31**
USAJPT	279	75	**27**
Study Design			
Clinical	382	58	**15**
Behavioural	238	75	**31**
Combined Methods[2]	75	12	**16**
Chart Review	36	3	**8**
Case Reports	75	66	**88**
Qualitative methods	40	9	**22**
Vulnerable Groups			
Children	101	16	**16**
Employees	91	32	**35**
Students	63	17	**27**
Other[3]	15	3	**20**

[1] Excludes Physiotherapy Evidence Database
[2] Clinical and behavioural methods
[3] Decisionally impaired = 5, critical care = 4, pregnant women = 2, survivors of sexual abuse = 2 army recruits = 1, sedated in-patients = 1

Rates of reporting confidentiality ranged from 19% in the South African Journal of Physiotherapy to 31% in Physiotherapy (Table 12). Case reports were most likely and chart reviews the least likely to report confidentiality protections (88% and 8% respectively). About one third of behavioural studies and one fifth of studies using qualitative methods mentioned confidentiality (31% and 22% respectively). When examined in terms of vulnerability, confidentiality was reported in approximately one third and one quarter of studies involving employees and students (35% and 27% respectively).

Most (80%) research using qualitative methods was undertaken among adult participants, a substantial proportion (58%) of whom were drawn from employees and students (Table 13).

TABLE 13
Characteristics of Research Using Qualitative Methods (N=40)

	N	%
Age of Participants		
Adults	33	**82**
Combined Ages	5	**13**
Not specified	2	**5**
Vulnerable Groups	23	**58**
Employees	12	
Students	9	
Decisional Impairment	1	
Survivors of Sexual Abuse	1	

Findings relating to vulnerable groups (children, students and employees) were further disaggregated according to study design and ethical protections (Tables 14 and 15).

Children were most often involved in interventional research published in PT journals and PEDro (66% and 100% respectively) (Table 14). About one fifth (19%) of children were involved in behavioral studies (Table 14). As already noted (Table 8), neither consent nor REC approval was obtained in 29% of studies using children reported in PT journals, with 13% of RCTs in PEDro failing to report either protection. No children were involved in qualitative research.

TABLE 14
Vulnerable Groups (Children) According to Study Design and Documented Ethical Protections

Children	**PT Journals[1]** **N=101**		**PEDro[2]** **N=86**	
	N	**%**	**N**	**%**
Study Design				
Clinical	67	**66**	86	**100**
Behavioural	19	**19**		
Combined Methods[3]	5	**5**		
Chart Review	6	**6**		
Case Reports	4	**4**		
Ethical Protections				
Informed Consent	66	**65**	68	**71**
REC Approval	61	**60**	58	**67**
Neither[4]	29	**29**	11	**13**
Confidentiality[5]	16	**16**		

[1] Physiotherapy Journals, [2] Physiotherapy Evidence Database, [3] Clinical and Behavioural Methods
[4] Neither informed consent nor research ethics committee approval, [5] PT Journals only

Students were generally involved in behavioural and clinical research (52% and 40% respectively) (Table 15). A minority (14%) of studies using students employed qualitative methods. As previously described (Table 8), the majority (68%) of students gave informed consent, whilst only half (51%) of the research was approved by an REC. Thirty percent of research using students had no documented evidence of either informed consent or REC approval (Table 15).

TABLE 15
Vulnerable Groups (Students and Employees) According to Study Design and Documented Ethical Protections

	Students (N=63)		Employees (N=91)	
	N	%	N	%
Study Design				
Clinical	25	**40**	7	**8**
Behavioural	33	**52**	79	**87**
Combined Methods[1]	1	**2**	1	**1**
Chart Review	4	**6**	4	**4**
Case Reports	-	-	-	-
Qualitative Methods	9	**14**	12	**13**
Ethical Protections				
Informed Consent	43	**68**	61	**67**
REC Approval	32	**51**	33	**36**
Neither[2]	18	**29**	27	**30**
Confidentiality	17	**27**	32	**35**

[1] Clinical and behavioural methods
[2] Neither informed consent nor research ethics committee approval

Employees were involved in mainly behavioural research (87%), with a minority (13%) taking part in research using qualitative methods (Table 15). Informed consent was reported in two thirds of the studies using employees, with much lower rates of REC approval (36%). Thirty percent of research obtained neither REC approval nor employees' consent. Confidentiality was addressed in over one third (35%) of studies involving employees.

Table 16 shows the journal requirements for ethical protections in the 'instructions to authors' sections of PT journals published between 1996 and 2001.

TABLE 16
Requirements for Documenting REC[1] Approval, Consent and Confidentiality in the 'Instructions to Authors' Sections of PT Journals

Journal	REC Approval	Informed Consent	Confidentiality[2]
AJPT	written statement	-	written permission
PTI	-	-	-
SAJPT	-	-	written permission
CJPT	written statement	written statement	written permission
UKJPT	signed certificate from REC	written statement	written permission
USAJPT	name of REC on title page	statement in 'methods'	written permission

[1] Research Ethics Committee
2 Confidentiality is limited to written permission to publish photographs in which subjects are recognizable and/or the use of fictitious names.

No ethical protections were stipulated in Physiotherapy Research International. Only confidentiality protections, introduced in 1997, were required by the South African Journal of Physiotherapy. Physical Therapy provided the clearest and most detailed guidelines, with written requirements for both REC approval and informed consent, and where this information must appear. Physiotherapy required a signed certificate from the REC as well as a written statement on informed consent. Physiotherapy Canada required written REC approval and written informed consent. The Australian Journal of Physiotherapy omitted informed consent and only specified the submission of written REC approval (Table 16). Of note, the Australian Journal of Physiotherapy's instructions to authors were available on their website only.

With the exception of Physiotherapy Research International, all PT journals published ethical requirements for confidentiality (Table 16). However, the guidelines were limited to issues relating to the publication of photographs. These journals requested written permission from patients and in the case of minors, the consent of parents or legal guardians. Physiotherapy Canada stipulated that subjects' eyes must be obscured with a black bar. Physiotherapy expected authors 'to obscure facial features'. Physical Therapy recommended that subjects or patients be allowed to see manuscripts of all types of research in order to protect their confidentiality. With respect to case reports, Physiotherapy suggested that authors use patients' names ('but they should not be their real names') for clarity and humanity. With the exception of Physical Therapy, no instructions to authors referred to subjects' 'rights' in research or to the Declaration of Helsinki. Physical Therapy required a statement that the rights of human and animal subjects had been protected in a study.

Ethical requirements and actual reporting practices regarding authorship, sponsorship/financial disclosure and conflicts of interest are presented in Tables 17 and 18 respectively.

TABLE 17
Policies on Documentation of Authorship, Financial Disclosure and Conflicts of Interest in 'Instructions to Authors' Sections in PT Journals

Journal	**Contributions**	**Funding**	**Conflicts of Interest**
AJPT	+	+	-
CJPT	-	+	+
PTI	-	-	-
SAJPT	-	-	-
UKJPT	-	+	-
USAJPT	+[1]	+	+

[1] Introduced from 1998 onwards.

Physiotherapy Research International and the South African Journal of Physiotherapy had no information for authors on contributions, funding and conflict of interest. Physical Therapy was the only PT journal that requested written information on authors' contributions, sources of funding which supported the study and commercial/financial interests or personal associations which might directly affect the 'subject matter or the materials discussed in the manuscript' (Table 17). 'Instructions to authors' in Physical Therapy directed authors to indicate precisely their contribution to a publication, for example, to conceptualization, design, data collection, data analysis, fund procurement, and provision of subjects, facilities or institutional liaisons.

Four out of six PT journals had written policies requiring information on funding, and two out of six requested information on authors' contributions (Table 17). The Australian Journal of Physiotherapy followed the ICMJE's Uniform Requirements on authorship.

According to Table 18, over two thirds (69%) of articles in PT journals compared to less than one third (30%) of articles in PEDro had 3 or less authors per article. Generally the trend in was towards higher authorship per article in PEDro, with 70% of publications having four or more authors. This was reflected in the mean number of authors per article in PEDro and the PT journals (3 and 5 respectively). About 1 in 5 and 1 in 10 articles in PT journals and PEDro respectively detailed the contributions of individual authors. Contributions were most often reported in Physical Therapy. About two thirds (65%) of research in PT journals had no sponsorship, about one third (34%) reported non-commercial sponsorship and less than 1% was sponsored by industry (Table 18). In contrast, over half (57%) and one quarter (24%) of trials in PEDro had non-industry and commercial sponsorship respectively (Table 18). Most articles in PT journals and PEDro provided no information on conflicts of interest (99.5% and 96% respectively) (Table 18).

TABLE 18
Frequency (%) of Documentation of Authorship, Sponsorship and Conflicts of Interest

	PT Journals[1] (N=806)		PEDro[2] (N=86)	
	N	%	N	%
Number of Authors per article				
1	111	**14**	3	**4**
2	223	**28**	8	**9**
3	217	**27**	15	**17**
4	121	**15**	17	**20**
5	74	**9**	16	**19**
6+	55	**7**	27	**31**
Mean	3		5	
Range	1-10		1-11	
Contributions to Authorship Specified				
Yes	179	**22**	8	**9**
Contributions by Journal				
USAJPT	121	**68**		
UKJPT	49	**27**		
Other	9[3]	**5**	8[4]	**9**
Sponsorship				
Industry	3	**0.5**	5	**6**
Non-industry	276	**34**	49	**57**
Both	3	**0.5**	11	**13**
None	524	**65**	21	**24**
Conflicts of Interest				
Declared	1	**0.5**		
None declared	1	**0.5**	3	**4**
No statement	802	**99.5**	83	**96**

[1] Physiotherapy Journals; [2] Physiotherapy Evidence Database
[3] CJPT=5, AJPT=3, PTI=1; [4] BMJ=2, Phys Ther=2, J Pediatr Orthop=1, J of Pediatrics=1, Lancet=1, NEJM=1

Chapter 4 Discussion

4.1 Introduction

Efforts to develop the evidence base and quality of physiotherapy practice rely on a solid empirical foundation of quantitative and qualitative research data obtained from a growing pool of patients, colleagues, students and healthy volunteers. Furthermore, history shows that as well as being scientifically sound, research must be ethically beyond reproach. The responsibility to ensure that research is conducted ethically rests with a number of individuals including the investigators, sponsors, REC members, journal editors, subjects and the public. As the ultimate gatekeepers of the research process,[24] this study examined the role of journals in the chain of protections in physiotherapy-related human subjects research.

Although physiotherapist-investigators do not need to be experts in research ethics in order to conduct ethically sound research, they do need to know and appreciate a few basic requirements and the ethical principles upon which they are grounded. Examples include the requirements for initial REC review and approval before subjects are enrolled, continuing REC review, reporting adverse events to sponsors and RECs (in the case of clinical research), and receiving approval for protocol changes. Each of these requirements is based on the Belmont Report's[101] principle of beneficence which mandates that benefits be maximised, risks minimised and the balance between the two weighed. The increasingly stringent requirements for informed consent and the protection of subjects' privacy and confidentiality reflect the increasing awareness and continued refinement of the ethical principle of respect for persons.[101] Additionally, there is a high likelihood that physiotherapist-investigators will undertake research among individuals who are not capable of self-determination and who lack the ability to determine the limits of their own research participation. Where research subjects have diminished autonomy, researchers must provide additional safeguards in the form of surrogate decision-making and proxy consent for mentally incompetent adults or child assent and restrictions on allowable risk for research involving children.[101] These requirements for independent committee review and informed consent are also spelled out in principles 13 and 22 to 26 of the Declaration of Helsinki respectively; whilst principle 21 promotes respect for subject's privacy and confidentiality.[7]

4.2 Documentation of Informed Consent and REC Approval

A powerful mechanism to encourage ethical research is the requirement underwritten by leading international journal editors[16-18,20] that authors include in their manuscripts submitted for publication written statements confirming that REC approval and informed consent were obtained and that confidentiality was protected. This study provides evidence via documentation in articles in Physiotherapy (PT) and related journals of reported use of basic ethical safeguards such as REC approval, informed consent and confidentiality during the performance of clinical and non-clinical research, roughly between 1996 and 2001. Of note, discussion of findings from PEDro is limited to the distinctive ethical issues relating to physiotherapy-related clinical trials undertaken in a vulnerable population, namely children (sections 4.4 and 4.5).

A word of caution is needed regarding the interpretation of findings in this study. Failure to document REC approval and informed consent in a journal article does not necessarily imply that the research was unethical, nor is it evidence that researchers failed in their ethical obligations or that subjects were put at risk. There are many reasons including lack of space, a belief that these requirements reflect standard practice and do not need to be reported, or non-specification of ethical requirements in journals' instructions to authors that might explain authors' failure to *document* compliance.[25,142] In other words these data do not reflect *actual* failure of compliance during the conduct of a study. Indeed, follow-up surveys of investigators who did not mention REC approval show far higher rates of compliance than originally reported.[29,33,43,142] For example, rates of informed consent and REC approval rose from 43% to 88% and from 52% to 86% respectively in a recent survey of reporting practices in leading paediatric journals.[33]

In keeping with the findings of Amdur and Biddle,[26] an analysis of PT journals' editorial policies revealed extremely variable requirements for documentation of ethical content. Of the six PT journals surveyed, four required a written statement of REC approval, one journal did not present or refer authors to any information related to human research ethics and another journal included no requirements for REC approval or informed consent but did specify guidelines for protection of confidentiality. Half the PT journals required written confirmation of informed consent. Comments made by Amdur and Biddle in response to the variability of their findings are pertinent to this study.[26] It is not possible, they said, to conclude that some journals lack awareness of human research ethics, whether some editors do not feel it is their role to ask about ethical issues or whether editors do not believe documentation of ethical issues is important.[26]

Findings in this study show that editorial policies exemplified in the instructions to authors do not necessarily reflect PT journals' publication practices. For example, of the four journals requiring written statements of REC approval, rates of non-documentation of REC approval ranged between a high 76% in the case of Physiotherapy to a low 18% in Physical Therapy, with 58% of articles in Physiotherapy Canada and 40% of articles in the Australian Journal of Physiotherapy providing no information on REC approval. However, it is conceivable that authors submitted separate documentation of REC approval to editors, for instance in a covering letter or in a standard checklist of compliance, instead of providing documentation in the actual manuscripts. Indeed, authors submitting articles to Physiotherapy are instructed to include a signed certificate from the REC. So whilst authors may well comply with this instruction, they may not always document adherence in their manuscripts. Likewise, despite editorial instructions requiring written statements of informed consent, over half (54%) the articles in Physiotherapy and approximately one quarter in Physiotherapy Canada and Physical Therapy (27% and 23% respectively) failed to document that written informed consent had been obtained.

Overall 48% of articles in PT journals had documentation of both consent and REC approval and 29% had no information on either ethical safeguard. When examined separately, consent and REC approval were reported in 65% and 54% of articles respectively. In general, Physical Therapy exhibited the highest rates of compliance. Almost three quarters of the articles reported both REC approval and informed consent, with only 14% of articles reporting neither requirement. When disaggregated, rates of documentation of REC approval (82%) and informed consent (77%) remained high. Possible explanations for these higher rates of documentation include strict editorial policy, US researchers' compliance with federal regulations mandating IRB approval and written consent, as well as an increased awareness among both researchers and editors of well-publicised research abuses among vulnerable populations in the United States.

The Australian Journal of Physiotherapy also reported relatively high rates (54%) of documentation of both REC approval and informed consent and a low rate (21%) of non-documentation of either requirement. Seventy two percent and 60% of articles reported consent and REC approval respectively. This Journal's listing on the prestigious Medline in 2001 may partly account for these rates of documentation.[143] It is probable that to achieve this status the journal placed greater emphasis on publication standards in general, including better documentation of compliance with ethical requirements. For instance, one criterion for inclusion is the quality of editorial work. This refers to features that contribute ' ... to the objectivity, credibility, and quality of a journal's contents, eg ... statements indicating adherence to ethical guidelines ...'.[143] (p. 159)

The low rates of documentation of consent and ethical committee approval in Physiotherapy is difficult to interpret. As already noted, authors may have notified editors of compliance but withheld this information in their articles. Speculation aside, recent developments in the UK research environment are likely to lead to stricter adherence to ethical guidelines in the future. New regulations issued in the Research Governance Framework for England, and parallel documents in Wales and Scotland, establish standards for research which will apply to all clinical and non-clinical studies relating to health and social care.[144] Crucially, high quality ethical practice is central to this Framework.[144] Moreover, according to Wiles of the Chartered Society of Physiotherapists, all physiotherapists involved in research at any level must be aware of the Framework and adhere to its standards.[144] Changes set out in this Framework were due to be fully implemented by April 2003.[144] Thus, it is likely that in the future the editorial board of Physiotherapy, the official mouthpiece of the Chartered Society of Physiotherapists, will play a more prominent role in ensuring that the research it publishes strictly adheres to the ethical requirements laid down in the Research Governance Framework, which include ethical approval of research proposals by a National Health Service or a university ethics committee, informed consent and confidentiality assurances.[144] Furthermore, REC approval will be required for 'All research involving people, their organs, tissues or data ... '.[144] (p. 642)

Paradoxically, articles in Physiotherapy International achieved the third highest rates of compliance, despite no editorial advice whatsoever on ethical requirements. In fact, their rates of documentation of consent and REC approval (67% and 54% respectively) compared favourably with the overall rates of consent and REC approval (65% and 54% respectively). These findings add weight to Amdur and Biddle's contention that ultimately ethical research depends as much on investigators' integrity as editorial policy regarding ethical requirements.[26]

Besides the absence of guidance in the instructions to authors section, there is no obvious explanation to account for the low combined rate of documentation of consent and REC approval (25%) in the South African Journal of Physiotherapy. When disaggregated the rate of REC approval remained low (27%) whereas the rate for consent was more than double (57%). Despite its status as a developing country, since 1992 medical research in South Africa has been governed by ethical guidelines published by the South African Medical Research Council.[112] Moreover, South Africa has been in the forefront of debates around contentious issues in human subjects research.[145] Arguably, ethical safeguards were adhered to during actual studies but authors did not mention this in their manuscripts. Indeed, it is unlikely that the minority of authors (12%) from developing countries could explain the overall uneven rates of documentation found in this study. Furthermore, published findings comparing rates of REC approval in research conducted inside the

US and outside the US found no significant differences in documentation; although it is not clear if these studies were conducted in other industrialised or non-industrialised countries.[32,38,39]

Compared to other published studies, the overall rate of documentation of REC approval (54%) in PT journals was comparable (range: 40% - 61%),[31,33,37,38,40] sometimes better (range: 3% - 30%),[25,32,35,36] and in some instances it was worse (range: 96% to 71%).[28,29,39] In similar vein, the overall rate of documentation of informed consent (65%) in PT journals was at least as good as some studies (range: 43% - 57%),[30,33,34] better than others (range: 23% - 26%)[36,38,40] and much lower then the rest (range: 80% - 90%)[28,37,43,45]. Thus, the rates of documentation of ethical requirements in PT journals are comparable, better and worse than their counterparts in medicine and psychology. However, these combined findings from research in several disciplines, suggest a lack of consensus among authors and editors regarding documentation in articles of adherence to basic ethical standards. This confusion is reflected in journals' uneven advice to authors and authors' (seemingly subjective) decisions as to what information regarding ethical safeguards is included in their manuscripts. Recent publication of ethical guidelines by groups of editors[16-18] and specialist journals[54-57] may go some way towards reaching an agreement.

Encouragingly, there is evidence of a statistically significant improvement in the overall rate of documentation of REC approval in PT journals between 1996 and 2001 (from 46% to 64%). In addition, the rates of documentation of both ethical safeguards improved from 42% to 56 percent. Other promising findings in articles that did report ethical safeguards are the high rates of identifying detail about RECs (such as the numbers of committees and their names, 81% and 93% respectively), and the use of written consent more frequently than oral consent regardless of study design or study population. This finding is consistent with a previous study.[45] Arguably, further educational efforts to promote awareness of research ethics at undergraduate and postgraduate level will improve these trends even further. Ongoing education in research ethics is an important function of RECs in hospitals and universities which provided the settings for most of the research undertaken in this study.

As listees on the Medline database, Physical Therapy and the Australian Journal of Physiotherapy[143] already report the highest rates of compliance. However, all PT journals should bring their ethical standards for documentation in line with best international practice.[16-18,20] In order to remove variability in reporting requirements between journals and discrepancies within journals between their instructions and publication practices, Amdur and Biddle[26] recommend that journal editors standardise their publication requirements and make documentation of adherence to ethical requirements a prerequisite of publication. For example, findings in this study show that REC approval is reported in the 'methods' section or on a journal's second page. Standardisation would enable readers to expect to find this information in a particular section. Bauchner goes further by proposing the introduction of 'structured reporting' of REC approval, along the lines of structured abstracts which have improved the quality of scientific reports.[146] (p. 403) Bauchner recommends the inclusion of the following elements: the type of approval obtained (full board or expedited), if research was exempt and the reasons why, and the nature of the informed consent (oral or written).[146] Myles and Tan echo proposals that documentation of IRB approval and informed consent become a requirement of publication.[29] They contend that 'This is the final check in ensuring the highest scientific and ethical standards and a necessary step in protecting research subjects and maintaining public trust in the process'.[29] (p. 1212) Current COPE[17] and WAME[18] guidelines give editors discretion to publish articles that do not fully comply with requirements for

REC approval and written informed consent. Editors may also decide not to publish research they believe is unethical even if REC approval was obtained.[20] Yet, the absence of any indication on what grounds editors will make these decisions may lead to even greater uncertainty and inconsistency regarding publication requirements for ethical research.

4.3 Documentation of Confidentiality

Rights to confidentiality are distinguished from rights to privacy by noting that confidentiality implies that information revealed voluntarily must be used only in the agreed upon manner, and privacy implies that no consent to release the information has been granted.[124] Informed consent is needed to protect privacy and anonymity is the best guarantee for protecting confidentiality. Accordingly, confidentiality is the ethical duty not to reveal personal information about individuals in clinical care or research without their explicit consent. This duty is overridden only in select circumstances, for example suspected child abuse or neglect. In the context of research, adequate efforts are necessary to protect personal information about subjects and prevent confidentiality breaches during all phases of a study, including data collection, manipulation, disclosure and publication. The burden of safeguarding confidentiality is greatest in studies of stigmatising illnesses and in small community studies. As the risks of harm from data collection or disclosure increase, so must the protections to confidentiality.[136]

Except for Physiotherapy Research International, all PT journals instructed authors to obtain written permission from subjects, or parents in the case of minors, to publish identifiable information. However, these instructions mainly applied to the publication of photographs in case reports.

Overall, 26% of articles included documentation of confidentiality. This was better than previous findings in research involving medical students[35] and subjects with mental illness[25] (21% and 7% respectively). Whereas rates of documentation of confidentiality ranged narrowly between 19% and 31% depending on the PT journal, rates of documentation according to study design varied widely (between 8% and 88% for chart reviews and case reports respectively). Of note, the special confidentiality requirements in research with particular study designs and vulnerable populations are examined more fully in sections 4.4 and 4.5.

Barnitt and Partridge suggest physiotherapist-researchers must look beyond formal statements of confidentiality protections.[73] Based on a follow-up study of research subjects, they contend that confidentiality is as much about trust in researchers as it is about the use of pseudonyms.[73] Despite receiving assurances of confidentiality from researchers during the informed consent process, subjects who included disabled persons and physical and occupational therapists, worried about potential breaches of confidentiality.[73] Barnitt and Partridge wrote ' ... subjects were anxious about confidentiality even when no breach had occurred. Trust in confidentiality appeared to decrease once a researcher had left the research site. Confidentiality was viewed as part of the subject-researcher relationship rather than the system for gaining informed consent'.[73] (p. 259) These findings suggest that when undertaking sensitive research, physiotherapist-investigators offer confidentiality assurances and discuss subjects' perceived concerns about potential breaches throughout the research process. Arguably, these additional safeguards ought to be documented in publications in much the same way as Sigmon and colleagues[25] recommend that psychologist-researchers report the use of interventions such as debriefing and referral for counselling or support in order to manage difficult ethical issues or crises.

4.4 Documentation of Informed Consent, REC Approval and Confidentiality According to Study Design

Decision-makers in health care need high-quality evidence to support clinical and health policy choices. Pervasive and persistent unexplained variation in clinical practice, high rates of inappropriate care and limited resources have fuelled the demand for evidence of clinical effectiveness. Because the quality of available evidence is often inadequate, researchers and funders, in particular the pharmaceutical industry, increasingly rely on RCTs, the generally accepted gold standard, to obtain high quality evidence of clinical effectiveness.[79] In the present study, data on clinical interventions were extracted from articles in PT journals and PEDro. Clinical studies in PT journals included clinical trials and studies with interventions such as massage, chest X-rays, walk/run tests, electrical stimulation and the like (Appendix 2). Almost half (47%) the articles in PT journals reported using clinical interventions.

Since clinical research involves therapeutic and non-therapeutic interventions, subjects may be placed at risk of physical harm. Thus, subjects must be told about all the risks of all the study interventions even if an intervention is standard care.[109] In order to give a fully informed consent to randomisation, a subject must be told about known risks and possible benefits of both treatments.[109] All clinical trails must receive REC approval.[109]

However, there is evidence that clinical research subjects have trouble appreciating the implications for their clinical care of taking part in a clinical trial. When this failure is based on lack of appreciation of the impact on individualised clinical care of elements of the research design, it is called the therapeutic misconception.[125] Failure to distinguish the consequences of research participation from receiving ordinary treatment can undermine the quality of subjects' informed consent. Worryingly, subjects may underestimate the risks for themselves of participating in a trial and they may not realise that decisions about treatment are based on a study protocol rather than a subject's best interests.[125] The therapeutic misconception is more likely to arise when a patient-subject's clinician is also the trial investigator.[125] Hence, researchers carry an added responsibility in the informed consent process if they are also clinician-investigators.

Compared to other study designs, clinical interventions and PEDro RCTs had the highest reported rates of informed consent and REC approval (78% and 69% and 79% and 67% respectively). Both these requirements were reported in 64% of PT journals and 61% of RCTs. These findings are consistent with other research which also showed higher rates of documentation of ethical safeguards in interventional studies and clinical trials compared to observational studies such as chart reviews and analysis of existing databases. [28,29,31,33,36,39,44,45] Indeed, some articles report almost complete compliance with ethical requirements. For example, rates of compliance were 100% when the sponsors were pharmaceutical companies,[39] and 98%[28] and 97%[31] when trials were undertaken among children and anaethetised subjects.

Although the reported rates of documentation in this study are comparatively better than the other study designs, they are far from complete. Almost one fifth of articles in PT journals failed to report either protection in interventional studies with the potential to injure participants. Researchers have a moral obligation to assure participants in trials that meticulous attention is being paid to their security and for reasons of accountability this needs to be publicly reported in journal publications.[45]

Although not as high on the hierarchy of evidence as clinical trials, properly conducted observational studies (such as cross-sectional surveys) have a role in modifying clinical practice by reducing uncertainty. About one third of the research examined in PT journals employed a behavioural design which included interviewing and/or questionnaire techniques for data collection. Whereas, over two thirds of these articles reported that consent was obtained, only 39% documented both consent and REC approval. In addition, one third of articles made no mention of either safeguard. The finding by Weil *et al*[33] that when investigators were approached directly about their ethical practices, rates of IRB approval and consent for behavioural research rose from 51% to 82% and from 42% to 81% respectively, suggests that physiotherapist-researchers may also have provided these ethical protections at a higher rate but failed to report this in their publications. Again, the solution requires definitive editorial guidelines that documentation of ethical safeguards is a precondition of publication.[26]

Wagner makes the further point that in medical settings, surveys and interviews can involve the collection of sensitive information, such as medical diagnoses, drug use or sexual preferences, that could be harmful if it became known outside the research setting.[109] Yet, only one third of behavioural research in the present study provided additional confidentiality assurances. This is disturbing since 47% of subjects included in behavioural research came from vulnerable groups, in particular, employees and students, where inadvertent disclosure of sensitive information carries heavy psychological, social and economic penalties.[35,133,136] More optimistically, behavioural designs had the highest reported rates (59%) of written informed consent.

Consistent with the potential risks in poorly conducted behavioural studies, the careless use of qualitative methodologies can lead to significant social and economic harms, such as stigmatisation, embarrassment or loss of insurance.[136] Despite these potential harms, properly executed designs using social science methodologies are necessary so that physiotherapist-researchers can collect in-put from patients regarding their experience of their condition and its treatment.[70,116] Ritchie contends that the technical as well as subjective aspects of care need to be appraised, and he believes qualitative methodologies provide the best means to do so.[70,116] Although only a minority (5%) of studies used qualitative methods, over half involved vulnerable subjects such as workers, students and survivors of sexual abuse. Whereas documented rates of informed consent were high (75%), less than one third of studies reported both ethical requirements. Even fewer (22%) documented confidentiality safeguards.

There is disagreement regarding the role of RECs in the review of research employing qualitative methodologies. Critics contend that most REC members, schooled in the methods of quantitative sciences, are ill-equipped to evaluate qualitative methodologies.[120,121,147,148] Consequently, researchers who use these methods may perceive RECs as impediments to research.[121] As a solution, it is recommended that more social and behavioural scientists and experts in qualitative methodologies be appointed as REC members.[121,147] Gordon also proposes that investigators '... educate and negotiate with IRBs'.[121] (p. 317) Negotiation can entail appearing at IRB meetings and personally addressing members concerns and questions.[121] Since governmental oversight is unlikely to become less burdensome,[144] a set of guidelines is needed for RECs to review protocols that use social science methods, in other words that provide a set of standards capable of establishing the credibility of qualitative research. To this end, Cutcliffe and Ramcharan offer an ethics-as-process approach for judging the ethics of qualitative methodologies.[149] Because much qualitative research is an emergent process which makes it difficult to establish *in advance*, beyond doubt, the balance of risks and benefits (particularly in comparison to quantitative studies in which the range of questions and procedures is known beforehand), they recommend that RECs monitor studies over time to check the ratio of emerging risks and benefits.[149] IRBs should also check that informed consent is obtained and reaffirmed during the conduct of research, that subjects are repeatedly reminded of their rights to withdraw, that subjects have the opportunity to check how researchers have represented them in notes and transcripts, and that researchers provide safety nets if necessary for vulnerable subjects.[149] Preferably, researchers should describe these added ethical protections in their publications to reassure readers that subjects' dignity and welfare were a constant concern whilst undertaking the study.[25]

Interestingly, several years earlier, Barnitt and Partridge in a follow-up study of subjects of physiotherapy research, identified shortcomings that had occurred during the process of the studies.[73] These included, among others, a consent process that left some individuals ill-equipped in their role as subjects as well as ignorant of potential psychological risks, poor interpersonal skills among the physiotherapist-investigators, and unfulfilled expectations regarding the outcomes of the studies. In response, these authors strongly recommended a monitoring role for RECs to ensure ethical conduct throughout the research process. Ideally, these extra safeguards ought also to be included in subsequent publications.

Whether or not consent and REC approval are needed for collection of existing data, for example, via the use of chart audits, is controversial.[113,117,118] On the one hand, it is argued that REC approval is not necessary because these activities represent routine clinical care and findings will not affect individual patients' management or their outcomes.[138] Furthermore, it is claimed that chart audits carry minimal risk of harm. On the other hand, it is held that a variety of people such as research assistants, students or clinicians gain access to personal patient information to which they would not normally be entitled outside the research situation.[109] Moreover, critics maintain that if presentation or publication of such activities is planned, the systematic collection of these data by definition constitutes research, and consent and REC approval are needed.[109,117,140]

Findings in this study suggest that a minority of physiotherapist-investigators felt consent and REC approval were necessary for when undertaking chart reviews (14% and 31% respectively). Indeed, a high proportion (69%) of articles had no documentation of consent or ethics approval. These data are similar to other studies which also noted low levels (range: 26%-52%) of compliance.[29,33] However, the reported rate of 26% in the study by Weil and co-workers considerably underestimated actual practice which showed that 60% of investigators obtained consent and IRB approval for their studies of pre-existing data.[33]

Only 8% of articles classified as chart review in the present study had documentation that confidentiality had been protected. Unquestionably, if during an audit, researchers intend to record personal information that could identify individual subjects (such as patients' names, medical record numbers or a combination of items including birth date, initials and diagnosis that could identify the patient) REC approval is indicated.[139] Indeed, potential harms from identification of individual subjects is part of the motivation for the US HIPPA Act,[119] which grants patients the right to know when and why their health data are being used. In the present study, it is not possible to determine whether breaches of confidentiality did in fact occur. As a simple rule of thumb, it is recommended that, when in doubt about a study, investigators should seek advice regarding ethical requirements from a local REC or even an editor if there is a chance the findings might be published.[29,109] If data are to be extracted anonymously from medical records, RECs will likely waive consent requirements.[109,118] Myles and Tan consider it inappropriate for researchers to make these decisions without independent, expert advice.[29] In the closely associated field of quality improvement, Williams acknowledges that defining clinical research 'within day-to-day physiotherapy management' can be problematic.[71] (p. 80) She advocates that if physiotherapist-investigators' primary intent is to assemble knowledge, rather than relieve patients' symptomatology (although both outcomes may occur), then they must first obtain REC approval.[71]

Partridge extols the benefits of case reports in physiotherapy.[115] She explains that 'In this evidence-based world it is worth considering the role of the Case Report ... They describe actual patients and their treatment in clear detail, and have a specific point to make ... the role of description is also important in identifying links between treatments and adverse effects ... in terms of education ... nothing makes more attractive reading than descriptions of real patients ....'[115] (p. iv) In addition, ' ... case reports can provide a rich source of information and help identify the characteristics of patients who are likely to benefit from treatment and those who are not ...'.[115] (p. v) But, Partridge is careful to point out that publication of case reports has ethical implications, in particular, the chance that individual patients may be identified, hence consent must be obtained from patients or their relatives.[115] Significantly, she does not mention the need for REC approval for publication.

Although higher than a previously reported finding (2%),[29] only 13% of case reports documented REC approval in the present study. Wagner does not think reports of single cases represent research.[109] On the other hand, he reckons the systematic collection of information on say six patients would probably require REC approval.[109] REC approval aside, case reports raise tricky ethical issues concerning patients' or families' privacy. Whilst 88% of case reports included confidentiality protections, only 17% mentioned informed consent. Here consent would necessarily include permission for publication of potentially personal information. Even though investigators conscientiously remove personal identifiers from patients' photographs or case histories, patients' and families' privacy can be difficult to protect when the institution is specified and a patient's clinical details are presented.[109] Furthermore, an author's geographic location may be a giveaway.[141] Anonymous authorship is not an attractive option to many authors who belong to a system that measures the value of academics and their institutions by publication output.[141] Thus, because complete anonymity is difficult to achieve, Wagner advocates that before submission, case reporters discuss publication with patients and their families.[109]

The takes a somewhat stronger line. In their statement, they say 'Patients have rights to privacy that should not be infringed without informed consent. Identifying information should not be published in written descriptions, photographs, or pedigrees unless the information is essential for scientific purposes and the patient ... gives written informed consent for publication ... IC for this purpose requires that the patient be shown the manuscript to be published ... when IC has been obtained it should be indicated in the published article'.[16] On this view, 83% of case reports in this study would not have been accepted for publication.

In a study that examined investigators' attitudes towards privacy and confidentiality issues in the publication of pedigrees, about half the respondents most of whom had experience in genetic research, were not personally concerned about subject confidentiality.[141] It is unlikely that this reflects a complete insensitivity to confidentiality concerns, in much the same way as most case reports included some confidentiality protections. Rather it implies that an increased effort to educate the broader biomedical community on these issues is warranted. Already identified as a problem in clinical practice,[74,150] further education and critical debate around ethical issues raised by confidentiality would benefit physiotherapist-practitioners and physiotherapist-researchers alike.

Botkin and co-authors propose that journals request that peer reviewers and the editorial board formally assess risks to subjects' privacy and confidentiality; that they require documentation of informed consent in published articles; and they detail requirements for managing identifying information in the instructions for authors.[141] Whereas these authors would support the ICJME's recommendation that subjects view photographs or case reports before submission, they reject this approach for family pedigrees ' ... since this practice itself risks breaching the privacy and confidentiality of family members and risks disclosing genetic information to subjects without counseling and, perhaps, prior validation'.[141] (p. 1812)

4.5 Documentation of Informed Consent, REC Approval and Confidentiality According to Vulnerability

Research involving vulnerable subjects raises many challenges for researchers and RECs. Charles Weijer makes the point that determining exactly who counts as vulnerable is a matter of judgment, which involves consideration of susceptibility to harm as well as capacity to provide free and informed consent.[151] He continues that attention to ethical protections requires a balanced approach in which the benefits and potential harms of research participation must be carefully weighed.[151] Specific protections for vulnerable subjects include enrolling subjects in a study only with strong justification, ensuring that consent is free and understood, and setting limits on the level of risks subjects must endure.[151]

Loosely based on Kipnis's categorisation,[129] one third of subjects in studies in PT journals were classified as vulnerable. These comprised mainly children, employees and students. By definition all participants in the paediatric RCTs extracted from PEDro were classified as vulnerable. Less than 5% of subjects constituted other vulnerable populations such as the decisionally impaired, critically ill patients, pregnant women, victims of sexual abuse and members of the military. These latter frequencies were too low for meaningful subgroup analyses or interpretation. Whereas in the past women were unfairly excluded from research,[134] this was not apparent in the present study.

One in ten subjects in this study was elderly (>65 years). Rates of documentation of consent and REC approval for elderly subjects were almost identical to those for adult subjects (64% and 55% and 63% and 51% respectively). Moreover, the rates of REC approval were better than published rates of 21%[36] and 40%[37] in comparable populations. Unless cognitively impaired, elderly subjects are not considered vulnerable. The South African Medical Research Council guidelines make this point strongly: 'Old age alone does not render a person incapable of consenting to health research. In the absence of any indication to the contrary, elderly persons are generally assumed to be competent to consent to research'.[112] (p. 10) The Medical Research Council adds the proviso that investigators must keep in mind the possibility of mental deterioration, elderly subjects' ability to comprehend and their dependency on others.[112] Where elderly persons are institutionalised[37] or cognitively impaired,[130,152] they may need added protections if they take part in research. In the US, research involving adults with decisional impairment is governed by the Common Rule's general provisions which merely direct IRBs to include 'additional safeguards' to protect the rights and welfare of 'mentally disabled persons'.[10]

Almost three quarters of the research reported in PT journals took place in a hospital setting. For paediatric RCTs this was 90 percent. Physiotherapist-researchers must remember that in some senses sick persons may be vulnerable simply by virtue of their illness.[151] Indeed, 'Illness may render a patient temporarily, intermittently, or permanently incapable of making an informed choice to participate in research'.[151] (p. 23) In the case of chronically ill patients for whom there is no effective treatment outside a research study, the voluntariness of their decisions may be in question.[126] Kipnis calls patients who lack treatment options medically vulnerable.[129] Investigators and RECs must constantly balance over protection which may deprive individuals and groups to which they belong of important benefits with potential harms incurred by needlessly including vulnerable groups in research.

If inclusion of certain population groups in a research study is potentially controversial, investigators ought seriously to consider providing justifications for their recruitment decisions in subsequent publications. This could, at once, show that the investigators were sensitive to the ethical issues and open critical debate over contentious choices.

4.5.1 Children

Medical research in general and clinical trials in particular has largely been avoided among children because of their encompassing vulnerability[128] and their inability to give fully informed consent. Yet these attempts to protect individual children from exposure to research risks may harm children as a class by inhibiting research in children's health and disease.[81,82] Based on this concern, children have been termed 'therapeutic orphans' in the drug development and pharmaceutical industry.[153] Frequently clinicians must adapt medicines, studied in adults, for use in children.[81,82] So, whilst intuitively it seems reckless to involve children as subjects in clinical research, prescribing interventions (especially drugs) not properly tested in children is unscientific and may be dangerous.[153]

Accordingly, research on children continues to present an ethical challenge. On the one hand, society must protect individual paediatric subjects of research from being harmed or improperly used. On the other, the welfare of all children depends on research to test the safety and effectiveness of medical procedures, drugs and public health measures such as vaccines.[80] Such research is essential to provide benefits and prevent harms within the population of children as a whole.

For the most part, ethical guidelines do not allow individual subjects to assume significant risks unless there is some prospect of benefit to them as individuals. Although a purely utilitarian perspective might permit harming a small number of individuals in order to achieve great good for a larger number, the codes and principles governing research ethics, such as the Declaration of Helsinki[7] and CIOMS[8], are explicitly non-utilitarian. The level of risk to the individual subject must be limited by investigators and RECs regardless of the potential value to society. In the case of children who are unable to consent to their own participation, the level of risk is limited even more carefully.[10,112,154] RECs play a fundamental role in research with children. Their main function is to protect patients, and child-subjects need maximum protection. Each REC should include a member with practical knowledge and experience of healthy and sick children.[154]

In research with children, parental permission and children's assent (if they are over seven years of age) are necessary.[80,81,155] Although the terms consent and permission are often used interchangeably, they have distinct conceptual differences.[155] Parental permission, not parental consent, is needed for a child's participation in research.[155] Only a competent individual (usually of legal age and with decisional competency[152]) may give consent. Parents, in representing their child, give permission not consent to the child's participation.[155] Assent (the active affirmation by a research subject) allows a child to refuse to take part and generally this ought to be respected.

In this study approximately two thirds of articles involving research with children documented REC approval. When compared with similar research in children, this finding was as good and better. These latter studies reported REC approval rates of 27%[32] and 52 percent.[33] Overall, the reported rates of parental permission in PT journals and PEDro trials (69% and 79% respectively) were better than analogous paediatric research.[30,33,34] In contrast, documentation of children's assent in articles in PT journals was lower in the present study compared with other research.[30,34] In turn assent rates in PEDro paediatric trials compared favorably with published findings.[30,34] Arguably, given children's vulnerability as research subjects, parental permission and children's assent (where appropriate) should be documented in all manuscripts as a condition of publication. This requirement is even more important when children are subjects in clinical studies. Positively, only 13% of paediatric RCTs in PEDro had no evidence of consent or REC approval. Unfortunately, almost a third of paediatric studies in PT journals reported neither ethical safeguard.

One in five children in PT articles was a subject in behavioural research. Generally, where observing, questioning or measuring form the basis of the research, studies are judged as minimal risk.[10,112] Even though child-subjects are unlikely to feel physical discomfort in such studies, parental permission and assent remain basic requirements for ethical research. Whether children's verbal, as opposed to written, assent is sufficient for participation in minimal risk research remains a matter of debate.[155]

4.5.2 Students and Employees

Two distinctive ethical concerns in research using students and employees are the voluntariness of the consent and beaches of confidentiality. If the person obtaining consent is in a position of authority or commanding influence over the participant, subjects may enroll in a study through fear of retribuition.[126] Thus subjects are vulnerable because they are more likely to be unduly influenced or controlled by an investigator's behaviour.[126]

Students make particularly good research subjects because they are available, often have free time and do not expect high levels of compensation.[126] However, students may feel obliged to take part in research if approached by faculty, especially when their grades are conditional on participation (as happens on some psychology courses).[126,132] Furthermore, because many students have limited financial resources, they may be more susceptible to modest incentives. These pressures may undermine the voluntariness of students' consent when considering whether or not to participate in research.[126] Inadvertent disclosure of sensitive information about students (such as debt burden, drug habits or sexual practices) may cause unintended psychosocial harms.[35] In addition, investigators who act in a dual role of teacher-researcher may gather confidential information which might negatively bias their perspectives towards individual students when serving in the teaching role.[35] Hence, sensitive information revealed in the research context might make them vulnerable to discrimination if information were inappropriately used in non-research settings.[35]

Despite these potential ethical breaches, only half the research involving students in the present study had REC approval and just over one quarter documented confidentiality protections. More encouragingly, over two thirds of articles documented consent. These rates of documentation were much better than findings in a study using medical students, in which rates for consent and IRB approval were 23% and 3% respectively.[35] To safeguard against possible social and psychological harms, investigators and RECs must pay special attention to recruitment, consent and confidentiality practices in protocols involving students. It may also be prudent for RECs to evaluate institutional policies relating to research with students.[35]

Most (87%) research in PT journals that included employees utilised behavioural methodologies which carry inherent social, psychological and economic risks.[70,136] Yet, about two thirds of studies failed to document REC approval or confidentiality assurances. Although rates of informed consent were somewhat higher (67%), it is not possible to determine the validity of the consent. It is reasonable to suppose that employee populations in PT journal articles consisted of physiotherapists or physiotherapist-assistants with different levels of seniority. Thus more junior employee-subjects might have been vulnerable to subtle pressures, particularly from management, to take part in order to benefit the organisation or institution. There is also a danger that researcher-managers may view research in the workplace as a quality improvement exercise not needing REC approval.[133] Rose and Pietri contend that a study becomes research when the intent of the project is to gather data and contribute to generalisable knowledge as well as to extend the findings beyond the individual study subjects.[133] They acknowledge that the 'paycheck vulnerability' between subjects and employers is complicated by the ambiguity that characterises definitions of research and legitimate managerial activity.[133] (p. 801)

Although the seriousness of these concerns confirms the need for additional protections, currently there is no formal ethical framework that addresses the unique vulnerability of workers as research subjects.[133] Rose and Pietri have identified loss of privacy and confidentiality as specially problematic in workplace research.[133] For instance, employees might realistically fear researchers' access to their confidential records.[133] Accordingly, these authors recommend added safeguards for the protection and management of study data to cover use of personal identifiers, use of data by others, an indication of whether data will be analysed in aggregate or individual format, and use or inclusion of study findings in employees' personnel or medical records.[133] Critically, consent procedures must detail these safeguards for potential subjects. To address existing shortcomings and to protect workers in research in the future, Rose and Pietri have developed a Worker Study Participant Bill of Rights.[133] Whatever extra ethical measures are included in a study, these need to be acknowledged in ensuing publications.

4.6 Documentation of Authorship, Sponsorship and Conflicts of Interest

According to principle 22 in the Helsinki Declaration potential subjects ' ... must be adequately informed of ... sources of funding, any possible conflicts of interest, institutional affiliations of the researcher ...'[7] In turn, principle 27 charges authors and publishers to declare in publications 'sources of funding, institutional affiliations and any possible conflicts of interest'.[7] Principle 27 continues that if reports of experimentation do not accord with the principles laid down in the Declaration they must not be published.[7]

Likewise, ICMJE Uniform Requirements provide unambiguous instructions on these issues.[16] With respect to authorship, the requirements stipulate that all persons designated as authors should qualify for authorship. Authorship credit must be based only on 1) substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; 2) drafting the article or revising it critically for important intellectual content and; 3) final approval of the version published.[16] All three conditions must be met and authors must provide a description of what each has contributed and editors must publish this information. Further, authors must disclose financial and other conflicts of interest that might bias their work, as well all financial support for the work and other financial or personal connections to the work.[16] COPE acknowledges that there is no universally agreed definition of authorship and directs authors to the target journal's instructions to authors in light of current uncertainties.[17] COPE notes that conflicts of interest may be personal, commercial, political, academic or financial.[17]

Despite these international principles and guidelines, there is no uniform policy or standardisation among PT journals regarding documentation of authorship, sponsorship and conflicts of interest. Only Physical Therapy, a Medline-listed journal, mentioned all three requirements in their instructions to authors. Nor did formal policies necessarily influence editors' or authors' practices. For example, Physiotherapy had no policy on authorship, yet over one quarter of its articles reported authors' contributions. In turn, the Australian Journal of Physiotherapy instructs authors to comply with the guidelines on authorship but none of its articles reflected detailed authorship. However, in light of a recent article on authorship in this journal there may well be better compliance with the Uniform Requirements in the future.[156] Since many articles in PT journals and PEDro had a minimum of three authors (58% and 87% respectively), all PT and related journals should provide clear-cut instructions requiring authors to specify their contributions and take responsibility (and hence accountability) for the contents of a manuscript.

Four out of six PT journals required documentation of sponsorship, yet only two out of six required written confirmation of conflicts of interest, despite the possibility that a source of funding can lead to a conflict of interest.[50,51] Arguably, in light of the very low rates of funding from industry (<1% and 6% in PT journals and PEDro respectively) potential financial conflicts of interest in physiotherapy research are less problematic than in medical research.[52]

In summary, there are certain ethical principles that investigators must keep in mind when submitting their findings for publication. Although attention to ethical issues in research publications is no guarantee of ethical adequacy, directives to address ethical issues as a condition of publication should enhance the ethical quality of both the conduct of a study and the dissemination of the findings. In the final chapter, recommendations are made to improve documentation of ethical practices in published physiotherapy research.

Chapter 5 Summary of Main Findings and Recommendations

5.1 Summary of Main Findings

5.1.1 Instructions to Authors in PT Journals

Whilst all people deserve the remarkable benefits that biomedical research involving human subjects generates, they also deserve assurances that their rights and welfare will be protected if they take part in research. One method of promoting ethical research is for journal editors to state clearly in their instructions to authors section that no study will be published unless there is documentation in the manuscript of compliance with basic ethical requirements, such as REC approval and informed consent.

In this study there was no standard editorial policy in the instructions to authors sections of the six PT journals for reporting basic ethical safeguards in manuscripts submitted for publication. Five journals required a written statement that subjects' confidentiality had been protected. This assurance generally applied to the publication of identifiable photographs or personal information in case reports. Four journals requested confirmation of REC approval. One journal required a signed certificate from the REC and another stipulated where in the article information on the REC was to be located. Three journals requested documentation of informed consent, with one directing authors to place this information in the 'Methods' section of the journal. Two journals had no statements on REC approval or informed consent. Four journals wanted information on researchers' sources of sponsorship, two had policies on authorship, and two included statements on conflicts of interest.

Furthermore, journals' publication practices often did not reflect their advice to authors. So even when journals provided explicit instructions to authors regarding ethical requirements, articles not complying with these criteria, were published nonetheless.

5.1.2 Documentation of REC Approval and Informed Consent

Overall, 48% of articles in PT journals had evidence of both REC approval and informed consent. When disaggregated, rates of REC approval and informed consent were reported in 65% and 54% of PT journal articles respectively. Yet, despite increasing concern about the protection of human subjects, about one third of papers did not report either ethical requirement. It is not clear in the absence of documentation whether some authors did obtain REC approval and consent but omitted to mention this in their papers, whether they provided this information directly to the editors, or their studies did not meet these requirements at all. Additionally, informed consent was defined liberally in this study which may have inflated the true rate of documentation. Encouragingly though, there was a significant increase between 1996 and 2001 of documented rates of REC approval in PT journals.

The Declaration of Helsinki and the CIOMS guidelines mandate REC approval and informed consent in human experimentation. Although the process of informed consent has been criticised, it remains central to upholding patient autonomy, a key tenet of ethical research. Indeed, informed consent and REC approval (where risks and benefits are carefully weighed) are *both* required because of well-described shortcomings in the consent process, such as the therapeutic misconception where subjects fail to distinguish between clinical research and clinical care.

A reasonable proportion of investigators obtained REC approval and informed consent for clinical interventions and RCTs (64% and 61% respectively), study designs widely recognized as requiring stringent ethical safeguards. In light of the disagreement about what ethical requirements are needed for chart reviews and the use of large data sets, researchers may have been uncertain whether or not REC approval and informed consent were necessary in studies employing these designs. Only 17% of chart reviews reported both requirements. Although no article specifically mentioned quality assurance, some of the chart reviews may have been quality improvement exercises and there is no consensus about when such projects become research, although intent to publish is considered a useful rule of thumb. If researchers are undecided about ethical requirements for some research designs, they should seek an opinion from the REC as to best ethical practice, and report the results of such a consultation in their publications.

Likewise, researchers probably did not consider case reports to be a form of research. This would account for the low rate (11%) of reporting of both REC approval and informed consent. Whilst there is general agreement that single case reports do not constitute systematic collection of data (that is, research) requiring REC approval, they do carry the risk of disclosure of personal information and many would argue that informed consent for publication from the patient or the family is essential to protect privacy and confidentiality.

Although the rate of documentation of informed consent was high (75%) in studies using qualitative methods, REC approval was reported in only 32% of articles. Debate about the role of ethics committees in the evaluation of research using qualitative methods is intense, particularly amongst social scientists and cultural anthropologists who maintain REC members lack expertise in the qualitative methodologies. Whilst this view has merit and REC members should become better informed about qualitative approaches, it should not imply that REC review is best avoided. Over half the subjects, mainly employees and students, involved in qualitative research could be considered vulnerable and therefore requiring added ethical protections rather than less. The voluntariness of consent and potential breaches of confidentiality provide important justifications for requiring both informed consent and REC approval when undertaking qualitative research. Nevertheless, there is scope for modifying these requirements because much qualitative research is an emergent process making it difficult for instance, confidently to determine in advance likely risks and benefits of a study. In similar vein, it may be more appropriate to obtain consent throughout a study rather than as a once off ethical obligation. If researchers deviate from standard ethical practices, authors should provide ethical justification for using a more morally controversial approach.

Only about two in five articles using behavioural designs, including interviews and questionnaires, documented both REC approval and informed consent. Rates of consent were documented more often than rates of REC approval (68% versus 44%). This finding is consistent with the qualitative methodologies and most likely reflects a degree of overlap between the sets of findings. Behavioural designs may involve the collection of sensitive information, the disclosure of which can cause psychosocial harms. Hence informed consent and REC approval are basic ethical requirements which should be documented in published articles reporting research using these methods.

Approximately one third of subjects was vulnerable and included mainly children, employees and students. Historically, children have been excluded from research by virtue of their vulnerability, in particular their questionable maturity to give fully informed consent. This has led to their being called therapeutic orphans. However, children are increasingly being included in research in order to benefit them individually and as a class. In research with children, parental permission and children's assent are minimum ethical requirements. Whereas rates of parental permission in PT journals and PEDro were reasonable, reported rates of assent were far lower (10% and 26% respectively). Considering their vulnerable status, it is worrying that 29% of PT journals reported neither ethical requirement. Although the inclusion of children in research is commendable, this research must meet the highest ethical standards and journals have a central role in ensuring that only research that meets stringent ethical requirements is published.

Research among students and employees raises special ethical issues. These include susceptibility to incentives and undue pressure to participate in order to satisfy the wishes of persons in authority, such as teachers, lecturers, bosses, and unions. Although valid informed consent is generally the paramount protection against unwilling participation, additional protections such as independent subject advocates and careful scrutiny of the balance of risks and benefits by an REC are needed. Whilst, reported rates of informed consent (68% for students and 67% for employees) were relatively sound, respective rates of REC approval were less satisfactory (51% and 36%). Clearly subjects should not be excluded from research merely because of their vulnerable status but they do need protection. Journals can influence researchers' behaviour by only publishing research that provides evidence that it was conducted ethically.

5.1.3 Documentation of Confidentiality

Confidentiality is the ethical duty not to reveal personal information about individuals in clinical care or research without their explicit consent. In total, only 26% of PT articles reported confidentiality. Appropriately, most (88%) case reports included confidentiality protections. Yet, despite the risks of inadvertent disclosure of sensitive information, rates of reporting for studies using behavioural and qualitative methodologies were disappointingly low (31% and 22% respectively). The inclusion of employees and students in these studies in the absence of confidentiality assurances is especially worrisome because of potential social, psychological and economic harms that could arise should information obtained during a study be used beyond the research setting.

Less than one in ten studies classified as a chart review reported that confidentiality had been protected. If data are extracted anonymously breaches of confidentiality are unlikely to occur although REC approval is nevertheless desirable. If investigators intend to extract personal information that could identify individual subjects, REC approval which would include an assessment of the risks to privacy and confidentiality is indicated. As already discussed, the ethical requirement to obtain informed consent for anonymous chart review or audit is controversial, with detractors complaining that consent is impractical and an impediment to records-based research. Significantly, current legislative efforts in many countries especially industrialised nations, support escalating measures to protect personal information during the conduct of research. Editors must require, and investigators must document where appropriate in their publications, whatever measures were taken to protect subjects' privacy and confidentiality.

5.1.4 Documentation of Authorship, Sponsorship and Conflicts of interest.

The Declaration of Helsinki is unequivocal in its requirement that publications reflect authors' sources of funding for their research along with any conflicts of interest. If articles do not comply with these requirements they must not be published. Most articles in PT journals and PEDro contained no information on conflicts of interest (99.5% and 96% respectively). Because it is unclear whether investigators had conflicts of interest and did not report them or they actually had none, journals should require a statement that no conflicts are declared even when no conflicts exist. In this way, authors would be held accountable. In total, only eight studies received commercial funding, suggesting that physiotherapy research may be less susceptible than medical research to potentially negative incentives from commercial sponsorship. Still, other conflicts of interest such as political and personal may be associated with publicly funded research. Therefore, PT journals must uniformly mandate documentation of sponsorships and conflicts of interest, and any connections between them.

Increasingly, editorial bodies, such as the ICMJE, COPE and WAME, expect explicit specification of authorship in publications in order to prevent, among others, guest or ghost authorship. PT journals' own editorial policies and practices in this regard are uneven. Whilst, there may never be a universally agreed-upon policy regarding authorship, PT journals at the very least should develop their own guidelines and, as importantly, ensure their implementation.

5.2 Limitations

This study could not corroborate whether investigators' failure to report ethical safeguards, reflected actual failure or simply failure to document whether ethical safeguards were followed. This study's findings, based on information in published articles, reflected only what was reported, not the actual conduct of human subject research. This is important in view of follow-up surveys of investigators that show they do in fact obtain REC approval and informed consent but for many reasons do not always include this information in their final manuscripts.[27,31,33,43,142] Conversely, attention to ethical detail in published reports does not automatically mean the research was conducted ethically.[47]

Likewise, the study did not determine whether ethical dimensions of research were explicitly addressed in cover letters to editors and peer reviewers at the time of manuscript submission, a practice consistent with the recommendations of some journals' instructions to authors. Thus, low rates of reporting may not imply that the research was unethical, merely that authors failed adequately to inform their readers.

The rates of documentation in articles were taken at face value. None of the journals' editors was directly interviewed and there was no confirmation of ethical approval from any RECs. Nor was there any confirmation from research subjects that informed consent had been properly obtained.

The generalisability of findings is limited to PT journals included in this study. However, in light of their consistency with the published literature in PEDro and in other fields, it is likely they will apply to other PT publications. Additionally, articles in PT journals spanned a six year period.

5.3 Recommendations

Publications are the public face of physiotherapy research and although careful attention to ethical issues in published reports offers no guarantee of a study's ethical satisfactoriness, a requirement to address ethical issues as a condition of publication would enhance attention to ethical detail in the planning, execution and dissemination phases of a research project. Accordingly, it is recommended that:

1. The instructions to authors sections of all PT journals should contain a clear and detailed description of the ethical standards that are required to publish articles on human subject research, including case reports.

2. PT journals should consider stating explicitly in their instructions to authors that manuscripts will only be considered for publication if the research they describe complies with ethical guidelines of international ethical codes such as the Declaration of Helsinki or CIOMS. These include, at a minimum, documentation in manuscripts of REC approval, informed consent and proxy consent or assent, confidentiality and disclosure of sources of funding and conflicts of interest. More detailed discussion of ethical issues may be warranted for studies considered ethically problematic.

3. PT journals should bring their authorship requirements in line with those of international bodies such as the ICMJE, COPE and WAME.

4. PT journals should standardise their ethical requirements for publication and it would be useful if these were added to editorial and peer review checklists.

5. PT journals should be consistent in where information on ethical issues is located, for example in the 'Methods' sections of published articles.

In conclusion, although primary responsibility for ensuring ethical conduct of research rests with investigators, PT journals can be more active in protecting subjects by making compliance with a uniform set of ethical safeguards a condition of publication. These requirements would serve as the final check in ensuring the highest scientific and ethical standards in human subject research.

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Appendix 1: Protocol for Review of Physiotherapy Journals and PEDro Articles

Article number:

Journal: SAJP UKJPT USAJPT CJPT AUSJPT PTI

Journal Title (PEDro)

Year: **volume:** **pages:**

Authorship: number on byline university affiliation: Y N

Country of origin:

SA Rest of Africa USA Canada UK/Europe Australia

Middle East Far East Asia Other (specify)

Contributions specified: Y N

Conflicts of Interest: declared none declared no statement

Sponsorship: industry non-industry both none

Setting: hospital Y N other (specify)

Ages: children adults elderly combinations not specified

Gender: male female both not specified

Vulnerable groups:

children students pregnant women HIV/AIDS critical care

decisionally impaired employees other (specify)

Design: clinical behavioural chart review combination of methods

Case report: Y N

Quality assurance study: Y N

Qualitative methods: Y N

Presence of informed consent in article: Y N not applicable

Format: written oral both waived not specified

Proxy consent: familial non-familial not specified not applicable

Assent: Y N not applicable

Format: written oral both not specified

Presence of REC approval in article: Y N

Number of committees: name of REC specified Y N

Location of REC approval: 'methods' title page both

Confidentiality: Y N

Appendix 2: Coding Sheet for Physiotherapy Journals/ PEDro

Article number: code consecutive protocols for each new article with a number beginning with 1.

Journal (Physiotherapy): Circle the appropriate journal source for each article.
- SAJP - South African Journal of Physiotherapy
- UKJPT - Physiotherapy
- USAJPT - Physical Therapy
- CJPT - Physiotherapy Canada
- AUSJPT - Australian Journal of Physiotherapy
- PTI - Physiotherapy Research International

Journal (PEDro): Write journal title in full.

Year, volume and pages: specify for each article.

Authorship:
- indicate number of authors on the title byline
- does 1st author have a university affiliation?
- circle country of origin of 1st author

Contributions: indicate whether individual contributions of each author are identified e.g. wrote paper, designed study, collected data, managed data, analysed or interpreted data, performed statistical analysis.

Conflicts of interest: circle whether authors acknowledge any conflicts of interest e.g. consulting fees, service on advisory boards, research grants, honorariums for lectures.

Sponsorship: circle appropriate source of sponsorship. Industry includes private sector funding e.g. drug companies; non-industry includes funding from non-profit organisations, university grants, foundations and government agencies such as the medical research councils.

Setting: hospital includes in-patient and out-patient settings. Specify other settings such as schools, community centres, nursing home, sports tournament, private practice.

Number of participants: includes number who actually took part in the study.

Age of participants: children refers to participants ‹18 years, elderly refers to participants >65 years.

Vulnerable groups: 'children' refers to participants ‹18 years, 'students' refers to participants who are receiving higher education (i.e. not scholars), 'critical care' includes persons in intensive care and emergency care settings, 'decisionally impaired' refers to previously competent persons who are mentally ill, unconscious or suffering from severe dementia, and the mentally retarded.

Design:
- **clinical:** includes clinical trials and studies with interventions such as massage, blood tests, blood pressure, chest X-rays, walk/run tests, electrical stimulation etc.
- **behavioural:** includes studies where data are collected using interviews, questionnaires or health services research.
- **chart review:** includes use of pre-existing and publicly available data bases, chart reviews and clinical audit.
- **Combination of methods:** includes more than one method, e.g. clinical intervention plus questionnaire.

Case report: includes articles in which the phrase 'case report' is used in the title, abstract or key words of the article.

Quality assurance study: includes articles in which the phrase 'quality assurance' is used in the title, abstract, key words or methods section of the article.

Qualitative methods: includes articles in which words 'qualitative methods' are used in the title, abstract, key words or methods section of the article.

Presence of informed consent in article: refers to those articles which document that informed consent (written or oral) was obtained or waived. Articles must include either a strict or implied definition of informed consent. Informed consent is present if the following kinds of statements are reported:

- Patients/ proxy gave written informed consent to participate in the study (strict definition).
- All subjects gave written/ oral consent (implied definition).
- Investigators received approval from the REC to use deferred consent (waived consent).

All articles will be counted once for informed consent but may include multiple counts on other outcome measures. For example, BOTH oral and written consent may be circled if both are obtained in a study.

Proxy consent:

- **familial** consent refers to consent from a parent or guardian in the case of a child, and to a family member in the case of an adult.
- **non-familial** refers to consent granted by a legal proxy or a caregiver.

Assent: refers to articles which document that assent was obtained from child participants.

Presence of REC/IRB approval: refers to articles in which REC approval or exempt status is documented. Articles must contain either a strict or implied definition of REC approval. REC approval is present if the following kinds of statements are reported:

- The study protocol was approved by the ethics committee (strict definition).
- The study adhered to the Helsinki declaration (study performed according to Helsinki...) (implied definition).
- Approved by a government or professional body (e.g. MRC, National Institutes of Health).

Number of committees: refers to the number of ethics committees that granted ethical approval for the study.

Name of REC: Was the actual REC named? For example, the REC of the Faculty of Health Sciences, University of Cape Town. (Because of variation in practice and effectiveness of RECs, naming a committee may increase accountability).

Location of REC approval: indicate where in the article mention of REC approval is made.

Confidentiality: refers to articles which documented that participants' confidentiality, privacy or anonymity was respected, for example, data were collected anonymously, identifying information was removed.

Appendix 3: Protocol for review of 'instructions to authors' in physiotherapy journals

Journal: SAJP UKJPT USAJPT CJPT AUSJPT PTI

Year of publication:

How often during the year are instructions issued:

EXPLICIT statement in instructions concerning:

Informed consent: Y N

If yes, IC to be located in: covering letter manuscript not specified

REC/IRB approval: Y N

If yes, approval to be located in: covering letter manuscript not specified

Compliance with Helsinki declaration: Y N

Protection of human rights and dignity: Y N

Financial disclosure/sponsorship: Y N

If yes, disclosure to be located in: covering letter manuscript not specified

Conflict of interest: Y N

If yes, statement to be located in: covering letter manuscript not specified

Confidentiality: Y N

Authors' contributions: Y N

Do instructions refer authors to the Uniform Requirements: Y N

No guidelines for ethical standards: Y N

OTHER/ COMMENTS:

Appendix 4: Coding sheet for 'Instructions to Authors'

Presence of informed consent in instructions: refers to a documented statement that informed consent should be obtained when conducting human subjects research. For example, Physiotherapy states that ' ... for reports of research involving people, written confirmation of informed consent is required'.

Presence of REC approval in instructions: refers to a statement indicating that REC approval of studies involving human research is required for publication. For example, Physiotherapy Canada requires that '... for research conducted on human subjects, authors must include a written statement documenting informed consent of subjects and approval of this study by an institutional review board or similar body'. Phrases such as 'IRB', 'responsible committee on human experimentation', 'institutional approval' may be used interchangeably with REC.

Compliance with Helsinki Declaration: refers to a statement to this effect. Compliance would imply that the study meets with the following ethical requirements: REC approval, informed consent, assent, proxy consent, disclosure of funding and possible conflicts of interest (articles 22, 24, 25, 27 of Declaration).

Protection of human rights and dignity: refers to instructions to authors that they must protect subjects' rights and dignity. For example, Physical Therapy requires a statement in the 'methods section' that ' ... the rights of human and animal subjects were protected.'

Financial disclosure: refers to a statement requiring authors to document all sources of funding. For example, Physiotherapy Canada states that '... funding sources supporting the work should be acknowledged in a footnote on the title page'.

Conflicts of Interest: refers to instructions requiring authors to acknowledge possible conflicts of interest. For example, Physiotherapy Canada expects authors '... to disclose in their covering letter any commercial or financial association that might pose a conflict of interest in connection with the submitted paper'.

Contributions of individual authors: For example, Physical Therapy requires that authors' and non-authors' signatures appear next to a list of itemised contributions which include, *inter alia*, writing, research design, data collection, fund procurement, clerical/secretarial support.

OTHER journal requirements: refers to additional ethical guidelines in the 'instructions'. For example, Physical Therapy adheres to the use of 'people-first' language. A subject should not be referred to by disability or condition (e.g. 'patients with stroke' NOT 'stroke patients') and terms that could be considered discriminatory should be removed.

Confidentiality: refers to specific instructions to maintain privacy and confidentiality. For example, Physiotherapy states that '... the use of names in case studies is encouraged for clarity and humanity, but they should not be their real names'.

Comments: should include any *additional points* of interest in the 'instructions' not captured in any other section of the protocol. Verbatim descriptions of instructions might be useful.

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3rd February 2003

Professor Trevor Gibbs
FHS Dissertations Committee
Faculty of Health Sciences
Barnard Fuller Building
Medical School
Observatory.

Re: Resubmission of Dissertation Proposal - Reporting Ethical Requirements in Published Physiotherapy Research (Student Number: WLFDEN001)

The attached comment refers.

At a full meeting of the Research Ethics Committee held on 31st January 2003, members overwhelmingly indicated that ethics approval for research of this nature was unnecessary. The aim of the proposed study is to examine journal articles which are available in the public domain and as such there is no human subject involvement.

Yours faithfully

Lesley Henley

CC Professor C. Swanepoel (Chairman, Research Ethics Committee, FHS)
Professor S. Benatar (Course Director, MPhil in Bioethics)

Research Ethics Committee
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06 February 2003

Dr L Henley
Paediatrics

Dear Dr Henley

REPORTING ETHICAL REQUIREMENTS IN PUBLISHED PSYCHOTHERAPY RESEARCH

Thank you very much for your letter to the Research Ethics Committee dated 03 February 2003.

We agree with the contents of the letter as the reflection of the position of the Committee on the matter.

Please quote the above Rec. reference number in all correspondence

Yours sincerely

PROF CR SWANEPOEL
CHAIRPERSON