



Pacific Rim International Journal of Nursing Research

Ethical Issues in Research on Children

One of the most common ethical concerns in research is related to the dilemma of using children as subjects, because young children are one of the most vulnerable groups who are open to exploitation by adults.¹ It is imperative that nurse researchers appraise themselves of their research obligations when considering the ethical issues of their subjects or participants, whether adults, adolescents or children. Importantly, nurses and other health professionals should always consider the additional issues and research requirements involved in gaining consent or involving children or adolescents in their studies. This editorial will explore some issues related to ethical principles and practice about this to help avoid research misconduct with children.

Historically, research in children before and during the World War II was marked by unethical practices in Europe and Asia. For example, in a study at Kobe Medical School in Japan in 1958, infants were used as “objects” in clinical experiments, without parental consent, to identify the best density of lactose in artificial milk. A small gastric plastic tube was inserted into the infants’ gastrointestinal tract to analyze the gastric content along the tract after feeding with various milk formulas. A number of babies in the study suffered from high fever, diarrhea, and vomiting². In another example, in 1952 infants of the Nagoya City Infant Nursery in Japan were inoculated with coliform bacillus, resulting in severe diarrhea among the babies, and death.² During WWII, twin children in Nazi concentration camps were subjected to cruel experimental studies, e.g. injection of different dyes into eyes to change the color of their eyes.^{3,4} In the Nazi Neuengamme Camp in Germany, children were deliberately infected with tuberculosis and later killed after the experiment.³ Therefore, following the Nuremberg Trials after the WWII, some of the medical researchers involved were punished and the world medical community urged for ethical principles for research. Ethical research among children was also reinforced.

Gradually in a number of countries, a paradigm shift began to occur, where children became viewed as “subjects” rather than “objects” in research. However today, ethical issues still exist in many countries,⁵ including Thailand, where ethical review committees (or institutional review boards) for human research are not established in many places across the country, and there is a dearth of both experts with experience and knowledge in both adult and child research ethics. However, Thailand is now in the final process to enact a new law requiring all human research to be approved by standard Ethical Review Committee.⁶

There have been a number of statements of ethical principles produced over the years for example, The Declaration of Helsinki⁷ and The Belmont Report⁸. In 1964, The World Medical Association developed a set of ethical principles for medical research, The Declaration of Helsinki, consisting of 32 items, and which has become the foundation of human ethics for research across the world.⁷ This Declaration recognizes the vital significance of medical research to advance understanding and development of medical interventions. But it is the researcher’s duty to promote and safeguard the health, wellbeing and human rights of their human subjects. It is therefore important to weigh up and evaluate the potential risks, burden or benefit of the research to the subjects. Only if the benefit(s) of a study is greater than the risks, it is acceptable.⁷

Later in 1977, the National Commission of the Protection of Human Subjects of Biomedical Behavioral Research in the USA produced the Belmont Report, which had three core principles: a) respect of persons

(autonomy protection), b) beneficence (do no harm and maximize benefit), and c) justice (no bias for risk and benefit).⁸ These three principles can apply to research in both adults and children.

1. **Respect for persons.** The two requirements are that the researcher should a) respect the autonomy of subjects, and b) protect those with diminished autonomy. In respect of autonomy, it is required that any subject needs to enter into any investigation process voluntarily and with adequate information from the researcher. Parental consent/permission for children aged below 18 to participate in any research is also required. Children aged 7–18 are able to provide their assent in research participation.¹

2. **Beneficence.** It is the obligation of the researcher to secure the health and wellbeing of the subjects by: a) doing no harm and b) maximizing possible benefits and minimizing possible harms. Throughout the research, the researcher should have carefully thought in advance of any possible risk or discomfort that might occur and plan ahead to prevent them. Emergency care or alleviating measures should be planned in advance. In most clinical trials trying to find effective treatments for pediatric illnesses, the subjects themselves may not directly gain benefit from the experimental research, but hopefully this will further benefit the future advancement of knowledge for treating illness in the future.^{1,9}

3. **Justice.** – Questions to ask in terms of this are: Who will gain benefit and who bear the risk/burden? Why are the children subjects? Why not adults? What are reasons to justify the need for study? Are the subjects treated equally? It is critical that the burdens and benefits should be equally distributed with respect to the merit of a study.⁹

Children's autonomy and the assent form

The autonomy of subjects can be better ensured by providing informed consent and informing them they can withdraw from the study without any negative consequences from the researchers. Parents and caregivers are important persons for researchers to involve, for they need to grant permission for studies on their children. The researcher needs to try to gain children's *active* agreement using an assent form and *passive* agreement using a consent form signed parent(s) or caregiver(s). For passive agreement or permission, the researchers should provide parents with clear and understandable information about their research in order to try to gain truly *informed consent*. Older children are able to actively explore the information provided by the researchers and express their wish as to whether to participate.⁹ The child and adolescent permission form, the so-called *assent form*, is used among children aged 12 and above, as their normal cognitive ability is at formal operational stage.

The process of getting assent from children needs to include:

1. Giving content about the research activities, offering information as appropriate to their age and reading ability.
2. Avoiding medical/technical terms that unfamiliar to them. Pictures and user-friendly language for explanation is recommended.
3. Providing in writing the necessary information about research background, process, risk and benefit of the study and persons to contact (addresses and telephone numbers of both researchers and a contact person within the ethical review committee should be given).
4. Avoiding coercion and informing them that if they want, they can withdraw from the study at any time without negative effect on their usual service such as health care or education processes.
5. Allowing sufficient time for parent(s) or caregiver(s), and children to make a decision as to whether to join the study.

6. Inviting any questions before, during, and after the study period.
7. Inviting parents to stay with children when administering drugs or other interventions.
8. When children understand and are willing to participate, with the permission of their parents, they are invited to sign their name.^{1,10,11}

Parental permission or informed consent can be *waived* in cases of research:

1. Involving child protection, such as dealing with child abuse, child neglect, and domestic violence; or
2. Where, the privacy of the child or adolescent can be violated.¹¹ For example, when parents are asked to give permission in studies about drug use or sexual behaviors in adolescents, most parents will scrutinize their child's behaviors. This can cause a violation of privacy and make adolescents feel uncomfortable and not provide the truth about the topic to the researcher.

Ethical issues in research designs

Various research situations/designs may raise concerns in research on children. For example:

Clinical trials: When children are subjects of invasive treatment, researchers should carefully consider the risks of such treatment. For example, what is a safe dose for a new drug experiment? How much blood can be taken from children? According to Howie in the WHO Bulletin, the maximum allowable blood volume in healthy children is 0.8–4.0 ml./kg. of body weight within 24 hour and less than 8 ml./kg. within 4–8 weeks. In sick children, it is <3 ml./kg. within 24 hour.^{12,13}

Cohort study: In most descriptive and experimental studies among children, parents provide their informed consent and children provide their informed assent just once before data collection. However, when children are subjects in birth cohort or other cohort studies, renewal of their assent is required at different stages. It is recommended that researchers consider gaining re-assent in children when they reach 7, 13, and 18 years old, as at the time that they are contacted periodically as subjects in cohort studies.^{12,14,15}

Participatory Action Research: There may be additional research ethics issues when children are participants within this research design, because of the nature of direct contact between researchers and children during study processes. Carefully designed approaches in communicating and data gathering with children are essential. For example, the researcher must consider questions like: What are the research topics to be studied?; What methods of communication will be used? (For example, drawing, writing, and oral interview); and How can children take part in data interpretation?^{5,8}

Conclusion

All ethical principles for conducting research in adult subjects must also be applied to children. When children are subjects, special consideration includes four major issues. Firstly, a child's cognitive ability is usually aged-related and so appropriate assent forms should be used for those aged 7–18 years old. Secondly, children need special attention in research projects because they may be vulnerable to exploitation. Therefore, researchers are obligated to protect their health and well-being during and after the studies, and to protect their human rights at all times. Thirdly, parental permission is legally pertinent. Parents or guardians should be given adequate information and provided with informed consent forms prior to the beginning of the study. Lastly, when children grow older in a longitudinal study, it is recommended to renew their assent/consent at various important stages.

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References

1. Sueblinvong T., Morakot N., Panichkul S. Ethical Guidelines for Research in Children. Bangkok: Chula Book; 2015. (in Thai).
2. Tsuchiya T. In the shadow of the past atrocities: Research ethics with human subjects in contemporary Japan. *Journal of Asian and International Bioethics*. 2003; 13: 100-2.
3. Lifton RJ. *The Nazi Doctors: Medical Killing and the Psychology of Genocide*. New York: Basic Books; 1986.
4. Kubica H. The Crimes of Josef Mengele. In Gutman I., Yisrael M., Berenbaum M. *Anatomy of the Auschwitz Death Camp*. Bloomington, Indiana: Indiana University Press; 1998.
5. Einarsdóttir J. Research with children: methodological and ethical challenges. *European Early Childhood Education Research Journal*. 2007. 15(2): 197-210.
6. Draft Research on Human Subjects Law. Thailand Citation Index Centre. No date. [Cited 2016 Jul 1]. Available from <http://tcijthai.com/tcijthainews/view.php?ids=5428>. (in Thai)
7. World Medical Association. Declaration of Helsinki. Ethical Principles of Medical Research Involving Health Subjects. Amended 2013; c2013. [Cited 2016 Jul 1]. Available from <http://www.wma.net/en/30publication/10policies/b3/index.html.pdf>?
8. The National Commission for the Protection of Human Subjects on Biomedical & Behavioral Research. The Belmont Report. No date. [Cited 2016 Jul 8]. Available from https://videocast.nih.gov/pdf/ohrp_appendix_belmont_report_vol_2.pdf
9. Thomas N., O’Kane C. The ethics of participatory research with children. *Children & Society*. 1998. 12: 336-48.
10. UCLA OHRPP. Guidance and procedures: Child assent and permission by parents or guardians. Available from http://ora.research.ucla.edu/OHRPP/Documents/ChildAssent_ParentPerm.pdf?
11. Faculty of Medicine Siriraj Hospital, Mahidol University. Assent form for children. No date [Cited 2016 Jul 1]. Available from https://www.google.co.th/search?q+assent&ie=utf-8&oe=utf-8&gws_rd=cr&ei=eD0pV_j2LoKeuQSE8aOoDg. (in Thai).
12. Shaddy RE., Denne SD. the Committee on Drugs and Committee on Pediatric Research. Guidelines for ethical conduct of studies to evaluate drugs in pediatric populations. *Pediatrics*. 2010; 125(4): 850-60.
13. Howie SR. Blood sample volumes in child health research: review of safe limits. *Bulletin, WHO*. 2011; 89(1): 46-53.
14. National Research Council. *The Ethical Conduct of Clinical Research involving Children*. Washington DC: The National Academic Press; 2004.
15. Nuffield Council on Bioethics. *Involving Children and Young People in Health Research-Getting it Right*. No date. [Cited 2016 Jul 1]. Available at: www.nuffieldbioethics.org/children.