

Evidence-Based Complementary Medicine. State of the Evidence Methodological Challenges.

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ABSTRACT

“Ethical Approval of Research on Complementary Medicine”.

The increase use of Complementary medicine in the community has rightly led to the obligation by health care providers for a corresponding increase on evidence-based research in relation to their use. The term Complementary medicine includes a very diverse group of therapies, and it is well known that some are likely to have more risks than others. Furthermore, many may have little or no benefit, whereas others may prove to be ‘medical breakthroughs’ in terms of treatment. As with any medical intervention, researchers who wish to study the effects of a treatment on humans, generally require ethical approval before commencing their project.

The aim of this paper is to further raise awareness among researchers of the ethical approval process, to facilitate research into Complementary Medicine. For example, some questions that have arisen in my experience on an Ethics Committee will be addressed, including - should the study of aromatherapy in hospitals be considered a drug trial, or is it only a perfume? What if approval had been given for research of a herbal remedy that was found to be banned? Who would be held accountable if a serious unexpected harm occurs as a result of a research project involving complementary medicine?

In relation to informed consent, how much information can be given about a therapy if little or no studies have been done in the past? To what extent should the Ethics Committee insist on evidence of efficacy and potential harms, and how confident must the researcher be that the potential harms of any therapy have been identified before commencing the study?

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Slide 1.

I would be surprised if most of you at this congress could claim never to have had concern about the ethics of research for some projects on Complementary medicine.

Slide 2. Yet, as an academic, on a University Ethics Committee, I have frequently observed frustration from researchers who see gaining ethical approval for their projects as an obstacle they would rather ‘do without’.

However, my experience on the committee has shown me that a research project that has not addressed the ethical questions in sufficient depth will not only be highly criticized by their peers, but also by society in general. For example, I well remember a project carried out by the Family Planning Association in Melbourne that was put under a media microscope, for failing to address the informed consent aspects of the research sufficiently when introducing a new product. It was both embarrassing for the agency, and damaging of their reputation. The ethics committee that approved the project was also strongly criticized. Fortunately, no significant harm to patients occurred.

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Institutional Ethics Committees in Australia must follow the guidelines of the National Health and Medical Research Council (NH&MRC), and all Universities and generally all hospitals have a well established ethics committee to review research involving humans. For the purpose of this paper I assume that some form of ethical review takes place for all research in Complementary Medicine.

In the brief time available to me, I propose to use the criteria that we use at Monash University to consider the common issues that an Ethics Committee would focus on, and I intend to give examples of issues that have a particular relevance for research on

complementary medicine. In our committee, we have three different categories that are determined during the approval process. Category A projects are the more controversial, and it is this category that I will be mainly focusing on today. Category B are less controversial, although there still may be some problems with the recruitment and consent processes for participants. Category C are basically not able to be assessed at the time, usually because more information is needed to approve the study.

Category A. *Slide 4*

The first criteria, which must be discussed by a full committee is **‘using intrusive techniques’**. This would include taking blood, giving injections, using rectal thermometers, and I assume, any study involving acupuncture using needles. The committee may not have concerns about the processes, but would want to be assured that the risks were low, and that the practitioners (including research assistants or associates) are appropriately qualified to carry out the technique.

I hope Dr. Stephanie Joos will forgive me at this point if I use her research as an example of how an ethics committee would be likely to have considered the research project she presented on Thursday. Those of you that were there may remember that the study was randomized, and involved the use of acupuncture for patients with Crohn’s disease. I believe that an ethics committee would have had a lot of questions concerning the control group, who had needles inserted in up to 18 deliberately selected non-acupuncture points. Apart from the anticipated lower therapeutic response, the committee would, I believe, have wanted to ensure that all participants had been informed – prior to agreeing to take part in the study – that this could happen to them if randomly selected into the control group. If they all believed that they were receiving acupuncture, this would be ethically problematic. I also would hope that they were not paying for the so called ‘treatment’ given.

This example is also relevant to the second criteria, which is: **‘causing discomfort in participants beyond normal levels of inconvenience’**.

This includes the length of time required for the questionnaire, travel time to a venue, or undergoing specific intrusive tests or interventions. It may also include interviewing subjects who may be grieving or have experienced significant trauma. In these circumstances, the committee would want to know that steps have been taken to protect participants, such as being ensured that they can withdraw from the study at any time, and/or appropriate counselling is available.

Slide 5. The third criteria is **‘examining potentially sensitive or contentious areas’**. In my experience, the projects which would relate to this category would be those where confidentiality would be an issue, or if the data collected is culturally sensitive. For example, in Australia, some information from Aboriginal subjects, such as men’s or women’s business, would be highly sensitive, and when I worked in Africa, I was aware that some traditional medicines should not be passed on to the uninitiated.

The forth criteria is **involving vulnerable subjects** (children, mentally ill, unconscious patients, those in dependent relationships, e.g. wards of state, prisoners, members of armed forces, patients, students etc.) or in apparently coercive situations. If the research will be conducted with your own clients or patients, you generally need to ensure that a third party does the recruitment, and that it is confidential who ‘opts in’ or ‘opts out’ of the study. Furthermore, reassurance is usually given that if the patient does not take part in the study, it will not effect their current treatment.

In relation to children, recruitment and parental permission may be a problem. For example, I was invited to Sydney recently to speak at the New Children’s hospital where staff were concerned about their duty of care, when parents sought to use complementary medicine for their children. The staff were worried that the proposed treatment was not in the child’s best interests, particularly if conventional treatment was omitted in favour of the proposed therapy. This would also be a concern for a research ethics committee.

For research on children, the NH&MRC differentiates between ‘therapeutic’ and ‘non-therapeutic’ treatment. If non-therapeutic, there is an expectation that the level of

discomfort for the child should be no more than is experienced in everyday life. If therapeutic, the potential gains for the child must be balanced between the potential harms. This therefore generally requires strong evidence of previous research to support the use of the treatment.

Slide 6. Many of you have, or are conducting clinical trials. Ethics Committees in Australia seek reassurance from committees such as the Therapeutic Goods and Drug Administration for a number of homeopathic and other therapies. One of my colleagues studying homeopathic treatments has had a particular Ethics Committee perceive a project as acceptable, but several other similar (although he says less controversial) projects assessed by the same committee as ‘new research’. Therefore, this required approval and monitoring from a clinical trial notification ethics committee. Unfortunately, this has attracted a cost of \$15,000 per project. If funded by an organization that can afford this, that may not be a problem, but it could be a huge obstacle for others with a limited budget. It could also be argued that many complementary therapies are not in fact ‘new treatments’.

The fifth category is ‘**accessing personal records that identify individuals**’. This category is one that I am sure you are aware of, and in Australia, the Privacy Act has had a strong influence on who gets what information, and in what circumstances. Even if you own records, if not collected for research, it cannot be assumed you can use them if the patient has not consented to have them used for research.

The sixth category is ‘**potential conflict of interest for the researcher**’. I have come across this if research is funded or otherwise influenced by a group that has a significant vested interest in the result. To illustrate this point I would like to refer to a well known case in New Zealand, commonly called the ‘unfortunate experiment’, where women with cervical cancer were not treated in a way that was conventionally accepted at the time. It transpired that the chief researcher was the chair of the committee that approved of the project. Over at least a twelve year period, a number of complaints from other doctors had been sent to this committee, but they were not acted upon. Furthermore, the status of

the researcher was another reason that the research was not challenged more rigorously, and many women died a premature death.

The final category is **'other'**, and I would just like to mention degree of risks and benefits. As we have discussed at this congress, we know that not all so called complementary medicine is safe or effective.

Slide 7. From an ethics committee perspective, the greater the degree of risk, the more stringent the need is for informed consent and assessment of a persons competency to consent. It is the researcher's responsibility to thoroughly investigate any therapy that may be used in research, and to provide some evidence to members of an ethics committee regarding the benefits and possible harms of any proposed treatments. As we know, this can be problematic with complementary medicine, if there has been little or no formal research carried out in the past. The responsibility of the committee is both to approve the research if appropriate, and to monitor the research when underway. For example, if any adverse effects occur the researcher must notify the committee, and after investigation, they may well have to discontinue the study. We also include a 'complaints clause' in all explanatory notes to participants, to ensure that they can contact the committee if they have any problems with how the research is being conducted.

When we are not sure of the risks though, there is a need for caution. As with conventional medicine, there are examples of harms caused as a result of using complementary medicine - such as these given by Angell in 1998. She refers to the following as examples of "*what will be a rapidly growing problem*".

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Slifman and her colleagues report a case of digitalis toxicity in a young woman who had ingested a contaminated herbal concoction. Ko reports finding widespread inconsistencies and adulterations in his analysis of Asian patent medicines. LoVecchio et al. report on a patient who suffered central nervous system depression after ingesting a substance sold in health-food stores as a growth hormone stimulator, and Beigel and colleagues describe the puzzling clinical course of a patient in whom lead poisoning developed after he took an

Indian herbal remedy for his diabetes.

In this Congress, we have also been given many examples of therapies where research suggests it is both safe and effective, but it is subsequently shown to have the opposite effect. You can see the frequent dilemmas for Ethics Committees, who have to trust that the supporting documentation is both honest, up to date, and well researched.

In the last few minutes of this paper, I would like to mention the experience of one of my Masters students with the ethical approval process. She was researching the possible benefits of using aromatherapy for women in labour, to determine if it reduced pain, and facilitated the birth process. Prior to going to the ethics committee, she sought advice from the appropriate person approved by the committee with expertise in therapeutic goods administration. He believed that aromatherapy was basically like a perfume, and 'harmless', despite the fact that she chose a particular mix of oils under guidance from a qualified aromatherapist, precisely because other oils may have adverse effects.

However, both a hospital committee and a University Ethics committee was concerned about any possible adverse effects not only for the woman during childbirth, but for the visitors, other patients and hospital staff. The hospital committee was also concerned about the effects on the foetus. In retrospect, locally administered inhalation of the aroma would have been more prudent. Furthermore, a clinical trial would probably have been a more appropriate approach to the study.

With this study, we also had a problem using a placebo as a control. For example, fragrant oils have other possibly more toxic properties, and we were not prepared to risk that. We thought of using water, suggesting to participants that it was a homeopathic substance, to account for the lack of smell. However, this was deception and therefore ethically problematic, even in the interests of research. We did finally use water, but it was probably obvious to almost everyone what was the real thing and what was not. Although, strangely one husband had a problem with the 'aromatherapy', and wanted it discontinued, when water as placebo was used!

At the moment in Australia, the use of some placebos are causing all sorts of problems in relation to research on complementary medicine. Many can be bought from health food

shops, but they are not approved substances. Therefore their use comes under the category of 'new research', and approval is required from the 'expensive' committee' previously mentioned! I hope this will change soon.

Slide 10. In conclusion, I hope this paper has been useful, and that unlike many of my colleagues you do not judge ethics committees too harshly. History has shown us that the community needs to have checks and balances for research to be conducted safely and ethically. As I said at the beginning, I have assumed rightly or wrongly that the ethics processes that you will or have experienced are similar to those in Australia. If you would like to talk to me about a project, please do.....

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