Article

A Review of Innovative Treatment

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Innovative procedures are the way that medicine can progress, improving both the duration and quality of many people's lives. Innovation in health care has often been useless or harmful, so it is important to consider how to minimise harm and maximise benefit when introducing a new treatment protocol.

It is generally agreed that minimising harm requires analysing all the possible benefits and risks of a new procedure, including economic considerations, early in the process of introducing the innovation. There is less general agreement about the most appropriate ways to perform this analysis. Jennett suggests that the simplest way to do this is to keep a register of the use of a new technology.[1] This would not compare one procedure with another, but would allow easy identification of the weaknesses and strengths of a procedure.

There have been three key areas of discussion about innovative procedures: (i) proving that they are safe and effective; (ii) gaining the informed consent of patients to perform non-standard treatment; and perhaps most importantly, (iii) defining what constitutes an innovative procedure.

1. Definition

In 1988, after the Cartwright Report into the carcinoma in situ (CIS) study at National Women's Hospital in the 1960s (the 'unfortunate experiment'), where women were given unconventional treatment without being informed, it became necessary to gain approval from an Area Health Board ethics committee for all new treatment protocols.[2] But what constitutes a new treatment protocol? Surgeons are always refining and adapting operations to improve various aspects of surgery. Exactly what departure from a standard procedure is required to form an innovative procedure? There have been many attempts to find an appropriate definition, but there is not yet a concise and widely accepted description of innovative treatment.

Regional ethics committees have used the definition of innovative procedures found in the National Standard 1996: 'Those procedures which are new to a particular provider setting in New Zealand, or which are being used for a new purpose.'[3] This includes both diagnostic and therapeutic procedures.

Gillett expands on this definition, dividing innovative treatments into several classes:

- a procedure new to New Zealand that has been tried and tested overseas;
- a new use for an established treatment;
- a modification of an existing treatment;
- a new procedure devised by a New Zealand health professional;
- an unintentional discovery that leads to the development of a new treatment.[4]

This expanded definition is important in the ethical evaluation of innovative procedures, since each class of innovation poses different ethical issues. For a procedure that is new to New Zealand but tried and tested in other countries, for example, the issue may be whether the team proposing to perform the procedure has the appropriate skills and training to perform the procedure. For a procedure devised by a New Zealand health professional and not used elsewhere, however, there would be further issues to consider, since risks and benefits would be less well demarcated.

A legal opinion sought by the National Advisory Committee on Health and Disability Ethics suggested that an ethical review would be required for any treatment that differed enough from established treatment to make harm to a consumer a real possibility.[5] There are several questions which must be answered for this definition to have any useful meaning: What constitutes harm? How is it measured? Obviously only clinical evidence can really demonstrate the risk of harm involved in any innovation, but should some level of theoretical safety be reached before an innovative technique is actually used? For example, in introducing a hip joint prosthesis, investigators could hypothesise that inserting a piece of metal into the shaft of the femur would cause the bone to shatter, they could then use cadaver and animal experiments to establish whether this was actually a risk during hip replacement surgery. This is a very intensive way to exclude every possible harm however, often it may be necessary to introduce only special precautions. Obviously, even when innovators have established a treatment is safe in every way they can imagine before they attempt to perform the procedure on living humans, risks that they hadn't thought of, or even risks they thought had been excluded may be discovered. When innovations are less elaborate modifications of existing surgery, they need evaluation of whether they cause less harm than the standard treatment, or have no discernible difference. Who should decide what kind of testing an innovation needs before being used to treat humans?

This brings us to the question of assessment – should a regional ethics committee or other body decide if an innovation is safe enough before it is trialled in humans, or should ethical review only occur after implementing the new procedure?

2. Assessing the safety and effectiveness of innovative procedures

While innovations in drug treatments are subject to controlled trials and ethical evaluation before conclusions are made about their use in patients, innovations in surgical or other treatments tend to be tested by less controlled experimentation.

There are health professionals who advocate randomised controlled trials (RCTS) of all innovative procedures, pointing out that many procedures

which at first appeared to be fantastic innovations, were eventually discovered to have the same outcome as a more conventional or less radical treatment. This was the case for the extracranial/intracranial bypass surgery introduced in 1967, and later found to be no more effective than aspirin at reducing risk of stroke.[6] It is important to prevent situations like this – where many were harmed through unnecessary surgery and subsequent complications – from arising again.

Those who believe that innovation can only be evaluated through RCT ignore the fact that surgeons who develop innovative procedures are seldom in a position of equipoise, where they believe that the innovation is no more effective than any alternatives. It is impossible for these surgeons to perform RCTs because they cannot ethically allocate patients randomly to different treatment groups. If these surgeons were to establish a database of all cases, showing the indications for treatment and treatment outcomes, innovative procedures could be compared with their predecessors. Establishing such databases would be expensive and care would need to be taken to include enough information about cases to allow appropriate matching of patients. If retrospective studies show little difference in outcome between a new procedure and a more traditional one, it may then be appropriate to perform an RCT. When assessment is carried out by an RCT, it becomes important to decide when to stop randomising, a national guideline could recommend a level of certainty that should be obtained but not exceeded. In other cases, however, a comparison of innovative and traditional techniques may show a vast improvement in outcome with the innovation, and to then randomise patients would be unethical.

The public has tended to view controlled trials in general as 'human experimentation' and found this concept abhorrent, preferring that patients are given all the facts about an innovation and allowed to decide for themselves, rather than being randomly assigned to treatment groups. Despite this, when offered a new treatment that appears to have advantages over others, many people will accept the innovation without seeing themselves as participating in an experiment. However, if a surgeon is in an equipoise position with regard to an innovative procedure and its alternative, then she can communicate this to her patient and obtain consent for randomisation, since neither can genuinely know which procedure, if any, is more effective. Trialling innovative procedures in this way is comparable to trialling new drugs by RCT.

The risks and benefits of an innovative procedure can be compared with those found in retrospective case studies of a control procedure, but it is difficult to eliminate bias from these trials. Different trials use different indications for surgery and may also measure outcome via different measures, making it hard to compare one trial with another. To decrease the bias in retrospective studies, it would be useful to have standardised scales used to measure both outcomes and indications for surgery. Examples of such standardised scales include the Neurological Cervical Spine Scale (NCSS),[7] which measures the impact on quality of life of cervical myelopathy, and the Astler-Coller classification of carcinoma of colon and rectum,[8] which grades colon cancers based on the distribution of the tumour. These scales allow case-mix comparison between different treatment groups and also facilitate large scale studies of many centres instead of restricting studies to one hospital or area.

There will always be difficulties when comparing studies, whether they are randomised controlled studies or otherwise, because it is impossible to adjust for the differing abilities of surgeons and the small differences in their operating techniques, which will affect outcomes. Jennett believes that these differences may be particularly apparent in controlled trials:

> Because controlled trials are so complicated and expensive to mount they are normally only conducted in centres of excellence that have a particular stake in their outcome. This has led to doubts as to how widely applicable the results will be in hospitals in general.[9]

The timing of the evaluation of innovations is also important, it takes time to learn the new techniques associated with an innovation, so the first few cases may not be representative of subsequent applications of the innovation. As Jennett points out, if surgeons had given up on dialysis or heart valve replacements when the first attempts at these were unsuccessful, many people would have missed out on valuable treatment.[10]

3. Ethics Committees in New Zealand

Ethics committees in New Zealand are concerned that there is no established mechanism for introducing innovative non-drug treatments in health care, despite the requirement for ethical approval of these innovations. Committees around the country are presently trialling submission processes for innovative procedures.

The application for ethical approval must justify the use of the new procedure, provide reports from the literature if available, compare risks and benefits, demonstrate the experience and qualifications of the clinician and the training required for nurses and other staff, provide copies of information to be given to patients and discuss how informed consent is to be obtained.

The application form does not include guidelines as to when in the evolution of an innovation ethical evaluation should take place. It would be reasonable to perform an innovative treatment on one patient, with informed consent, without gaining ethical approval, but it is difficult to define a point when ethical approval should absolutely be obtained. It would be difficult for the ethics committee to make a decision unless it could review a reasonable number of cases, and there needs to be a period of introduction, during which clinicians gain the necessary skills to perform the procedure.

It is also during ethical review that the differences between various classes of innovation described by Gillett become relevant. The application form should require different information depending on the class of innovation. Perhaps the timeframe of review could also vary for different classes of innovation. An innovation new only to New Zealand could undergo review prior to its introduction, because overseas data could demonstrate risks and benefits. A procedure devised in New Zealand and not used elsewhere would require review after introduction, so that the risks and benefits could first be established. It will be necessary to decide how many times an innovative procedure can be per-

formed before it must undergo ethical review. It is difficult to find a good median number, but it can be seen that performing a surgical procedure three times would not allow a surgeon to perfect the procedure, while performing a procedure one hundred times without establishing it is effective is obviously unethical.

There is overlap between the issues about staff covered in the application for ethical approval, and those covered by the Surgical Credentialling Committee, which determines skills needed for introducing an innovation and approves surgeons with these skills. Taylor asks whether the ethics committee is the appropriate place to deal with personnel in detail.[11] This is a valid concern: lay ethics committees were not established to determine the professional skills of medical personnel. A Surgical Credentialling Committee consists 'predominantly of medical practitioners'[12] and Royal Australasian College of Surgeons guidelines recommend that the committee takes appropriate training and experience of the surgeon into account when considering her ability to adopt new technologies. This kind of peer review is more likely to be able to evaluate effectively the capabilities of surgeons than the ethics committee.

However not all new procedures are surgical, and the competence of the practitioners of other innovations must also be established. Perhaps peer review is the best way to achieve this, so that ethics committees should require evidence of peer support of the innovator's abilities when considering innovative treatments. It would be useful to have peers who perform research, rather than those unfamiliar with research methods, on committees reviewing the competence of medical practitioners, so that both the competence of the practitioner and the proposed method of introducing an innovation can be reviewed. This review should ensure that the application includes a description of a means of assessment for the innovation which will actually allow the safety and efficacy of the innovation to be proven.

While hospital-based credentialling committees are a valuable way to oversee innovations, it would also be possible for a national review committee to investigate proposed innovations. Approval could be sought at this national level before the innovative procedure was used on humans. This is similar to having drugs approved for use in humans before clinical drug trials. Having one national committee would ensure that guidelines were enforced in the same way throughout the country, and also allow for expert input from all sources rather than just one hospital. Input from health professionals from other countries would also be valuable, because New Zealand's small size means that if an expert proposes an innovation, there could be few other professionals in the country with the appropriate experience and skills to review its risks and benefits. With the Medicines Act presently under review, now is a good time to investigate a national system for monitoring innovative procedures.

4. Informed Consent

Perhaps the most important issue in the use of innovative procedures is gaining the informed consent of patients. This consent was not obtained in the carcinoma in situ study at National Women's Hospital. In considering any innovative procedure, the person to place at the centre of ethical evaluation is the patient.

Under the 1981 Medicines Act, a clinician may provide a patient with treatment he/she believes is in the patient's best interests: this gives the clinician the right to use innovative techniques, but it would be inappropriate to deviate from standard practice without informing the patient. This would be abusing the partnership as Gillett describes between surgeon and patient:

> In such a partnership each participant has certain legitimate expectations. The patient expects the surgeon to act with due care and skill and in a way that accords with responsible medical opinion. He also expects his surgeon to present the options in a way that fairly represents their materially relevant features. The surgeon, on her part, expects the patient to present true information about his problem, and make a careful decision based on honest appraisal of the prospects of the various possible courses of management.[13]

If a surgeon is offering a patient a non-standard procedure, the patient should be informed of the difference from standard practice and the reasons the surgeon would prefer to use an innovative treatment. The patient would also be entitled to seek a second opinion from another specialist, giving her/him ample opportunity to decide which procedure would be preferable. This second opinion should be facilitated by the clinician so that it is not at the expense of several further months on a waiting list for the patient, which would provide an incentive to undergo the innovative procedure rather than seek further advice.

It is necessary to obtain informed consent because the patient may disagree with the surgeon about whether a treatment is in his best interests. 'Fewer than half of the first 30 patients receiving replacement heart valves survived the operation'[14] but for some patients with months to live without the operation the risk was worth it, while others preferred to make the most of their last few months rather than risk having even less time. This is a decision that no surgeon can make for a patient.

An advantage of discussing the innovative status of a procedure with patients is that they are much more likely to share their experiences of the procedure, providing useful material to aid in evaluating the procedure. This is particularly valuable when the outcome measures include subjective responses from the patient.

Patients also have the right to make decisions without sharing them with their families, and it is very important to keep good patient notes, so that it can always be demonstrated that the wishes of the patient have been complied with. Surgeons performing life-threatening innovative procedures may choose to send their patient a written copy of what they have discussed and agreed to, so that they can be confident that the patient has given fully informed consent.

Recommendations

1. That innovative treatment is defined by the possibility of increased harm.

2. That the safety and effectiveness of innovative treatments are assessed separately. Safety must be established early in the introduction of a procedure. Effectiveness should be assessed in a way that gives good statistical evidence.

3. Ethics Committees in New Zealand should utilise professional expertise but retain lay review of innovative procedures.

4. Informed consent to the procedure is always obtained.

References

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2 Cartwright, S. *Cervical Cancer Report* 1988
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4 Gillett, G.R. Innovative Techniques in Surgery. *Journal of Clinical Neurology* 1997
5 Taylor, G.D.S. NACHDSE *Innovative Treatment*. August 1997 para 17
6 Jennett, p.237
7 Kadoya, S. Grading and scoring system for neurological function in degenerative cervical spinal disease – Neurosurgical Cervical Spine Scale. *Neurol Med Chir* (Tokyo) 1992; 32: 40-41
8 Cotran, Kumar Robbins. *Pathologic Basis of Disease*. 5th ed 1994; p.817
9 Jennett, p.240
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11 Taylor, para 28
12 *The implications of new technology for surgical practice, quality assurance, accreditation and the delineation of responsibilities*; Policy of Royal Australasian College of Surgeons; 1994
13 Gillett, G.R. Ethics and Innovative Surgery. *Current Surgical Practice* 1998; 8: p.65
14 Jennett, p.244

Call for papers

Bioethics and Biolaw Second International Conference

Copenhagen 3-6 June, 1998

The second international conference on Bioethics and Biolaw under the patronage of UNESCO is to be held at the Parliament Building, Christiansborg, Copenhagen.

Participants will have the opportunity of presenting approved papers at a workshop. Those wishing to do so are requested to submit, before 15 April, 1998, a one page abstract with name, address and fax no to:

The Centre for Ethics and Law
Valkendorfsgade 30
DK 1151
Copenhagen
Denmark

For more information contact The Bioethics Centre, PO Box 913, Dunedin.

Visitor

William Evans Fellow

Professor Arthur Frank is the University of Otago's most recent William Evans Fellow. Professor Frank comes to the Centre from the University of Calgary where he is Professor of Sociology. Professor Frank is presently on holiday in New Zealand and will formally commence his visit to the Centre at the beginning of March.

He is the author of *The Wounded Storyteller: Body, Illness and Ethics* (1992). He is also the Case Stories Section editor of *Making the Rounds in Health, Faith and Ethics* (formerly *Second Opinion*).

As well as being a prominent figure in Bioethics, Professor Frank is especially interested in narrative ethics. The Centre's teaching in the medical curriculum has reflected the recent recognition of the importance of patients' narratives for medical ethics. Barbara Nicholas and Grant Gillett have active research interests in narrative ethics. This means that we are all looking forward to a productive time with Professor Frank over the next few weeks.

Professor Frank will be taking part in the centre's teaching. Dunedin readers will be able to hear him speak at a public lecture titled *A Bioethic of Reconciliation* on 16 March. This lecture will be held in the Colquhoun lecture theatre at 1pm.

FIFTH ANNUAL 'TEACHING RESEARCH ETHICS' WORKSHOP

24-27 June, 1998
Indiana University, Bloomington

The Teaching Research Ethics (TRE) project began in 1994 with support from the United States Department of Education's Fund for the Improvement of Postsecondary Education. The cornerstone of the project is an intensive workshop, which helps science faculty members to use existing materials to train their students in research ethics and to develop effective methods and materials of their own. The TRE project also provides support through an informal newsletter, an e-mail based electronic conference, and a World Wide Web site

(www.indiana.edu/~poynter/tre.html).

Attendance at the workshop is limited to 45; however, the two sessions on Saturday, 27 June, are open to a wider audience. The first Saturday session will be a two-hour panel presentation on 'Model Curricula in Research Ethics.' The second will be a four-hour seminar on 'Resolving Conflicts and Preventing Misconduct in Graduate Education.'

Registration is required for the workshop, panel, and seminar.

For more information:

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