

Clinical Research and the Provision of New Medicines: A Crisis in Confidence

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Dr Ken Paterson who acted as rapporteur at the Symposium, Clinical Research and the Provision of New Medicines: A Crisis of Confidence. This is his personal summary of the proceedings.

Clinical researchers, including pharmaceutical physicians, are hard-working, honest people doing their best, underpinned by the principle of beneficence and a sense of distributive justice. Their efforts improve and save many lives on a global scale, yet despite this reality there is a perception in society that all is not well or as it seems. Even in times dominated by cultures of litigation, regulation and public censure, clinical researchers, and especially those from the pharmaceutical industry, are held in low esteem, a situation not improved by increased regulation.

This apparent dichotomy was explored at the Faculty of Pharmaceutical Medicine Ethical Issues Committee Symposium “Clinical Research and the Provision of New Medicines: A Crisis of Confidence”. Two broad themes emerged, these being ‘bad practice’ (where the ethical issues are fairly easy and clear-cut) and ‘hard practice’ (where the ethical issues are more difficult or uncertain).

In the former category were described many practices, hopefully confined to the past, such as -

- poorly designed, even biased, studies
- poor publications practice (suppression of publication or multiple publication of the same data)
- poor practice with regards to authorship (both attribution of authorship to individuals with no real involvement in a study and suppression of the names of others who were involved)
- misleading or selective quoting of results and study findings.

In defence of researchers, other agencies may have to accept some of the blame –

- regulatory bodies (dictating conduct of clinical trials, selection of comparator therapies etc)
- Research Ethics Committees (not looking hard enough at the detailed science)
- medical journals (unwilling to publish data on negative studies or ‘failed’ drugs)

On balance, it was accepted that the research sector, both in industry and in the academic world, had needed to improve its performance standards and was now doing so – but it remains ‘work in progress’. In the pharmaceutical industry there frequently remain structural issues within companies, with the Medical Director often not being on the company Board, and with a lack of clarity over who has the prime role in ensuring patient safety. Medical

Departments had sometimes seemed to be 'AWOL', but there is still a concern that even a senior employee in a Medical Department who "blows the whistle" on unethical or inappropriate activity may risk his/her entire career.

In the area of 'hard practice' comes rationing of therapies, especially expensive therapies. This is inevitable but can be undertaken within an ethical framework and in a spirit of fairness, though the definition of 'fair' in this context is sometimes controversial. The science of health technology assessment needs to be informed by the voice of patients and the public, though even here the ethical issues of how this is to be achieved and by whom are not easy. Even the pricing of drug treatments raises questions, with the practice of charging what it is felt the market will pay being questionable, but perhaps excusable where the 'excess' profits are re-invested in clinical research and development.

Increasing globalisation of both research and drug development brings new areas of 'hard practice' which apply as much within countries as between countries. Excessive concentration on the new and innovative may lead to lack of focus on areas of greatest health need and failure to make the best use of existing treatments. Inequities (rich v poor, young v old, have v have not) affect all populations and impinge on ethical research. Recruitment to clinical studies may be easier among disadvantaged populations, but could be ethically questionable if reward of subjects (either financial or in terms of care provision) was possibly coercive. Vulnerable patients (very young children, pregnant women, patients in intensive care settings etc) require that researchers pay especially close attention to ethical issues, but also need the benefits which research can bring.

The use of normal volunteers in clinical research is also a matter of ethical concern, especially where new therapies may have unexpected, even unpredictable, dangers. It is open to particular question where patients with the disease being targeted are likely to behave differently from normal, limiting the extent to which normal volunteer studies can provide useful information on either safety or efficacy of a new treatment. It may well be that, in the future, some 'first-in-human' studies will most ethically and usefully be undertaken in patients rather than volunteers.

All 'hard practice' is about balancing innovation with risk, and managing that risk which cannot be removed. Ethically that means a flexible approach with partnership working, local involvement of patients and researchers and assessment on a 'case-by-case' basis. Perfection is unachievable in either science or ethics but researchers can work towards the highest standards which circumstances will allow, guided by advice such as the Guidelines of the Faculty of Pharmaceutical Medicine.

The Symposium showed the complexity of the issues, but also the means to move things forward and an enthusiasm to do so!

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