## **INNOVATIVE HEALTH TECHNOLOGIES PROGRAMME**



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## Innovations in Cancer Pain Relief: Technologies, Ethics, Practices

## **KEY FINDINGS**

How has cancer pain relief developed since 1945? What drivers have generated change, in drugs, their modes of delivery, and treatment approaches? Is freedom from pain a basic human right? In what ways do bioethical principles cast light on the problem of cancer pain relief? How can autonomy be promoted whilst ensuring that no harm is done? How can the principle of justice be understood when a small minority receive excellent pain relief but, globally, the majority do not?

- Unrelieved pain caused by cancer represents an epidemic of preventable suffering this is a clinical problem, a public health issue and a moral and ethical challenge.
- Over the past fifty years cancer patients have become more actively involved in their treatment and care, concepts of cancer pain have moved beyond the physical to encompass mental, spiritual and social suffering, and the understanding of pain mechanisms has deepened.
- The promotion of patient autonomy has been a driver of change leading to the introduction of long-acting pain relieving drugs, special technologies for their delivery and the vision of individually tailored pain management resulting from new research in pharmacogenetics.
- Benefits have come within the compass of those in affluent nations, elsewhere, in the poorer regions of the world, major problems persist.
- Our study contributes to several key debates about freedom from pain as a human right; the ethical and practical limits to its achievement; and the strategies that should prevail in the further development of innovative technologies for cancer pain relief.



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The global burden of cancer cases is set to increase from 10 million to 24 million over the next 50 years; 17 million of these additional cases will be in developing countries. Worldwide, we estimate that some 67-80% of people with cancer are currently suffering from under-treated pain. Yet it is estimated that the knowledge and skills required to alleviate cancer pain are well established in some settings, so unrelieved pain caused by the disease represents a global epidemic of potentially preventable suffering.

Our study set out to explore cancer pain at several levels: as a clinical problem, as a public health issue, and also as a moral and ethical challenge. We began by mapping out the complex history of cancer pain as a field of medical specialisation that first began to emerge after World War Two. From here we were able to identify a series of innovations that were explored through in-depth case studies, shedding light on how innovation takes place in this field and the factors that shape it.

In the second half of the twentieth century the clinical management of patients suffering pain from advanced cancer was transformed. In the UK, hospice innovators encouraged the frank use of powerful analgesics for terminally ill cancer patients, but harnessed this to a much wider understanding of the personal meaning of pain. In the USA, anesthesiologists began to take a special interest in pain assessment and management. This stimulated novel approaches to patient-centred analgesic evaluation and alongside these came new understandings gained from the individual illness narratives of people with cancer that started to proliferate at this time. As scientific, clinical and public interest in cancer pain relief began to grow, the stage was set for a period of significant innovation that occurred from the late 1970s through to the mid-1990s.

It had become clear that the regular administration of powerful analgesia could not only assuage existing pain, but also prevent its recurrence. But the modes of administering pain relief remained muddled. Complex mixtures combining powerful narcotics in an alcohol vehicle were still widely used, yet these were difficult to deploy with accuracy and careful titration of the dose to the individual patient was almost impossible. Regular injections of morphine and diamorphine worked adequately in hospital or hospice, but were inconvenient and intrusive and poorly adapted to the needs of the patient at home. And there were also continued anxieties among practitioners and patients about the addictive and euphoric effects of powerful opiate drugs.

A plethora of linked, but largely unorchestrated responses to these problems began to emerge. The pharmaceutical industry, observing the efficacy of the regular giving of analgesics, devoted effort to the development of slowrelease formulations of morphine, that would increase patient autonomy by requiring only a twice daily tablet regimen. This was further extended when the serendipitous innovation took place of using diamorphine in a 'syringe pump' capable of delivering the drug sub-cutaneously over extended periods. By identifying even more potent drugs than morphine or

diamorphine, it became possible to extend the period of active pain relief and to further enhance the patient experience through the development of 'patches' which adhere to the skin and deliver a continuous dose over 72 hours, without any external technology.

In the west, the field of pain and palliative medicine expanded and gained increased recognition. Clinical practice in cancer pain management became more refined and specialist knowledge was generated by research studies and disseminated in scientific journals. At the same time, and stimulated by the World Health Organisation, western experts in cancer pain relief began to take a more global interest in the problem. Studies showed massive problems in many parts of the world. Opioid analgesics were overregulated making their use for medical purposes impossible in many settings. Doctors and patients alike harboured major concerns about the use of powerful opiates. In a coalition fostered by WHO, a global strategy to address cancer pain relief was devised and 'rolled out' in many countries from 1982. It has proved only partially successful. The imbalance of 'regulation' against 'supply' still persists, along with many of the earlier fears and phobias. Moreover, commercial interests have fostered the promotion of more costly slow release formulations over an interest in the production of generic, immediate-release morphine. For resource poor countries these remain major barriers to achieving cancer pain relief at the population level; the problems have been particularly well documented in India, South America and parts of Eastern Europe.

Meanwhile there is growing interest in the west in the potential of pharmacogenetics to deliver even more personalised approaches to analgesia and pain specialists look to this area with growing anticipation. The likely gains will be for those patients whose pain fails to respond to what are otherwise considered the gold standards of cancer pain relief. Yet the pharmacogenetics innovation is unlikely to impact on the global problem of cancer pain, for which the technologies of attitude change and policy innovation are likely to be more significant.

The ethical dilemmas here are complex. Should freedom from pain be considered a human right? And in what ways do the principles of modern bioethics cast light on the problem of cancer pain relief? How can the principle of autonomy be promoted whilst also ensuring that no harm is done for example in relieving pain without producing unwanted side-effects? Has the principle of justice been obscured by the duty to do good for example when a small minority receive excellent pain relief in specialist settings but the vast majority do not?

Our study is unusual in bringing together historical, sociological, clinical and ethical perspectives on how particular ways of managing cancer pain have developed. The approach explores how these factors are reconciled with the consequences and costs of market led innovation. It is directly relevant to the UK government's current concerns to improve the quality and availability of cancer services and it can contribute to improvements in the way that cancer pain relief technologies are deployed in international contexts.

## About the Project

This project is part of a wider ESRC/MRC funded programme of research on Innovative Health Technologies. The research was carried out in two phases involving: wide-ranging literature reviews; a study of post World War Two cancer pain relief; interviews with key leaders in the field; and by tracing patterns of innovation in new drugs, modes of delivery and forces that shape clinical change.

The first phase constructed a narrative history of cancer pain relief since 1945, identifying key forms of technological innovation including new pharmaceutical inventions and discoveries, the redeployment of technologies from other areas of health care and the public health 'technology' of policy and strategic planning. The second phase explored contemporary debate and practice in three case studies of innovation emerging from our historical analysis. 1) Routes of administration methods available to clinicians for the administration of pain relieving drugs in advanced disease. 2) Pharmacogenetics the variability of patients' responses to analgesic therapies since this is a major issue in cancer pain management. 3) Pain and the public cancer pain relief in the wider social context. The latter explored ways in which cancer pain has been presented as a public health issue and the extent to which associated programmes have had an impact. One aspect of this is the barriers to cancer pain relief that exist in different countries and settings and the cultural, governmental, political and economic factors that shape them.

Anan ethical analysis was developed with each case study, incorporating a critical appraisal of the value of the four principles of modern bio-ethics (autonomy, nonmaleficence, beneficence, justice) and taking account of the potential for social inclusion and exclusion.

Three major meetings were generated by the study. A 'Witness Seminar' hosted by The Wellcome Trust History of Twentieth **Century Medicine Group in December 2002** enabled key figures in cancer pain relief to explain their work and its worldwide impact. This was invaluable in assisting our understanding of complex developments in this field. In March 2004, a two hour symposium at the UK Palliative Care Congress, University of Warwick, was attended by some 25 palliative care clinicians and researchers. While in March 2004, a seminar at 'Hospice House', London, brought together key individuals in the field of cancer pain relief to discuss and analyse issues uncovered during research. A major achievement in disseminating our research to a practitioner audience within the pain and palliative care field was the publication of five papers as a special series Journal of Pain and Symptom in Management, (29, 1: 2005), one of the world's leading journals in the subject.

The level of interest in our work, expressed by leading clinicians, suggests that the project provides a valuable contribution to the understanding of the recent history of cancer pain relief as a field of medical activity. Our case study analysis of specific innovations has opened up a space for more considered and critical reflection on the drivers of changing clinical practice in cancer pain relief and the limitations of approaches which concentrate on one benefit (mode of administration, side effect profile, analgesic potency) seen in isolation from the wider context of cancer, pain and the patient's experience.

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